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Translated from *Uspekhi Khimii* **60** 3–44 (1991) U.D.C. 530.145:547.354.9

Conjugation and the periodic system of the elements

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ABSTRACT. The knowledge of the characteristics and mechanisms of the interaction of the active centres of complex molecules is of primary importance for the development of theoretical and applied organic chemistry, promotes a more productive utilisation of the enormous amount of experimental data available, facilitates predictions and the search for new routes to and new varieties of the synthesis, industrial technology, and applications of organic compounds, and leads to more complete ideas about their functions in chemical, physical, and physiological processes. The studies in this field have been subjected to a critical survey and attention has been drawn to the possibility of distinguishing different forms of the mutual influence of atomic groups, the establishment of correlations between different parameters of conjugation and of the role of relativistic effects, the characteristics of conjugation systems incorporating heteroatoms from different groups in the Periodic System, and the study of the evolution of excited molecules.

The bibliography includes 188 references.

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I. Introduction

The properties and parameters of complex molecules made up of isotypical atomic groups are largely associated with the entire set of these groups; in the presence of heterogeneous fragments, a more or less marked relationship with individual fragments can be noted (examples: the colour of compounds with some kind of chromophoric centre; quasi-local vibration modes of the atoms; the dipole moment of a molecule containing a highly polar group). The application of mathematical methods makes it possible to obtain more detailed information (for example, the conversion of normal vibration frequencies of atoms into the force constants of individual chemical bonds) and leads to data for the distribution of electron density among the atoms, the interatomic distances, the structures of individual molecular orbitals having a bearing on the physical or chemical processes investigated, etc.

The more or less "local" characteristics of atomic groups or bonds obtained directly from experiment or by calculation make it possible to compare isotypical groups in various molecules. Slight variations in the corresponding parameters are usually attributed to the influence of adjacent and non-adjacent molecular fragments. Knowledge of the characteristic features of the mutual influence of atomic groups, to which the specific features of the physical and chemical properties of polyatomic (complex) molecules are in some way related, greatly expands the information afforded by the usual structural formulae and constitutes the most important problem in theoretical organic chemistry. However, one should note that the idea of mutual influence is based on comparisons with a selected initial basis, usually with a set of simpler molecules, simulating the fragments of a complex molecule, or with the classical structural formula. When there is an appreciable discrepancy between the real structures and such formulae, the choice of what one could describe as the "origin of coordinates" proves ambiguous and arbitrary. Difficulties of a similar kind and arbitrary features can arise also in other problems, for example, in the selection of a system of independent natural coordinates in the description of the force field (especially in cyclic molecules).

In order to expand and deepen our knowledge in the field under consideration, the constants and functions characterising reactivity (the Hammett, Taft, etc. constants), thermochemical properties, geometrical and electronic structures, the systems of electronic excitation levels, the force field in deformed molecules, optical and magnetic properties, various forms of relaxation, and biological activity have been resorted to. Computational quantum-chemical methods are being employed to an increasing extent. With their aid, it is possible to characterise the coordinates of chemical reactions and the transition states, to construct three-demensional electron density diagrams, to calculate (or if necessary to predict) the spectra of compounds of light and heavy elements, including electronic absorption spectra with identification of valence and Rydberg transitions, to assign the lines (bands) in the spectra and thus impart to them a much greater information content,[1–4] and to estimate the contribution of relativistic effects.[5,6] The latter are important for the chemical and phyiscal properties of molecules incorporating the atoms of heavy elements; it is sufficient to say that their contribution to the energy of the chemical bond reaches 50% in some cases.

Procedures for the productive employment of new physical methods for the investigation of molecular structures have been developed in the recent period. The electron-transmission spectroscopic technique[7,8] has been improved,[7–8] the use of

synchrotron emission has made absorption spectra in the range 1000–2000 Å accessible, and the technical possibilities of resonance Raman spectroscopy have been greatly expanded (the method has been extended to virtually all classes of organic compounds by employing excitations up to 1400 Å, the employment of recording times approaching the femtosecond range, and the measurement of spectra of microobjects, for example a *single* bacterium; the recording of the transformation of light by a single atom of molecule has been an outstanding achievement). Nuclear quadrupole resonance and binary (e, $2e$) spectroscopic data as well as non-linear optical methods have attracted attention. The formation of images of individual molecules with the aid of a scanning tunnel microscope has become realistic. The employment of light pulses with femtosecond durations (10^{-14}–10^{-15} s) has opened up new horizons; the determination of the characteristics of a chemical reaction of a molecule in a detailed time scan, eventually reflecting the evolution of the transition state and the possible rapid oscillations of the system within the limits of the coherence time ("femtochemistry",[9] reaction "vector dynamics",[10] attempts to analyse the photodissociation of a molecule by examining the dynamics of wave packets[11]) has become feasible.

Experimental and theoretical studies on numerous organic compounds have demonstrated the complexity of the entire pattern of intramolecular interactions. Here it is sufficient to draw attention to the multiplicity of (1) types of alternation of chemical bonds and heteroatoms in the chain, (2) three-dimensional forms of conjugated π-systems (quasi-linear systems—poly-ynes; two-dimensional systems—polyacenes, polyenes; three-dimensional, including spherical, systems—footballene), (3) couplings between different degrees of freedom, (4) degrees of stability (stable, and bistable, multistable, dynamic, unstable, non-rigid, and hypothetical systems), and (5) different versions of quantum states of the molecule.

The endeavour to make the enormous virtually non-encompassable accumulated data more readily available for practical use has led to numerous attempts to establish some kind of simple correlations between different properties of the molecule, on the one hand, and in series of structurally similar compounds, on the other (see, for example, Chau and McDowell[12] and Sacher[13]). The proposed relations with empirically selected constants are far from universal and have limited cognitive value; nevertheless many of them are extremely useful in practice.

The interaction between the active centres of a complex molecule† is reflected in one way or another in the energy and structure of the molecular orbitals, favouring their delocalisation, in the orders of chemical bonds and in the interatomic distances (promoting in most cases a certain degree of smoothing of the alternation), in the distribution of electron density, in the electronic and vibrational excitation energies, and in the possibilities of the evolution of the state of the system. These features can be greatly modified following the application of an external field as a result of association and solvation.

Henceforth, certain problems of conjugation and, in a broader sense, of the coupling between the active centres will be described in the text (see Sections II–IV and also Maier et al.[14] and Cook et al.[15]). Controversial problems, the limitations of the models employed, and contradictions in the estimates of the mutual influence of atomic groups will not be ignored.

II. Coupling between the active centres of a complex molecule

The distribution of electron density (the distribution of excitation energy in other problems) in a polyatomic molecule, for example, in a molecule involving a simple π–π conjugation system, can be in principle determined as a characteristic of the "stationary state". However, in the case of molecules, complexes, or ions incorporating weakly bound active centres, for example, a conjugation system of the π–σ–π type, one cannot rule out the practical possibility of recording the evolution of the state of individual centres, for example, oscillations in electron density or beats in the populations of the orbitals of fragments, provided that the vibration period is greater than 10^{-14} s [9,16] (see Section III). Whether or not a weak or strong coupling is produced between the subsystems depends on the molecular structure; the principal trend is towards a weakening of the interaction with increase in the distance between the centres R and in the number of intermediate units.

Compounds with a very *weak* but stable coupling between the active centres, including conjugation systems of the π–σ–π type or others, are of exceptional interest in connection with problems of biophysics and of the functions of biological systems. On the other hand, fundamentally new possibilities arise here for the use of molecules as systems susceptible to reproduction, regulation, and control by changes in the state of atomic groups as a function of time. Nowadays the study of these problems has been acquiring increasing importance. An active search is being prosecuted for new molecular structures which enable one molecule to perform the functions of a specific element or block in microprocessor ("submicroprocessor") technology—memory, logic, signal amplification, etc. functions;[17–19] an exceptionally high "packing density" and a greatly increased speed of operation can be achieved, in principle, in this way.

Polyconjugated π–π systems with a very strong coupling between the subsystems are closer to the other limiting case and have aroused special interest as a possible basis for the preparation of organic semiconductors, superconductors, and materials in which migrating excitation zones of various types, described as wave packets, can be created. They are suitable for the solution of certain technical problems, including the creation of systems for the transformation of information.

It would perhaps not be an exaggeration to say that the majority of other organic compounds belong to systems of an intermediate type. The entire wide variety of different kinds of coupling between the active centres can be seen in such compounds and the mechanisms of their functioning can be investigated.

The coupling between the electron clouds of adjacent or close atomic groups can be characterised in a fairly convenient form within the framework of ideas about stationary states: in asymmetric molecules, in terms of the degree of delocalisation of the molecular orbitals formed from the orbitals of the fragments and in terms of their displacements on the energy scale; in symmetrical molecules, in terms of the splitting of the molecular orbitals, reaching frequently 2–4 eV. In any case, it is useful to determine the matrix elements of the operator V of the excitation energy associated with the interaction between the orbitals a and b, i.e. $V_{ab} = \langle \varphi_a | V | \varphi_b \rangle$, where φ are electronic wave functions.

† Depending on the way in which the molecule is acted upon, different fragments can become the active zone or the reaction centre. The term "active centre" has the designation of a more or less local subsystem and therefore a conventional significance; in optical studies, the chromophoric group is usually implied.

However, these matrix elements cannot alone serve as a characteristic of the degree of mixing of the orbitals of the fragments (cf. Traven' and Stepanov[20]) or of the displacement of the molecular orbitals on the energy scale (ΔE), because data for the energy gap ΔE_0 between the initial orbitals are also necessary. We do not refer to the fact that in most cases one cannot make do with the "two level" approximations and data for only one element of the matrix $||V_{ab}||$; however, fairly simple relation (see Baidin et al.,[21] etc.)

$$\Delta E = 0.5\left[\sqrt{4V_{ab}^2 + \Delta E_0^2} - \Delta E_0\right],$$

should be used whenever possible. It is represented graphically in Fig. 1.

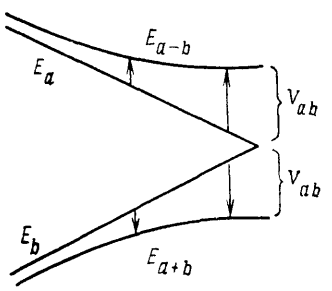


Figure 1. The shifts of the orbitals *a* and *b* on the energy scale induced by their interaction and the formation of orbitals of a mixed type with different initial splittings ($E_a - E_b$) but with a constant value of V_{ab}; the vertical arrows denote the shifts for two arbitrarily selected values of $E_a - E_b$.

Together with the molecular orbital energies, one can use also the set of ionisation potentials. The difference between these two variants is in most cases small and is determined by the contribution arising from the adaptation of the molecule to new conditions created as a result of the abstraction of an electron. The latter takes place very rapidly, approximately in 10^{-15} s, while the subsequent rearrangement of the molecule is slower and in principle one cannot rule out macroscopic time scales (the complete relaxation after a chemical reaction has taken place also requires a fairly appreciable time). In describing complex systems and processes to which correspond slight changes in electron density, it is more convenient to begin with molecular orbital energy data; otherwise, for example in the study of ionisation, it is best to resort to ionisation potentials and electron affinities (or to data derived from molecular orbital calculations with a parametrisation selected on the basis of photoelectron spectra[20]). There is no point in treating these variants as opposed procedures, since they are more likely to supplement one another.

If one is dealing with a coupling between remote active centres of the molecule, it is no longer possible to use the above criteria; in fact a splitting of the molecular orbital in terms of energy less than 0.1 eV is hardly susceptible to observation. However, under these conditions one still cannot rule out the possibility of the complete delocalisation of the molecular orbitals. On the other hand, among the manifestations of conjugation in different molecular properties, including reactivity, there may be some more sensitive to the interaction and even small differences in the structure of the interface can then prove of practical importance. As an example, one may refer to experiments[22] in which it has been shown that an increase in the number of units in the intervening polymethylene chain from 6 to 8 altered sharply the direction of a chemical reaction.

As regards the coupling between the vibrations of *atoms* in the subsystems under consideration, it is manifested by the establishment of delocalised modes and in the absence of interference can be readily observed in symmetrical molecules from the splitting of frequencies, which is associated, roughly speaking, with the rigidity of the entire intervening subsystem. The delocalisation of the vibrational modes has no direct bearing on the delocalisation of molecular orbitals and conjugation, which is unfortunately not always recognised (see, for example, Randhawa and Suri[23]); however, the contribution of non-diagonal force coeffcients has a bearing on the electronic interactions between different chemical bonds, manifested in the atomic vibration process.[24]

III. Comments on the mechanism of intramolecular interaction. What is the inductive effect?

The desirability of distinguishing different types of "electronic effects" (conjugation, the inductive effect, steric hindrance, etc.) and of the representation of their essential features has on the whole been evaluated in different ways in the literature; it has been noted that one is dealing not with physical phenomena but with a transition in describing the electronic structure of a molecule from the zeroth approximation to higher approximations. However, one should not go to extremes; the change in conditions in an intramolecular interaction and the appearance of definite specific features in properties, for example as a result of a transition from non-planar to planar diene systems, is entirely real. Avoiding the rather inappropriate but frequently resorted to references to "the delocalisation of electrons",[25–28] one can nevertheless speak of delocalisation of the molecular orbitals of conjugated systems. The presence of such molecular orbitals affects in one way or another the experimental data (see, however, the comments by Streitweiser and Vorpagel[29] and also Dewar[30] and Shaik et al.[31]). Speaking of conjugation, we have in mind the set of its manifestations in different properties of molecules, based on the overlap and mixing of the orbitals of the interacting fragments with a concomitant change in the orbital energies.[32] Deviations from a simple additive scheme, in which the property of a complex molecule is defined as the sum of the contributions of its fragments, are to some extent associated with conjugation. However, the specific features of the property or parameter investigated are then of primary importance and questions concerning "non-additivity" and its origin must be resolved separately for each property (see Section IV).

Among the possible manifestations of conjugation in chains with an alternation of chemical bond orders, for example, in polyenes and poly-ynes, one should mention the more or less pronounced smoothing of the differences in the alternating bond orders, lengths, and rigidities (it is frequently referred to as "delocalisation of bonds", which is in essence equivalent to "delocalisation of valence characteristics"). The set of distibine, diarsine, and certain others can serve as new interesting examples.[33,34] In such cases the

disposition of the Z–Z σ-bonds of a certain number of identical molecules on a single straight line favours the formation of delocalised orbitals, incorporating the entire chain of heteroatoms, or one may say the "conjugation of the σ-bonds of adjacent molecules". The molecules of diphosphine H_2P-PH_2 hardly interact with one another under such conditions (this is indicated by the symbol P–P P–P P–P). A very weak interaction with an insignificant smoothing of the bond alternation has been noted in diarsine (...As–As...As–As...); the molecules virtually retain their individuality, although, strictly speaking, delocalised orbitals must be used to describe the entire chain. The bonds between distibine molecules are more distinct; the large bathochromic shift of the absorption bands, which vanishes when the ordered arrangement of the molecules is lost, i.e. on breakdown of the conjugation chain, is striking.

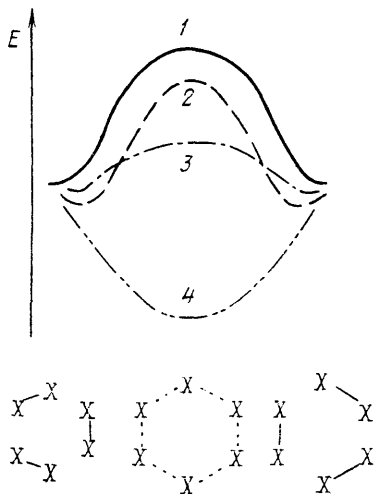
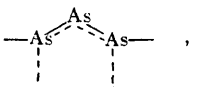


Figure 2. The energy of cyclic systems X_6. The extreme points of the curves on the right and on the left correspond to sets of three molecules X_2 (D_{3h} symmetry). Those in the middle correspond to systems in which all six X–X bonds are the same (D_{6h} symmetry). The H_6 system corresponds to curve *1*,[31] the benzene molecule corresponds to curve *4*,[31] molecules with only slight smoothing of bond alternation correspond to curve *2*, and the example of a structurally modulated (dynamic) system corresponds to curve *3*.

While there is an appreciable similarity in the manifestation of conjugation in distibines and poly-ynes, the forms of the bonds *between the fragments* of these structures differ greatly: in the former case, the overlap of the p_x orbitals of Sb, oriented along the chain, plays the main role, while in the latter case the main role is assumed by the overlap of the p_y and p_z orbitals oriented at right angles to the chain. In the first case, there is no rigid σ-skeleton ensuring the stability of the geometry and integrity of the system.

An almost complete equalisation of the bonds between the heteroatoms has been noted in dibismuthines (...Bi...Bi...Bi...Bi...).[34]

A symmetrical system, resembling the π-allyl system, i.e.

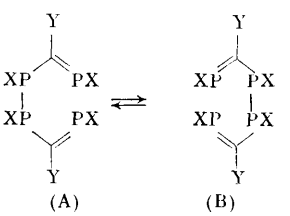


has been described.[35]

It is believed[31] that the equalisation of the carbon–carbon bonds in benzene is due to the σ-skeleton and that the π-subsystem is more likely to counteract this, the π-delocalisation being regarded merely as a concomitant factor. This interpretation is not convincing, but comparison of the six-membered C_6H_6 and X_6 systems is very appropriate. According to calculations,[31] the resonance energy in the H_6 system is insufficient to compensate for the energy expended on the deformation of the bonds and for the conversion of three H_2 molecules into the delocalised form H_6. However, in the Li_6 and C_6H_6 systems the energy is entirely sufficient (Fig. 2, curves *1* and *4*).

The smoothing of the bond alternation in the chain and certain other aspects of conjugation are frequently described[36] with the aid of a combination of resonance structures (to each of which the significance of a solution of the Schrödinger equation is attributed without due justification[37]); the use for this purpose of the symbolism of valence characteristics is unjustified, since one is dealing with the representation of wave functions and not their squares. The resonance structures do not by themselves provide an idea about the conjugation energy (and in general whether or not the proposed structures are suitable), the properties of molecules associated with the delocalisation of molecular orbitals, and the principal features of conjugation in chains of σ-bonds, for which intraatomic exchange integrals, etc. are important; the traditional description of the electronic structure of conjugated systems, for example, amides is not very satisfactory (see Sections VI, IX, and X), while in a more complete description one loses compactness (thus the description of one of the compounds mentioned in Section I requires the representation of more than 12000 (Kekulé structures). In any case, the data on the set of molecular orbitals provide much greater possibilities.

Among molecular systems with different forms of the potential, including those with two or several potential energy minima, it is easy to find examples of a high stability of *one* form, systems which readily isomerise (rearrange), structurally modulated (dynamic) rapidly oscillating systems, and, finally, "mesomeric" systems, where there is no justification for attributing their principal features to "oscillations". An interesting example[38] of a structurally modulated (dynamic) system can be represented by the following scheme:



On rapid oscillation (A)⇌(B) and for a relatively long recording time (τ_{rec}), we are able to observe a six-membered ring which is to a large extent equalised and in the absence of other information we can describe the system in terms of two resonance structures of types (A) and (B), which in a certain sense resemble Kekulé structures.

However, for a short τ_{rec} either structure (A) or (B) might be observed, which implies some similarity with the systems represented by curve *3* in Fig. 2.

The separation of the different forms of intramolecular interaction mentioned at the beginning of the Section is fairly problematical. These forms and simple summation of their contributions correspond to a fairly rough approximation. Thus the differentiation of the contribution by the inductive effect to the experimentally determined Hammett constants implies in essence a transition from reality to some kind of convention. Such a transition is justified if it facilitates to some extent the prediction of quantities (which are in principle observable); however, successes of this kind are fairly modest. The situation is complicated by the multiplicity of different versions of the interpretation of the very concept of the "inductive effect". This effect has been considered[39] as competition between acceptor ligands adjoining the atom, while in other studies[15,40–44] it has been regarded as the influence of a polar group on the σ-skeleton of the molecule, as a result of a change in the hybridisation of the atomic orbitals or of the involvement of unoccupied orbitals, etc. Some workers have calculated separately the contributions of the effects of the field of the polar group and of the inductive effect, while others assume that the latter in fact consists in the effect of the field; the use of this concept to account for the polarity of diatomic molecules has also not been ruled out. Such large discrepancies have created disadvantages but they can also have a humorous aspect.

In most studies the term "inductive effect" is understood as the polarisation of a molecular fragment induced by the static field of excess charges (+) or (–) on the atoms of other fragments, such polarisation not involving a redistribution of electron density between bonds[45] (cf. Cook et al.[15]); the latter is usually attributed to the donor–acceptor interaction as one of the aspects of conjugation with participation of unoccupied orbitals of the acceptor. Since in fact electron systems assigned to individual chemical bonds are not autonomous, the distinction between ideas concerning the distribution of electron density within the limits of bonds and between bonds can have no physical justification (see Section XI). The very differentiation of fragments and the corresponding part of the electron cloud (as well as the "electro-optical parameters" of chemical bonds) is fairly arbitrary. Thus the demarcation of conjugation and of the inductive effect is ambiguous and its possibilities should not be overestimated. It is not fortuitous that estimates of their relative roles based on the use of different criteria or schemes diverge appreciably. Thus the contribution of the inductive effect for nitrobenzene varies from zero to 100% according to the conclusions reached by different workers:[21,46–48]

The differentiation of the inductive effect has been of some interest as a route to the estimation of electron density from the form of the structural formula. Such estimates correspond to reality to some extent in certain simple molecules including a highly polar bond such as AlkF and AlkLi, but here too the involvement of hydrogen atoms and specific features of the cartesian component of the polarisability complicates the picture. In any case, the model with point charges on atoms and charge redistribution "along chemical bonds"[49] is clearly inadequate. As regards quantum-chemical calculations (see, for example, Topsom[50] and Shatkovskaya and Gineitite,[51] the latter yield more complete information but this is also by no means free of the influence of subjective factors associated with the choice of the method of separation. Under these conditions, the calculation of the resultant electron density on atoms without separating the contributions of the inductive effect on conjugation is entirely appropriate for the solution of the majority of problems without attributing great importance to the numerical estimates of these contributions obtained in different ways[21,44,52] (they have been frequently quoted with four significant figures), one can nevertheless assume that their qualitative comparisons are useful, particularly since they can differ sharply in terms of their conformational dependence (the orientation of specific orbitals is important for conjugation, while the orientation of the dipole is important for the inductive effect). However, judging from estimates,[52] the non-additivity of the influence of the effects considered can play a dominant role; if this is so, then the entire separation scheme is unjustified.

According to certain experimental and computational quantum-chemical data,[45,50–52] the influence of the inductive effect should diminish rapidly along the chain of C–C σ-bonds and more slowly along the chain of π-bonds. It is believed that the influence of conjugation diminishes more slowly (see the examples in Section X). However, one should not speak of conjugation "in general"—its different aspects (different manifestations) respond in different ways; thus one of the principal aspects is that the delocalisation of the molecular orbitals describing two identical active centres in a symmetrical molecule does not weaken at all with increase in the number of intermediate units, but its sensitivity to disturbances in molecular symmetry increases, while the conjugation energy actually diminishes rapidly. Examples of large differences between the coefficients of the transmission of influences on different parameters referring to the CHO group can be found in the paper of Yanovskaya et al.[52]

As the mechanism of the mutual influence of atomic groups was specified in further detail, the contributions of different channels leading to the interaction—through the intervening atoms or chemical bonds and through space—were considered.[53] The mixing of the electron wave functions of the above groups and the formation of delocalised molecular orbitals is possible as a result of the participation of the orbitals of the intervening bonds (an example is provided by the *n*,*n*-conjugation due to the slight involvement of the N–N σ orbital in the *trans*-conformer of hydrazine) or certain atomic orbitals of the intervening atoms (not necessarily the atomic orbitals which form the chemical bonds linking the active centres). Another channel is determined by the direct overlap of the orbitals of the active centres through space (for example, the overlap of two π orbitals in norbornadiene or the *n* orbitals in *cis*-hydrazine[54–56]). It is self-evident that the different forms of combination of these channels (leading to their enhancement or, on the contrary, to their weakening and even the disappearance of the observed signs of interaction) can be by no means ruled out (see Section XI).

The interaction between atoms or atomic groups of a complex molecule *through space* (TS) can be regarded, depending on how strong it is and what are the overlap populations of their orbitals, as an insignificant addition to the information yielded by classical structural formula, as a very weak chemical bond, or as a more important aspect of electronic structure which merits being reflected in the structural formula. Interaction through space is favoured by the diffuseness of atomic orbitals;[57] with increase in the distance between the centres, it diminishes faster than the interaction through the intervening subsystem. We have encountered this in the study of suitable conformers of non-rigid molecules as well as cyclic rigid structures in which the active centres approach one another in space (see Sections VII, VIII, X, and XI).

In this connection, the problem of the coupling between the active centres of molecules in close proximity has acquired great interest.[50,58] According to calculations,[59] the introduction of

extraneous molecules into the intervening region of space between two initial molecules (for a fixed distance R between them) promotes mixing, i.e. the delocalisation of orbitals within the limits of the entire system. One may add that the rate of electron transfer between the active centres of the molecule diminishes with increase in R, while the length of the intervening chain increases more slowly than the rate of transfer between two individual molecules.[60–62]

The question of the channel through which the influence of the inductive effect is transmitted[45] has been considered as a dilemma in which two variants are set in opposition (deliberate paraphrasing—the influence "through chemical bonds formed by intervening atoms" or "through space in which these atoms are located"). However, in reality, the atoms of a bridging group, side chains, the solvation shell, etc. are not always located in the particular part of the intervening space or near it. They influence in one way or another the strength of the field acting on the given object. Under these conditions, the presence of a continuous chain of intervening chemical bonds affects the "packing density", which is not by itself a decisive or essential apsect of the situation; among other things, one may mention that the polarisability of the butane molecule differs little from the polarisability of two ethane molecules and is described satisfactorily by the sum of atomic increments or, just as well, by the sum of bond increments. Under these conditions, the second variant (of the two quoted above in brackets) is less specific but more correct. It is not associated with limitations characteristic of the simple form of the LCBO (linear combination of bond orders) and the limitations in the multiplicity of the structures (cases) which actually exist.

In the estimation of the active field in practical studies, the intervening subsystem ("black box") was characterised by dielectric constants ε_{eff}; the values of ε_{eff} in the range from 1 to ∞(!) have been selected in different studies.[41,43,45,63] The arbitrary nature of the estimates of ε_{eff} naturally made the results worthless and made it evidently desirable to go over from macroscopic to "microscopic" characteristics and calculations at the LCAO level. We no longer speak of the inadmissibility (see Houk et al.[41] and many other studies) of the usual formula defining the Coulombic interaction between charges immersed in a medium for a model with an "intervening" medium (when the possibility of the intensification of the active field is not ruled out!).

A bridging group determines to some extent the distribution in space of the active centres and together with the latter can participate in the formation of delocalised molecular orbitals; the extent to which the subsystems are linked to one another and the possibility of the evolution of their state (the rate of energy or electron density transfer‡, the rate of even the direction of the chemical reaction) depend on its structure.

The possibility of an intramolecular energy transfer is associated with the overlap of parts of the emission spectrum of the emitter (excited chromophoric group) and the absorption spectrum of the receptor. The contribution of Forster's dipole mechanism then diminishes in proportion to R^{-6} and can be manifested for fairly long distances R between the π-subsystems (10–50 Å and more). The rate of energy transfer via Dexter's exchange mechanism, involving the overlap of the wave functions of the subsystem, diminshes exponentially and becomes insignificant for $R > 6$ Å; however, the participation of the σ-bonds of the intervening chain (for example, a polymethylene chain) in the $\pi-\sigma-\pi$ system can, according to some investigators,[59,60,62] alter the situation and enhance the role of the exchange mechanism. The rate of energy transfer $K_{en}(R)$ then diminishes with increase in R faster than the rate of electron transfer§ $K_{el}(R)$; in a series of studies[60–62] on compounds with $\pi_1-\sigma-\pi_2$ systems having different numbers of intervening units, $K_{en}(R)$ was found to be proportional to $K^2_{el}(R)$ and $K_{el} = 2.5 \times 10^{15}\ e^{-m}$, where m is the number of C–C σ-bonds in the intervening chain. Energy transfer along the receptor–polyene subsystem–emitter system has been considered by Maier et al.,[14] while the mechanism of the energy transfer as a result of the exchange of virtual photons (which is described by the non-diagonal elements of the decay matrix) has been examined by Morozov and Shorygin.[64]

We confined ourselves to brief remarks about the principal types of intramolecular interaction of atomic groups. Since even these principal forms are not clearly differentiated, it did not appear necessary (despite the inspiring terminology) to consider the numerous existing variants—homohyperconjugation and supra-annular, inductoelectromeric, and other effects.[56]

IV. Are correlations between different conjugation parameters possible?

The set of manifestations of conjugation in different properties of molecules includes numerous and varied parameters and naturally cannot be characterised by any one figure (provided that one does not postulate, contrary to facts, the existence of unambiguous correlations between all the properties investigated). The above parameters are by no means determined by identical factors. For example, the delocalisation of orbitals and the accompanying phenomena are favoured by the *similarity* in the disposition of the orbitals of the fragments on the energy scale, while the redistribution of electron density is favoured by *differences* between the latter.

One may refer to examples of complex molecules in which the deviations from additivity in some properties are clearly pronounced, while in others they are absent and also to systems in which the opposite picture is observed. Examples of compounds, similar to benzamide, in which an anomalously large dipole moment is associated with the preferential conjugation of the carbonyl group with one subsystem (NH_2) while the long-wavelength UV absorption is associated with its conjugation with another system (Ph), are no less instructive. Furthermore, it is seen from experimental data that the π-donors and π-acceptors in aromatic compounds influence the electron density in the benzene ring, the reactivity characterised by the Hammett constants σ_{para}, and also the ionisation potentials P_1 in opposite directions, but their influence on a number of optical properties[65] (the positions of the benzene UV absorption bands, the electron polarisability, the intensities of many Raman lines) and certain geometrical parameters of the molecule is in the same direction. Yet another aspect may be noted by referring to the compound $I-\Phi-NO_2$, where iodine is a π-donor and influences the optical properties like other π-donors, but its influence on the

‡ We have in mind the rate of change of the probability of recording the transfer and not the characteristic of the time scan of the process.

§ The energy and electron density transfer processes, which can be regarded as transitions between quasi-degenerate states of the entire system should not generally speaking, be contrasted. Depending on the structure of the orbitals of the subsystems and their initial state, these processes can differ sharply or can be of a mixed character; here it is appropriate to mention the electronic transitions with "charge transfer" or with "elements of charge transfer".

frequency of the nitro-group $\omega(NO_2)$ (on the dissociation constant in *p*-iodobenzoic acid) is more like that of an acceptor¶ (see also Sections VII, IX, and X).

In practice we have an exceptionally wide range of variants and a complex picture of interactions between subsystems and relations between different manifestations of non-additivity. However, these relationships are susceptible to analysis and can be adequately explained by studying the modification of molecular orbitals induced by the influence of substituents, in particular, their delocalisation and the changes in their energy and involvement in the redistribution of electron density.

The differences between the influences of intramolecular interaction on different properties of molecules have frequently led to contradictory conclusions and in some studies have served as a basis for conclusions concerning the suitability or unsuitability of particular parameters for the quantitative estimations of conjugation; such conclusions are based on a subjective choice of the criterion used as a reference standard or as a "measure of the conjugation effect" (according to Randhawa and Suri[23] as the "percentage resonance"!). In this connection, one may say that the majority of parameters are associated with the response of the molecule to external influences and characterise the possibility or probability of a particular transformation or transition to a new state, which occurs, for example, as a result of a chemical reaction or as a result of the application of the measuring procedure itself. The final state of the molecule is then specific to the observed process and possibly the conditions under which it takes place. The correlations between the parameters characterising the transitions to different final states would imply also correlations between the latter, which is fortuitous rather than the rule.

Nevertheless, it is possible to identify certain groups of parameters which are related to a greater or lesser extent. For example, the relation between certain optical properties of molecules can be established on the basis of known physical laws and is entirely explicable. However, even in this case the picture is not simple. It is determined by the involvement of a large number of electronic excitation levels of the molecule. Both low-lying and high-lying excitation levels, including those which determine the absorption spectrum in the range 500–1000 Å, then contribute to the static polarisability of the molecule. The long-wavelength part of the absorption spectrum, including the near UV region (2000–4000 Å) is somewhat more important for the refractive index of visible light; the longest-wavelength intense absorption zone or band has a major or even decisive importance for the dispersion of the refractive index and even more so for the intensity of Raman lines (especially for overtones).[66]

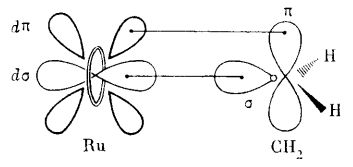
There is some chance of success in the search for correlations when different properties are considered in some specific electronic state of the molecule, for example, in the ground (unexcited) state. However, correlations with reactivity, which depends significantly on the presence of conjugation and its influence on the energy of the system in the transition and final states, are of greatest interest. The question what are the interrelations between the set of σ_{para} constants of the substituents X and the physicochemical characteristics of the compounds Y–Φ–X, for example R_2N–Φ–X, has been frequently dealt with in the literature. However, it is incorrect to formulate the question in this way. It is more logical to ask what are the correlations between the, by no means identical, sets of constants obtained from the corresponding types of initial data; it is even more appropriate to elucidate what relations exist between different kinds of initial data themselves (for example, between the basicity constants and the spectra). The establishment of certain relations of this kind would be extremely useful, but we are nevertheless faced by a complex set of conjugation parameters. Which of them will be usefully considered or adopted as the cornerstone depends on the aims of the investigator and perhaps on the ways in which he thinks.

¶ Here and henceforth the following notation is used: R = methyl group, Vy = vinyl group, All = allyl group, Φ = *para*-phenylene fragment, Π = π-bond system, and M = bridging group.

V. Chemical bonds and atomic groups incorporating heteroatoms

Before turning to complex systems, we shall note certain characteristic features of chemical bonds and atomic groups incorporating a heteroatom Z, which may constitute in certain combinations complex structures and conjugation systems. Comparison of the dissociation energies of the Z–Z and also Z–C, Z=C, and Z=Z chemical bonds formed by different atoms Z shows that the energy as a rule decreases on passing to bonds with heavier elements (as a result of the decrease in the overlap integrals of the more diffuse atomic orbitals) and in most cases with decrease in the atomic number of the element Z within the limits of the Period. This applies particularly to the π-component of double bonds. Thus, according to calculations,[67] the C=Al bond energy is smaller by a factor of 2 than the C=B bond energy, while the energy of the π-component (E_π) is correspondingly lower by a factor of 5; in the author's words, E_π for C=Z bonds decreases rapidly with decrease in the electronegativity of Z. According to calculations,[68] it amounts to 65, 35, 31, and 20 kcal mol^{-1} in the series C=C, C=Si, C=Ge, and C=Sn; estimates for the carbon–chromium bond yield a value less than 5 kcal mol^{-1}, so that the use of the double bond symbol is no longer necessary. The total energy ($E_\pi + E_\sigma$) of the C=Z double bond diminishes as Z varies in the sequence $0 \gg N > C > B \gg S > P \gg Ru, Al$.[67–70]

It is significant that the double bonds formed with participation of the atoms Z of different elements are by no means uniform in their nature. For example, whereas the C=Ti bond is described satisfactorily by two localised equivalent orbitals (with an appreciable participation of the 3*d* atomic orbital of titanium), the C=Mn bond represents a set of very different contributions of the σ- and π-components and involves a π-component which is very weak and markedly asymmetric as regards the contributions of the atomic orbitals of the manganese and carbon atoms.[69] According to calculations,[70] the $\rangle Ru=C\langle$ bond is covalent and is formed from 4*d* atomic orbitals of ruthenium:



The fragments must be arranged not as in ethylene but in mutually perpendicular planes. Judging from the arguments put forward by Zilm et al.,[71] the Sn=Sn bond can be regarded preferably as a mutually-dative linkage; the unoccupied *p* orbital of the adjoining atom participates in each of the two contributions to this bond.

Table 1. The compounds ZR_m.

Li	Be				B	C	N	O	F
7	10.5				10.9 —	11.4 6.0	12.5 4.8	13.4 6.0	17 6.5
0.8	(2)				3.9 162	4.5 157	5.0 199	5.2 184	6.2 132
0.9	1.8				2 —	2.2 —	2.7 —	3.1 —	4 —
50	(55)				88 —	86 —	75 —	87 —	110 —
Na	Mg				Al	Si	P	S	Cl
6	8.8				9.8 —	10.6 3.9	11.4 3.1	12.5 3.3	14.4 3.5
(0.7)	(1.6)				2.4 189	3.0 170	2.9 200	3.3 203	3.7 170
0.8	1.6				1.7 —	1.9 —	2.3 —	2.6 —	3 —
(45)	(45)				68 —	75 —	68 —	72 —	84 —
Ti	V^V	Cr^{VI}	Cu^I	Zn	Ga	Ge	As	Se	Br
9.4	—	—	(9.5)	9.4 —	9.6 —	10.2 3.7	10.7 2.7	12 —	13.5 —
2.2	—	—	(1.8)	2.4 202	2.35 195	2.7 180	2.6 200	2.7 235	3 180
1.6	2.0	2.2	1.8	1.4 —	1.7 —	1.8 —	2.1 —	2.4 —	2.7 —
65	(35)	(25)	55	45 —	60 —	60 —	57 —	59 —	70 —
Zr	Nb^V	Mo^{VI}	Ag^I	Cd	In	Sn	Sb	Te	I
9.4	9)	—	(9)	8.8 —	8.9 —	9.7 2.9	10.3 —	11.3 —	12.5 0.2
1.9	(2)	(2)	(1.6)	2.0 215	1.95 212	2.2 186	2.25 210	2.4 250	2.4 196
1.5	1.9	2.2	1.8	1.4 —	1.6	1.8 —	2.0 —	2.1 —	2.4 —
75	(52)	(32)	40	36 —	40	54 —	53 —	51 —	56 —
Hf	Ta^V	W^{VI}	Au^I	Hg	Tl	Pb	Bi		
9.7	8.8	8.6	—	9.3 —	— —	9.3 —	9.8 —		
2.0	2.3	2.05	(2.8)	2.45 202	1.8 220	1.9 205	1.9 (220)		
1.4	1.8	2.1	2	1.5 —	1.6 —	1.75 —	1.9 —		
80	62	38	(60)	31 —	32 —	37 —	35 —		

In general, double bonds with participation of a heteroatom Z in most cases bear little resemblance to the C=C bond; in conformity with their specific features, the manifestations of conjugation with adjoining fragments can differ greatly (see Section VI).

The available data suitable for a comprehensive characterisation of simple compounds ZR_m and their Z–C bonds are compiled in Table 1. These compounds imitate in a certain sense the fragments of complex conjugate systems incorporating groups of the type ZR_n. Each box in Table 1 indicates the heteroatom Z and its valence state if it is not the usual one; the following data are presented in the form of a column or two columns: (1) the vertical ionisation potential (eV) (the first of those corresponding to the Z–C bonds);[39,72–77] (2) the force constant of the Z–C bond (mdyn $Å^{-1}$) (indicated in bold type);[78–84] (3) the electronegativity of the $-ZR_n$ group;[85,86] (4) the *average* Z–R bond dissociation energy (kcal mol^{-1}).[87–89] In the second column we have (1) the electron affinity of the ZR_m molecule (eV) [90–92] and (2) the intense long-wavelength UV absorption band (in most cases the $\sigma \rightarrow \sigma^*$ band; gas phase, nm).[73,93–100] Approximate estimates based on analogies and comparisons with molecules having similar structures are indicated in brackets. The arrangement of the data in Table 1 was dictated by the need for compactness.

The principal trends noted when compounds ZR_m are compared are as follows: as Z varies across the Periodic System from right to left and from above downwards, the force constant K(Z–C) and the ionisation potential decrease; the electronic polarisability per Z–C bond increases; there is a sharp increase in the intensity of the Raman lines[32,66] and the Z → C electron density shift becomes more pronounced (in LiR, it corresponds to a transfer of a charge amounting to ~0.6 e); the electronic excitation energy decreases, at least within the limits of a particular Group in the Periodic System (comparisons along Periods are difficult because of the lack of uniformity as regards symmetry types and the unreliability of the assignments of the absorption bands). Similar trends have been noted also on comparing data for Z–Z bonds as well as Z=C and Z=Z bonds. However, all the foregoing features cannot be fully extended to compounds of the heaviest elements such as Au, Pt, and Hg, which is associated to a large extent with the contribution of relativistic effects and the corresponding contraction of the valence shells.

We have presented data for molecules with fairly simple structures. One may note that *almost any increase in the complexity* of the molecule (attachment of additional atomic groups) *reduces* the electronic excitation energy and in many cases (excluding the addition of active acceptors) also the ionisation potential. Naturally, in individual instances the appearance of steric hindrance can lead to the breakdown of conjugation as a result of a change in conformation, but one cannot rule out also the converse possibility where the real conformation which is relatively unfavourable for conjugation (say in hydrazine) is converted into a more favourable conformation as the structure becomes more complex or when the bond angles are greatly distorted (for example, in cubene compared with alkenes).

The assignment of molecules of the type ZR_m to the class of comparatively simple ones does not imply that they do not exhibit the non-additivity and mutual influence of fragments. In relation to the $H_3C-Zn-CH_3$ molecule, one may note an appreciable splitting (~2.2 eV) of the delocalised σ molecular orbitals of the Zn–C bonds, the non-zero value of the non-diagonal Zn–C/Zn–C force coefficient, etc. However, these aspects will not be considered here.

VI. π−π conjugation

The principal types of conjugated systems (π−π, σ−π, *n*−*n*, etc.) and the characteristics of their reactivity were at one time examined in detail.[101] At the present time compounds with conjugated π-bonds have been most thoroughly investigated by physical and chemical methods. Almost all the most important features of the physical, chemical, and technical properties of polyenes, poly-ynes, polyphenylenes, and other similar systems are related directly or indirectly to π−π conjugation; the functions of polyconjugated systems constitute the basis of many most important physiological processes; the photochemical reactions of π-conjugated systems can be seen among chemical processes which occur in the interstellar space, for example, on dust particles.[102,103]

It is know that the C−C central bond in the molecules of butadiene, diacetylene, and dicyanogen is shortened and its rigidity has increased more than might have been expected judging from the C−C bonds in propene, propyne, and acetonitrile; the specific features of the π-bonds are much less marked. According to new data,[104] the alternation of bonds in *trans*-polyenes is slightly smoothed out and to a greater extent in the centre of the chain where the rigidity of the double bonds (compared with the terminal ones) is reduced by 5−10% and the bond lengths are greater by approximately 1%. The changes in interatomic distances as the conformations are varied can be demonstrated in relation to glyoxal, whose conjugation energy (~3 kcal mol^{-1}) is close to that of butadiene. According to calculated data,[105] presented in Fig. 3, in the planar conformers there is a small amount of double bond character in the region of the central C−C bond (which according to R Bader's calculations should be accompanied by the breakdown of axial symmetry, i.e. by some ellipticity of the distribution of electron density). In *gauche*-conformers, all the manifestations of π−π conjugation, including effects in the bond lengths, are reduced to a minimum.

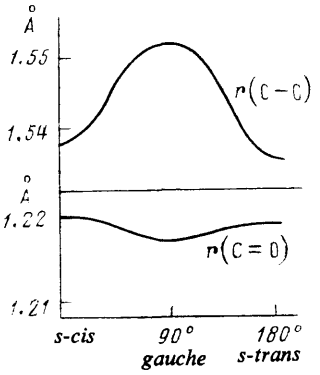


Figure 3. The C−C and C=O bond lengths in the OHC−CHO molecule in different conformations (θ = 180° for the *s-trans*-conformer).[105]

The conditions governing the conjugation of the C=C double bonds with the C=Z and Z=Z bonds can vary within wide limits. The transition for systems incorporating heavy atoms Z should be accompanied by the mutual approach of the frontier orbitals (which in general favours an increase in conjugation energy) and by a tendency towards an increase in the contribution of the C=Z fragment to the long-wavelength region of the electronic absorption spectrum. According to calculations,[106] the conjugation energy in the C=C−C=Ti system should be somewhat greater than in butadiene; in other cases, there is a possibility of its decrease and of the weakening of other manifestations of conjugation, which is partly associated with the contribution of relativistic effects.[57,107]

VII. Does the methylene bridge break the conjugation chain?

This question has been discussed for a long time in the literature but hitherto contradictory views have been expressed; the interest in this question has increased in connection with new problems, in particular the search for the possibility of creating organic conductors on the basis of polyconjugated systems, for example, polyacetylenes (see Section II). In a recently published study,[108] the authors confirmed the version stating that conjugation and π-electron delocalisation are retained in the presence of a methylene bridge but in another study[109] this version was rejected; semiempirical calculations of the interatomic distances and carbon−carbon bond orders led to the conclusion that in polyacetylenes there is no conjugation of the π-subsystems through the methylene group. A more complete idea about this problem is provided by calculations of the energies and structures of molecular orbitals.[110,111] The reasons for the contradictions are associated partly with the choice of different criteria (see Section IV) and with the differences in terminology. By invoking the delocalisation of π orbitals as the criterion, one must bear in mind that, when the π-subsystems are identical, such delocalisation should, generally speaking, be complete not only in molecules such as those of butadiene but even in the presence of a very weak bond between the subsystems (say between two ethylene molecules separated by a distance of 5−10 Å). However, under the conditions of a weak bond, a slight difference between the structures of the π-subsystems is sufficient to cause a breakdown in delocalisation; furthermore, the defects in the π−π conjugation chain in real polyacetylene specimens are not arranged regularly, the defect-free conjugation zones are not identical and, furthermore, they are not uniform as regards conformations at the locations of bridging groups. The question stated in the heading can therefore be answered in the given instance only by taking into account statistics and, naturally, the specific features of the criteria employed.

We shall consider in greater detail the simplest dienes with a symmetrical structure. Here the π orbitals of two vinyl groups, π_1 and π_2, can be mixed and can form two delocalised molecular orbitals, in one of which π_1 and π_2 are incorporated with the same signs (π_+) while in the other they have different signs (π_-). The energies of the new orbitals differ by Δπ. In the case where the interaction of the π-bonds through space predominates, π_- lies higher on the energy scale than π_+ and, when interactions through a bridge predominate, the opposite arrangement is possible.[54–56] The mixing of the unoccupied π* orbitals leads to a splitting Δπ*, which frequently differs greatly from Δπ. The mechanisms of the mixing (see Section III) of the occupied and unoccupied orbitals may not in fact be the same.

Henceforth in the text the deviations from the Koopmans theorem, the allowance for which in many problems is absolutely essential[56] and merits consideration in a special review, will not be discussed; we shall therefore retain the conventional designations of

the type $\Delta\pi$ and $\Delta\pi^*$ in the analysis of experimental ionisation potentials, etc.

According to experimental data, $\Delta\pi$ = 2.4 eV and $\Delta\pi^*$ = 2.2 eV in the planar *s-trans*-butadiene molecule. The values of $\Delta\pi$ and $\Delta\pi^*$ diminish rapidly in the series of compounds butadiene, penta-1,4-diene, hexa-1,5-diene, etc.; this can also be said about diynes, dinitriles, and diketones. However, in compounds containing a chain of methylene groups $-(CH_2)_n$ there are too many conformational possibilities† and this makes a simple comparison of experimental data relatively unproductive—the conformation is in this instance one of the decisive factors on which depend the degree of overlap of the orbitals of the fragments and the values of $\Delta\pi$ and $\Delta\pi^*$. One can also mention that, for a large chain length, one cannot rule out the possibility of the mutual approach the appreciable interaction of the terminal C=C bonds through space, i.e. the occurrence of a conformation resembling a ring.[112]

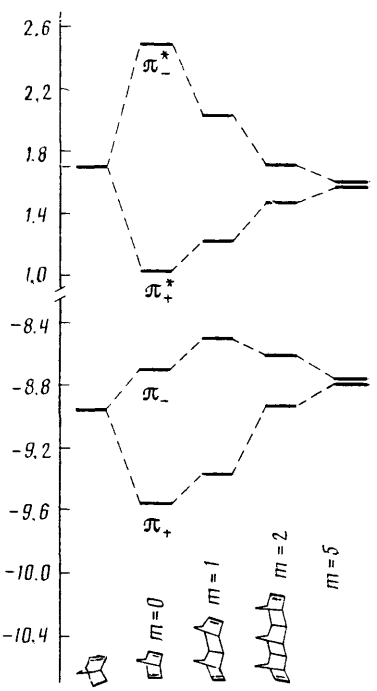
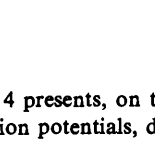


Figure 4. The energies of the π orbitals of type I diene hydrocarbons with an increasing number of intervening C–C σ-bonds.[55]

Fig. 4 presents, on the basis of the data of Balaji et al.,[55] the first ionisation potentials, designated by the indices π_+ and π_-, as well as the electron affinities (indices π_+^* and p_-^*) of symmetrical dienes (I) with a fixed relative orientation of the C=C bonds.



(I)

† The relative distribution of the double bonds in space can be described taking into account six degrees of freedom.

Fig. 4 presents experimental data for compounds with m = 0, 1, and 2, and the results of an approximate extrapolation for compounds with $m > 2$; the extrapolation for m = 7 (16 intervening C–C σ-bonds) yields $\Delta\pi \simeq 0.003$ eV.[55] Such a low value of $\Delta\pi$ is naturally not susceptible to detection by photoelectron spectroscopy, but, under suitable conditions, the possibility of investigating the interaction by other methods is not as yet ruled out. In particular, the study may be based on the rate of the photoinduced electron transfer, which was found to be in the subnano-second range in experiments[113] in the presence of ten intervening C–C bonds and was an order of magnitude lower in the presence of twelve C–C bonds. If the "conductivity" of the interface is still smaller, the transition time may run to seconds, i.e. may correspond to the possibility of clear representations.

With increase in m and hence in the distance R between the double bonds in dienes (I), the direct overlap of the π orbitals through space (TS) diminishes rapidly. Whereas in norbornadiene (m = 0, R = 2.4 Å) such overlap largely determines the real splitting ($\Delta\pi$ and $\Delta\pi^*$), for m = 1 and R = 4.8 Å it becomes very small and less significant than the interaction through the intervening C–C bonds (TB), which weakens much more slowly—by a factor of 2–3 when m increases by unity.[55]

In connection with these comparisons, one may mention that the influence of the inductive effect of the polar groups on the dissociation constants of carboxylic acids weakens by a factor of 2–3 with increase in the length of the intervening chain by one additional C–C bond,[45] while the induced charges on the C atoms of the alkyl group should diminish along the chain even faster according to calculations.[50,51]

Quantum-chemical studies of $\pi-\sigma-\pi$ systems have shown that the weakening of the interaction with increase in the number of intervening σ-bonds is not an immutable rule; under suitable conditions, one cannot exclude the possibility of the introduction of an additional unit such that the bond between the terminal active centres would be enhanced.

In norbornadiene, the dihedral angle θ between the planes of the two "ethylene" fragments is 116°. In other dienes with a similar structure but with a larger angle θ, the direct overlap of the π orbitals is less marked; in the almost planar cyclohexa-1,4-diene it becomes very small whereas the interaction through bridging groups (TB) is to a large extent retained and thus comes to the fore; accordingly, the π_+ orbital is located higher on the energy scale than the π_- orbital. Signs of non-additivity in the UV and Raman spectra of norbornadiene have been noted.[114]

If the two π-subsystems are arranged at right angles to one another, then, without the involvement of suitable intervening units, we have $\Delta\pi$ = 0; this is the case with the spiropentadiene



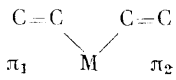
We shall designate such a system by the symbol ||=. Without going into specific structural details, one can say, in principle, that the introduction of an intervening double bond, oriented at a certain angle in such a way that there is a possibility of its interaction with each of the initial bonds (symbol ||⁄=), gives rise to the possibility of the formation of delocalised molecular orbitals with an appreciable energy splitting. A structurally suitable combination of σ-bonds can also serve as an active intervening unit; thus the

involvement of the orbitals of the intervening ring in the tricyclododecatetraene molecule



promotes the mixing of the highest occupied orbitals of the two diene fragments and the splitting of the HOMO reaches 1.5 eV.[115]

The question arises how the bond between the π-subsystems depends on the nature of the bridging group. Some information about this can be drawn from the results of studies on divinyl compounds.[116]



The coupling between the orbitals π_1 and π_2 is determined by the fact that they both overlap simultaneously with a suitable orbital of the bridging group M and thus (even for a very small contribution of the latter) form a conjugation system with delocalised orbitals of the type π_+ and π_- (see above).

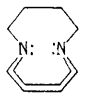
The difference between the energies $\Delta\pi$ of the new molecular orbitals is greater the closer is the energy of the orbital of M to that of the $\pi_{1,2}$ orbitals and the greater the overlap population in the M–C bonds. The difference $\Delta\pi$ is a maximum for planar conformers and reaches 3.5 eV for M = C=C, i.e. in the case of hexatriene. In the series of dienes with M=NH, O, CH_2, SiH_2, SnH_2, and $-CH_2-CH_2-$ the quantity $\Delta\pi$ diminishes and approaches zero but the orbital π_+ nevertheless lies higher than π_-, which is consistent with the conditions under which the bond through the bridge predominates (TB > TS). However, when M = CF_2 or CCl_2, the energy of the atomic orbitals of the bridging carbon atom is reduced under the influence of the electronegative ligands and the overlap population in the C–C bond of the C–$CHal_2$–C fragment diminishes appreciably; the conjugation of the π-bonds through the bridge is therefore weakened so much that even their slight interaction through space predominates and the delocalised orbitals π_+ and π_- are arranged on the energy scale in the opposite order characteristic of this type of interaction.[116]

VIII. *n*–*n* and σ–σ conjugation

Turning now to examples of *n*–*n* conjugation, we may note that the interaction of the *n* orbitals of adjoining atoms is unimportant for the formation of a chemical bond between fragments; however, the wave functions of the lone pairs (LP) in the Z–Z systems are mixed and their (+) and (–) combinations are split as regards energy for suitable molecular conformations with the accompanying destabilisation of the highest occupied molecular orbital (HOMO).

The difference (Δn) between the first two ionisation potentials, which corresponds approximately to the splitting of the above combinations of the atomic orbitals forming the two highest occupied orbitals, is illustrated by several examples in Table 2. The data for the first two compounds refer to the *s-trans*-conformations (the angle of rotation θ about the central σ-bond is 180°) corresponding to the maximum splitting; they were obtained on the basis of calculations and using analogies. The table also includes experimental data for the *n* orbitals of the oxygen atoms and certain dicarbonyl compounds, more precisely for those where the maximum splitting has been noted owing to a more favourable conformation (by no means in all cases optimal) for conjugation.[117]

Table 2. The gap between the first and second ionisation potentials corresponding to the delocalised n_+ and n_- orbitals.[54,72,77,117,118]

No.	Compound	Δn, eV	No.	Compound	Δn, eV
1	R_2N-NR_2	2.5	9		2.1
2	$R_2As-AsR_2$	1.6			
3	Cl–Cl	2.5			
4	I–I	1.8			
5	Diketones: α	2.6			
6	β	0.9	10		1.1
7	γ	0.5			
8	δ	0.3			

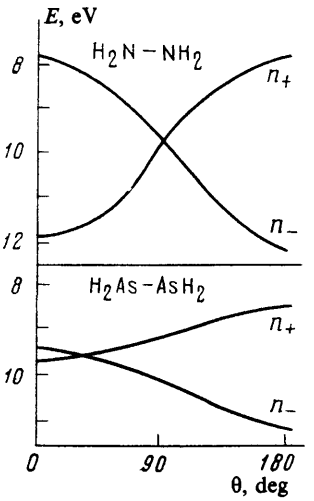


Figure 5. The energies of the delocalised *n* orbitals of N_2H_4 and As_2H_4, designated by the symbols n^+ and n^-, for different conformations including the *s-cis*-conformation (θ = 0°) and the *s-trans*-conformation (θ = 180°) (data obtained in Galasso's non-empirical calculations[54]).

Fig. 5 shows how the energies of the n_+ and n_- orbitals of H_2N-NH_2 and $H_2As-AsH_2$ should change as the conformations are varied according to calculations.[54] The splitting Δn in the *cis*-conformers is determined by the direct overlap of the *n* atomic orbitals of the heteroatom "through space". In the *trans*-conformers, it takes place as a result of the mixing of the low-lying σ orbitals of the central Z–Z bonds; despite the fact that the energies of these σ orbitals in the compounds of heavier atoms approach those of the *n* orbitals of the heteroatoms, the splitting diminishes, which is apparently associated with the change in the

nature of the lone pair and the decrease in their overlap with the molecular orbital σ_{Z-Z}. The lengthening of the Z–Z bond also has an effect in the *cis*-conformer.

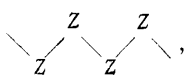
The principal conclusions drawn from ionisation potential data are as follows: (1) the manifestations of $n-n$ conjugation are associated with the interaction both through the intervening chemical bonds and through space; the relative roles of these channels depend on the molecular conformation; (2) with increase in the atomic weight of the heteroatom, Δn diminishes, which can be assessed as the weakening of conjugation as a result of the decrease in the contributions of both channels; (3) the difference Δn diminishes with increase in the distance R between the active centres; (4) in the molecules of compound (IX), which appears in Table 2 ($R \simeq 2.5$ Å), the interaction through the C–C σ-bond predominates, while in compound (X) ($R = 2.6$ Å) the interaction through space is dominant, which is favoured by the orientation of the n orbitals of the two nitrogen atoms "towards one another".[118] If the orientation and the distance R are kept constant, then in the bimolecular system $R_3N...NR_3$ one may expect approximately the same value of Δn.

The molecular orbitals of σ–σ conjugation systems, consisting of isotypical units, are delocalised. With increase in chain length, the number of occupied molecular orbitals and their maximum splitting on the energy scale increase, while the energy gap between the frontier orbitals, the first ionisation potential, and the electronic excitation energy diminish.[77,119,120] In this respect, there is no fundamental difference between the σ–σ conjugation chains (including those in *n*-paraffins) and polyenes, but the linkage between the electron clouds of the fragments and the features of non-additivity enumerated above depend on the nature of the atoms Z and become more explicit[119] in the series of chains formed by the following groups:

$$CR_2 < SiR_2 < SnR_2 < CH=CH.$$

The coupling between the orbitals of the atoms in a chain of σ-bonds was described on the basis of estimated intraatomic [interatomic? (Ed. of Translation)] exchange integrals $\langle\varphi_1|V|\varphi_2\rangle$ and also the weak overlap of the atomic orbitals of non-adjacent atoms;[42] the overlap and order of the bonds between non-adjacent atoms cannot, however, be regarded (contrary to what has been stated by Gineityte and Shatkovskaya[121]) as "criteria of the delocalisation of electrons".

We may note that, in systems involving "conjugation of the σ-bonds of adjacent molecules" ···Z–Z···Z–Z··· (Section III), the optimum geometry is attained more readily than in the chains



noted above, where the α-skeleton imposes certain limitations. Accordingly, among the entire wide variety of systems (chemical compounds), we have in the first case a wider range of possible interaction conditions.

IX. The donor–acceptor interaction of atomic groups

Considering a wide range of X–Y and X–M–Y systems in their *stationary* states, one may say that conjugation or, more precisely, the mixing of the orbitals of molecular fragments may not be accompanied (as happens, for example, in the C=C–C=C–C=C system) or may be accompanied (for X ≠ Y) by a redistribution of electron density between the groups X and Y– which is slight or appreciable depending on the structure of these groups. If it is appreciable and can be described as the electron transfer X → Y, then in the majority of problems it is more practical to employ another terminology and to begin with another procedure for the differentiation of the initial "fragments" with the corresponding excess charges; in this case, it may not be necessary to introduce the terms "redistribution", "interaction", etc. in describing the system.

In any case, the contribution of the donor–acceptor interaction can be estimated approximately *a priori* on the basis of empirical rules and approaches and can be determined from experimental data (from the molecular dipole moment μ, from IR absorption band intensities, etc.) or from information about the systems of unoccupied and occupied molecular orbitals, whose analysis provides a more detailed picture and fairly understandable explanations.

The electronegativities of the atomic groups χ tabulated in the literature are attractive because of the possibility of inferring directly the donor–acceptor capacities of the substituents in which we are interested. However, in fact we have a set of extremely heterogeneous data obtained in different ways, frequently without information about the type of atomic partner-groups and about the molecular conformations, although such information is of primary importance (as well as the information about the influence of the medium and especially the solvation of the active centres, which may greatly modify the donor–acceptor properties and the conditions governing the mutual influence of the atomic groups). For this reason, the values of χ quoted in the text below can be used only for qualitative comparisons.

In view of the multiplicity of methods proposed for the determination of χ, this constant has come to be adopted as an independent property inherent in the atomic group; there is no need for comments and it is sufficient to quote some of the large number (more than 30) of the published values of χ for the amino-group: 1.361, 2.992, and 3.63 (quoted after Vereshchagin[86]).

A step towards a more correct analysis consisted in the differentiation of two types of donor–acceptor interaction—with increase or decrease in the order of the bond connecting the molecular fragments under consideration.[122] Thus combinations of atomic groups favouring a redistribution of electron density between them and accompanied by manifestations of non-additivity in other properties have been noted. The designations "π-donor + π-acceptor" and "σ-donor + σ-acceptor" began to be used widely subsequently for the designation of such combinations. This problem was reflected indirectly much earlier by the introduction of the Hammett constants σ^+ and σ^-.

Even after the more concrete specification indicated, the designations "donor" (D) and "acceptor" (A) should not be treated as a classification of the atomic groups. Depending on the "partners" and the molecular conformation, the latter can behave differently. Thus the systems of carbon–carbon π-bonds (Π) can be π-acceptors in Π–D molecules, for example in aniline, and π-donors in Π–A molecules, for example in nitrobenzene.

The dipole moment of nitrobenzene is known to be greater than that of nitromethane by 0.8 D, which corresponds by convention to a Ph → NO_2 charge transfer of the order of (1/20)e. When the nitro-group is displaced from the plane of the benzene ring up to an angle of rotation of approximately 90°, the contribution of the π–π conjugation is virtually ruled out and the difference from nitromethane diminishes by a factor greater than 4 and, according

to quantum-chemical calculations,[46] by a factor of 1.5 (see also Baidin et al.[21]); according to the generally accepted view, only the contribution of the inductive effect then remains and the nitro-group becomes a σ-acceptor. The appreciable $H_2N \rightarrow Ph$ charge transfer in aniline molecules justifies the usual classification of NH_2 as a π-donor, but in an unfavourable conformation the amino-group (as well as the SR group) becomes a σ-acceptor.

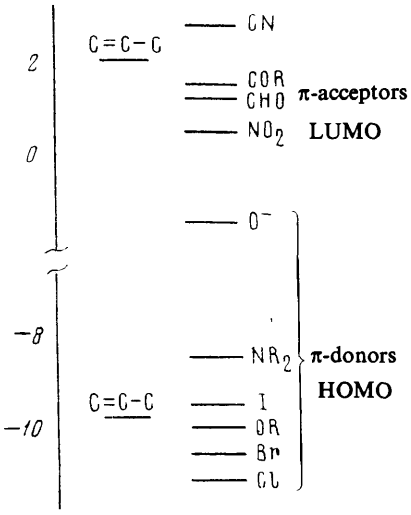


Figure 6. The positions on the energy scale of the HOMO of the π-donors and LUMO of the π-acceptors (simulated by the D−R and A−R molecules);[123] the possibility of the involvement of the groups D and A in the donor−acceptor interaction is related to them (however, cf. the data for PR_2 and AsR_2!).

The π-donor → π-acceptor redistribution of electron density depends significantly on the energy gap between the occupied orbital of the donor and the unoccupied π-orbital of the acceptor (Fig. 6) and also on the structure of the interface. It is self-evident that the electronic excitation of the molecule can alter radically the donor−acceptor properties of the substituents.

Table 3 provides data on the first vertical ionisation potentials (P_1) corresponding to molecular orbitals with an appreciable contribution of the *n* orbital (the lone electron pair) of the amino-nitrogen for compounds containing an active π-donor (amino-group) and intervening units of various types.[72,77,124] The values of ΔP_1 quoted denote the changes in P_1 on passing from simpler amines (X = H) to derivatives incorporating other groups X. Thus, whereas P_1 = 8.95 eV and ΔP_1 = 0 for R_2NH, the corresponding values for R_2N-NO_2 are P_1 = 9.75 eV and ΔP_1 = 0.8 eV. The influence of substituents on the amino-group can be inferred also from other data.[125–128] These include the experimental and calculated relative proton affinities (PA) of the amino-group in the compounds H_2N-CH_2-X (seventh column in Table 1—PA, kcal mol^{-1} [125]); the results of the calculation of the changes, induced by the influence of the group X, in the extremum of the electrostatic potential (EPE) generated by the lone pair,[128] which indicates the degree of involvement of the lone pair in conjugation (the fourth, eight, and twelfth columns—EPE, kcal mol^{-1}; the values for X = H were adopted as zero). The tenth column lists the Hammett constants σ_{para} [127] which are suitable for the investigation of the influence of X on reactions in electron-donating groups.

Some idea about the way that the amino-group influences in its turn the group X is provided by the changes induced by it in the stretching vibration frequency of the π-bond in the group X ($\Delta\omega_X$, cm^{-1}) (the fifth, ninth, and fifteenth columns).[32] For comparison, Table 3 includes electronegativity (χ) data for all the substituents X [85,86] in the form of the difference $\chi - 2.3 = \Delta\chi$.

Table 3. Signs of the mutual influence of the substituents in the D−A and D−M−A* systems.

Group X	Δχ for group X	R_2N-X (*a*)			R_2N-CH_2-X (*b*)				σ_{para} for group X	$R_2N-\Phi-X$ (*c*)				
		ΔP_1, eV	EPE, kcal mol^{-1}	$\Delta\omega_X$, cm^{-1}	ΔP_1, eV	PA, kcal mol^{-1}	EPE, kcal mol^{-1}	$\Delta\omega_X$, cm^{-1}		ΔP_1, eV	EPE, kcal mol^{-1}	Δμ, D	Δλ, nm	$\Delta\omega_X$, cm^{-1}
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
NO_2	1.4	0.8	50	−70	[0.8]	[−25]	16	[−30]	1.0	0.6	30	1.5	100	−17
CN	1.0	0.6	40	−40	0.7	−16	15	−24	0.9	0.5	—	1.2	35	−11
COR	0.4	0.3	25	−50	0.2	[−10]	—	−4	0.7	0.2	—	1.0	65	−13
Cl	0.7	[0.1]	30	—	[0.2]	[−10]	15	—	0.2	0.2	—	0.3	8	—
C=C	0.25	−1.0	17	−15	−0.1	2	—	0	0.1	−0.4	—	0.4	40	0
H	0	0	0	—	0	0	0	—	0	0	0	0	0	—
R	0	−0.4	4	—	−0.1	3	0	0	−0.1	−0.2	—	0	3	—
NR_2	0.35	[−1]	15	—	[−0.3]	[3]	[−2]	—	−0.3	−0.6	[−3]	0.1	10	—

* Approximate estimates are indicated in brackets.

The values of $\Delta\mu$ characterised the redistribution of electron density in the direction $R_2N \rightarrow X$, or, more precisely, the deviations of the dipole moment of $R_2N-\Phi-X$ from the vector sum of the moments of PhX and $PhNR_2$.[65] In the fourteenth column, $\Delta\lambda$ denotes the bathochromic shifts of the intense absorption band, which is in the region of 250 nm for $PhNR_2$ and corresponds to an element of charge transfer.

All the figures in brackets in Table 3 were obtained by quantum-chemical calculations or are approximate estimates based on analogies.

We shall consider in greater detail compounds of the type H_2N-A with $n-\pi$ conjugation systems in which the $D \rightarrow A$ shift of electron density has been noted. The formamide molecule can serve as the simplest example. In order to describe its large dipole moment, one usually refers[128] to the contribution of the structure $H_2N^+=CH-\overline{O}$, which reflects qualitatively also the shortening of the N–C bond, the coplanarity of the molecule, and the large energy barrier (18 kcal mol^{-1}), which prevents the rotation of the amino-group. According to calculations,[129] on rotation about the C–N bond with transition from a non-planar to a planar conformation, favouring $n-\pi$ conjugation, the electron density on the O atom increases slightly (cf. Refs. 49 and 130), while the C–N bond is shortened by 0.1 Å and its rigidity increases significantly.[131] However, certain other data do not correspond to the above methods of describing the structure of amides. Thus the length and force constant of the carbonyl bond, $R(C=O)$ and $K(C=O)$, differ little from those of simple aldehydes and the redistribution of electron density concerns, according to Wiberg and Laidig,[129] mainly the C–N region. One may add that the available data for the R_2N-NO_2 [132,133] and R_2N-CN molecules (but not for the just as polar R_2N-SO_2R group in which many features of conjugation are manifested weakly or are absent[134,135]) are in broad outline of the same kind.

The manifestations of $n-\pi$ conjugation in $PhNR_2$ molecules are well known. The energies of the p orbital in the PR_2, AsR_2, SbR_2, and BiR_2 groups differ little from that of the orbital in NR_2 (± 0.1 eV), but, as shown by the dipole moments of the compounds $PhZR_2$ and the Hammett constants σ_{para} which are close to zero,[127] are not active π-donors. The neutral character of the AsR_2 group ($\sigma \simeq 0$) has been treated[136] as a result of the annihilation of the contributions of the inductive effect (+0.28) and conjugation (–0.28), but in all the ZR_n substituents investigated, NR_2 and OR, the constants σ_{para} are close to zero despite the large differences between polarities! At the same time, the characteristic features of conformational equilibria were not considered by Gel'fond et al.[136]

Studies on specific $PhZR_2$ conformers yielded more information. According to calculations,[137] in the $PhPR_2$ conformer, where the two groups R are located on one side of the plane of the benzene ring, the PR_2 group behaves as a weak π-donor, while in the conformer with the symmetrical disposition of the methyl groups on either side of the plane of the benzene ring, the above group behaves more as a weak acceptor; a more significant bathochromic shift of the UV bands and appreciable intensification of the 1600 cm^{-1} Raman line of the benzene ring—almost the same as in $PhNR_2$—are characteristic of the first conformer. In $PhAsR_2$, which consists mainly of the conformer of the second type, the substituent exhibits stronger electron-accepting properties, which are usually attributed to the participation of the unoccupied d orbital of the As atom. The energy of the $n-\pi$ conjugation in the $PhNR_2$ molecule reaches 8 kcal mol^{-1}; for comparable conformations, it should be smaller by a factor of 1.5–2 in the $PhPR_2$ molecules.[138]

Judging from the data presented and also from the results of calculations,[20] NMR spectra,[139] and other data,[39,140,141] one can assume that the features of $n-\pi$ conjugation weaken in the series of compounds $PhZR_2$, where Z = N, P, As, Sb, and Bi, and in the PhZR series, where Z = O, S, Se, or Te. This applies particularly to the π-overlap and the $C_{arom}-Z$ bond length,[142] to the mixing of the n and π orbitals,[20] to the deviations from additivity in the dipole moments,[140] to the electron density on the carbon atoms of the benzene ring and the σ_{para} constants, to the conjugation energy[141] and the tendency by the molecule to assume the planar conformation favouring conjugation, and to the HOMO energy and the sensitivity of all the above parameters to changes in the angle of rotation θ of the ZR_n group about the $C_{arom}-Z$ bond. However, the above principal trends do not occur in the compounds PhX (X = halogen) and also in the compounds $O_2N-\Phi-ZR$,[65,140] where transition to heavier atoms Z entails the intensification of many manifestations of non-additivity; one of the causes is associated with the absence of the "problem of conformations" in the compounds PhX (X = halogen).

Allowance for the difference between the width of the energy gap ΔE between the n and π orbitals (which is smallest for PhI) is clearly insufficient to account for the entire observed picture; thus, one may turn ones attention to the appreciable decrease in the degree of $n-\pi$ mixing for almost identical values of ΔE in the series of compounds N ··· Bi. The latter is usually explained by the enhancement of the s character of the n orbitals, although this is not easy to test because of the lack of experimental data for the conformations being compared.

The sequences of Z based on the changes in the UV spectra of PhZr ($\Delta\lambda$) differ appreciably from those presented above. Within the limits of Group V elements, only nitrogen is outstanding. In the PhOR ··· PhTeR series and also in VyOR ··· VyTeR, a gradual shift of the region of intense absorption towards longer wavelengths is observed[143,144] (in conformity with this, a tendency towards an increase in the intensity of the Raman lines can be seen[143,145]); these data do not constitute an incontrovertible sign of the enhancement of any particular aspects of conjugation but it appears that the orbitals of heavy atoms are much more involved in the long-wavelength absorption (here one can turn ones attention to the energy of the n, σ, σ^*, and Rydberg orbitals and the UV spectra of the SR_2 and SeR_2 molecules and even more so TeR_2 molecules (see Table 1 and Refs. 73, 146, 147). Unfortunately, the interpretation of the PhX absorption bands is unreliable and incomplete, which applies particularly to the Rydberg transitions.

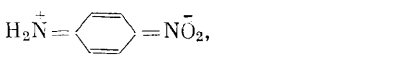
The overall pattern appears fairly complex and does not fit within the framework of a simple scheme; however, quantum-chemical calculations make it entirely possible to achieve qualitative explanations.

X. Donor–acceptor interaction in systems with a D–M–A bridging group

The question arises how the conditions governing the donor–acceptor interaction change on passing from D–A systems to D–M–A systems, where M is a bridging group. We shall consider initially the special case where the intervening unit is a system of carbon–carbon π-bonds. The degree of charge transfer in the $D-\Phi-NO_2$ molecules is smaller by a factor of $\sim 2-3$ than in $D-NO_2$. However, in the presence of the most active π-donors

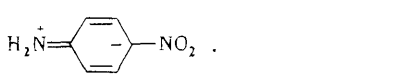
($-CH_2^-$, $-O^-$, $-NH^-$, $-S^-$), it is nevertheless extremely pronounced‡ and reaches 0.1 ... 0.2 e within the framework of the conventional D → A scheme according to calculations.[148]

The charge transfer in the *p*-nitroaniline molecule can be estimated as approximately 0.03 e; here the interatomic distances[149] correspond to an approximation to the quinonoid structure



and the C–NO_2 bond is shorter than in nitrobenzene by 0.03 Å. This led to the conclusion that conjugation involves the participation of both substituents; according to Furukawa et al.,[150] the conjugation energy, the amount in excess of the energy yielded by the interaction with each substituent separately (this is ~5 kcal mol^{-1} for $PhNO_2$ and ~8 kcal mol^{-1} for $PhNH_2$), is approximately 2 kcal mol^{-1}.

This interpretation has been rejected in a number of investigations;[46,151,152] it is believed[151] that the nitro-group is subjected to the inductive influence by the excess negative charge (about 0.06) generated on an adjacent carbon atom as a result of the influence of the amino-group, i. e. as a result of $n-\pi$ conjugation:



In certain other studies, the decrease in the basicity of the amino-group was considered and it was attributed to the interaction of the substituents in the cation, and not in the initial nitroaniline molecule, or to the influence of solvation.

The set of experimental data is not fully consistent with these conclusions. It is sufficient to state that the displacement of the nitro-group (as well as R_2N-) from the molecular plane weakens the signs of the interaction of the substituents.[32] These signs include the high intensity of the long-wavelength and charge-transfer absorption bands (~3000 Å), the shortening of the $C_{arom}-N$ bonds,[149,152] the fairly appreciable energy barrier hindering the free rotation of the nitro-group, the predominant influence of the amino-group on the frequencies ω_{as} of the antisymmetric vibration of the nitro-group (more local, with small involvement of the C–NO_2 bond), the influence of the latter on the NH_2 frequencies, the anomalously large molecular dipole moment, the high intensity of the IR bands due to the symmetrical vibrations of NO_2 and NH_2 (much greater than for the monosubstituted benzene derivatives), which can be interpreted as an indication of the migration of electron density during the atomic vibrations to the region of the conjugation system, and the fairly high absorption intensity due to the antisymmetric vibration, indicating an appreciably greater polarity of the N–O bonds[153] (whereas in the $H_2N-\Phi-CH=CH_2$ and similar molecules the substituents hardly influence one another). As regards solvation, its influence on different signs of conjugation and on the electron-donating capacity of the amino-group is very appreciable (for example, see Refs. 154 and 155), but is nevertheless of secondary importance; the clear non-additivity of the influence of the substituents on the spectra of isolated molecules has been established experimentally (see Table 3 and also Refs. 154, 156, and many others).

‡The symbol D → A should not be accepted literally; the redistribution of electron density involves to some extent also the atoms of the intervening chain.

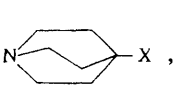
Whereas in the case of *p*-nitroaniline there are still some grounds for considering the structure of the quinonoid type (see above), in the presence of a longer intervening chain of π-bonds this becomes completely unjustified; the smoothing of the bond alternation induced by the substituents in the intervening poly-yne or polyene system is known to be observed only in the vicinity of substituents.

As the intervening subsystem lengthens, the D → A transfer of electron density diminishes, but, despite this the deviations from additivity in the dipole moments ($\Delta\mu$) increase owing to the increase in the effective length of the dipole. Thus $\Delta\mu$ = 0.6 D for R_2N-CHO, while in $R_2N-(CH=CH)_4CHO$ $\Delta\mu$ reaches 5 D.[52]

The changes in the force constant *K* (rigidity) of the π-bond in the group A can be traced in relation to nitro-compounds. According to experimental data, *K*(N–O) is reduced owing to the influence of the amino-group by more than 8% in the R_2N-NO_2 molecule, by approximately 3% in the $R_2N-\Phi-NO_2$ molecule, and by less than 0.5% in a system of the type $R_2N-\Phi-C\equiv C-\Phi-NO_2$.

In the presence of even longer chains of carbon–carbon π-bonds, the influence on the rigidity of the N–O bonds (and also the changes in the basicity of the amino-group itself under the influence of the nitro-group) are no longer susceptible to observation, but the non-additivity of the influence of substituents on certain optical properties actually becomes even more explicit. This is apparently associated with the fact that the absorption bands (electronic transitions) appear in the long-wavelength region, which is readily accessible to observation; they affect the colour and make a particularly large contribution to the electronic polarisability of the molecule (and also to the intensity of the Raman lines—some of them are more intense by a factor of 100–1000 than for nitrobenzene). However, the additional bathochromic shifts of the UV absorption bands following the increase in the length of the intervening chain by one unit gradually diminish. Thus the different properties respond in different ways to the lengthening of the chain, but these differences have a completely definite physical basis.

We shall now turn our attention to compounds of the type $D-CH_2-A$ and the entire set of data in Table 3. Despite the heterogeneity of the parameters listed there, which in general bear little relation to one another, one may note certain features common to them. Thus, the non-additivity in the influence of heterotypical atomic groups, where the electron-donating amino-group is coupled to the electron-accepting group X in one way or another, is most marked in almost all cases. Among electron-accepting groups, the nitro-group is outstanding, which can be accounted for by the lower position of its π* orbital (Fig. 6). On the other hand, a qualitative similarity may be seen in many aspects of the influence of the substituent X in the series of compounds R_2NX, R_2N-CH_2X, $R_2N-\Phi-X$, and 4-X-quinuclidine. Such similarity apparently extends to a significant degree also to systems consisting of D–Y and A–Y molecules in close proximity. Contrary to expectation, some of these parameters differ little in the above series (ΔP_1), others are weakened (EPE, PA, $\Delta\omega_X$), while some parameters are actually strengthened ($\Delta\mu$). Furthermore, in compounds of types *a*, *b*, and *c* the π-acceptor and π-donor substituents X influence the parameters associated with the amino-group—P_1 and the rigidity of the N–H bonds[126]—(as well as the dissociation constants of the acids $X-\Phi-COOH$) in opposite directions, while in the quinuclidine derivatives



they exert their influence in the same direction; this agrees with the fact that the values of $\Delta\chi$, which are very close to the characteristics of the σ-donor–acceptor capacities of the substituents, have the same sign for all the groups X considered (cf. the values of σ_{para}).

The similarity in the manifestations of the intramolecular interaction in the R_2N-CH_2-A and $R_2N-\Phi-A$ molecules does not imply identity of the mechanisms; one may say that the group A = CN, NO_2, Cl, or F (but not COR [157,158]) in the compounds R_2N-CH_2-A acts as a σ-acceptor, while in aromatic nitriles and nitro-compounds it acts as a π-acceptor:

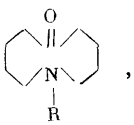


The influence of the σ-acceptor properties of the above groups has been described as a tendency to assume an electronic structure of the type $R_2\overset{+}{N}=CH_2A^-$.[128,157] The shortening of the bond with the amino-group and the lengthening of the $C-NO_2$ bond, which follows from non-empirical calculations[159] for $H_2N-CH_2-NO_2$, is consistent with this; similar results have been obtained for H_2N-CH_2-Cl.[128]

The similarity noted above does not extend to UV spectra. The point is that in aromatic compounds the combination of the groups D and A promotes an intense absorption in the long-wavelength region where the band involving an element of the D → A charge transfer but also with an appreciable participation of the benzene ring is located (see the molecular orbital in Fig. 6 of Ref. 160). In the observed long-wavelength part of the absorption spectrum of R_2N-CH_2-CN, the contribution of the amino-group predominates; the electron-acceptor group promotes the stabilisation of the lone pair orbital and the zone of intense absorption moves away into the region of 1800 Å (see Figs. 1 and 2 in Ref.157). This example indicates the necessity to study and to interpret fully the bands over a wider region in the spectrum.

The quantitative conclusions which might be drawn from the entire data obtained require more detailed calculations. One has to bear in mind that in reality the structures of the molecular orbitals, for brevity referred to as lone pair orbitals, differ greatly in the compounds being compared; the description of the principal trends depends to a considerable extent on the choice of the reference standard (in Table 3, this is X = H); there is no certainty that the dominant conformations in compounds R_2N-CH_2-X are isotypical. Finally, the data for diamines, and in the first place for hydrazines, are not treated unambiguously. The question arises how the group $X=NR_2$ in these compounds influences the other amino-group. Here $\Delta P_1 = -0.65$ eV, while $\Delta P_2 = -0.15$ eV, but both P_1 and P_2 characterise not one amino-group but the set of two such groups and, in considering the processes involving one-amino-group, it is therefore better to employ the average (−0.4 eV). In this case, both variants yield a negative sign but in diazaadamantane with the N–C–N system analogous variants give rise to different signs; thus, in describing different processes, even qualitative differences may appear in estimates of the influence of intramolecular interaction.

Table 3 may be supplemented by data for molecules in which the groups A and D are located in such a way that they can interact appreciably through the intervening free space; the transannular interaction in atranes and in various cyclic and polycyclic bifunctional compounds in which the active centres are fixed at a comparatively short distance from one another by a rigid skeleton of chemical bonds which does not itself participate in the conjugation has long been known. The aminoketone



may serve as an example.

Despite its unusual structure, in terms of the value of ΔP_1 it differs little from other ketones included in Table 3, while in terms of $\Delta\omega_{C-O}$ it is actually superior to some of them.

It is even more useful to compare a molecule of the type D–M–A with a set of two molecules one of which includes the group A and the other the group D. In an experiment, it is possible to immobilise an AX + DY pair of this kind by a solid inert matrix (for example, argon). It is easy to imagine that, after the formation of the AX + DY system, there is a possibility of its further evolution involving several stages with the modification of the wave functions and hence of the electronic structure. Under suitable conditions, one of the stages may be the electron transfer D → A. The knowledge of the characteristic features of the generation of the potential within the limits of the entire system (AX + DY or D–M–A) and of the parameters of all types of relaxation facilitates the selection of the molecular structure of a compound or complex to be used in "submicroelectronic" devices. The symbolic representation of one of the simplest elements of such a device, incorporating one molecule of the type D–M–A, is presented in Fig. 7; the possibility of creating controllable elements has been described.[17,18,161]

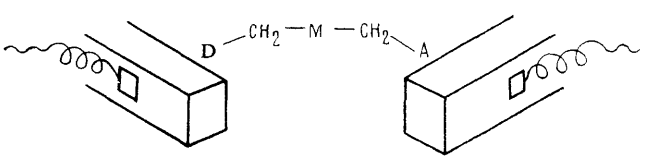


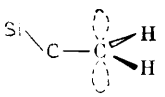
Figure 7. Model of an element in the microprocessor technique incorporating one molecule of the D–M–A type.

The study of the functions of D–M–A systems is of fundamental importance for the understanding of the mechanisms of many most important chemical, physical, and physiological processes.

XI. Conjugation in molecules of allylic compounds

The bond systems separated by the methylene bridge have been attracting increasing attention recently. It has become evident that the usual ideas about the weakness of the interaction between the subsystems cannot be extended to all molecules with a methylene

bridge; the manifestations of non-additivity are much more striking in certain cases than, say, in butadiene. We may refer to the examples of the solvolysis of derivatives of pentacyclononyl nitrobenzoate: under the influence of certain hydrocarbon substituents of low polarity, extending through two–three C–C σ-bonds, the rate of reaction increases by a factor of $10^{12}-10^{14}$.[162] Even more interesting examples may be quoted if one turns to ions, radicals, and electronically excited molecules, while the conjugation energy may prove to be an order of magnitude higher than in dienes. Thus such energy in the 3-silapropyl cation in the optimum conformation



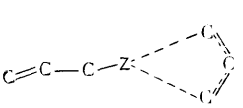
exceeds 25 kcal mol^{-1}.[163]

Allylic, benzyl, and similar compounds of heavy elements have attracted attention.[53,101,107,164–169] It was necessary to establish the principal features of their structure and, as far as possible, to find answers to the following questions:

1. What determines the tendency towards the formation of π-complexes or σ-structures?
2. How do the manifestations of conjugation in σ-structures depend on the nature of the heteroatom and of its valence state and also on the conformation of the molecule?
3. What is the mechanism of this interaction?
4. How are relativistic effects reflected in the signs of conjugation?
5. Do the unshared electron pairs of the heteroatom contribute to conjugation?
6. How are the manifestations of conjugation in the electronic and vibrational spectra and the redistribution of electron density between the fragments of the molecule interrelated?

As regards the first question, one should note in the first place that in allylic compounds different structural variants may occur depending on the nature of the heteroatom and the types and positions of the substituents. These variants include symmetrical π-complexes (characteristic of transition metal and alkali metal compounds), slightly or appreciably asymmetric systems, and, finally, typical σ-allylic structures which will in fact be the subject of our attention.

In contrast to π-complexes, in the σ-allylic structures there is a fairly strong σ-bond between the heteroatom and one of the terminal carbon atoms and only weak or negligible overlap of the atomic orbitals of the heteroatom and other carbon atoms. In individual instances, it has been suggested that there is an equilibrium between the σ-allylic form and the π-complex.[170–172] In complex molecules, one cannot rule out the participation of one heteroatom simultaneously in bonds of two types—characteristic of π- and σ-structures:



The study of the reactivity of a series of σ-allylic systems led to the concept of σ–π conjugation,[101] which can be described, in terms of LCBO, as the mixing of orbitals localised on bonds—the C–Z σ orbitals and the C=C π orbitals. Subsequently spectroscopic studies on the compounds $\Pi-CH_2-ZY_n$ with the atoms Z belonging to different Groups in the Periodic System led to the conclusion that compounds of heavy elements and the elements in the first Groups have specific features.[53,107,164] Manifestations of conjugation clearly occur in these compounds. These include, in particular, the deepening of the colour,[160,164] an increase in electronic polarisability, a sharp increase in the intensity of the Raman lines of the π-bonds,[32,53,165] and specific changes in reactivity;[21,101,173,174] a decrease in the heat of hydrogenation of the double bond (by 1–10 kcal mol^{-1}), a decrease in the vibration frequency and rigidity of the C=C bond, and, in certain cases, a slight smoothing of the differences between the C–C and C=C bond lengths (complete equalisation occurs in symmetrical π-complexes).

The mixing of the above π and σ orbitals (with the corresponding delocalisation) leads to the expansion of the energy gap between them and to the destabilisation of the highest occupied molecular orbital (HOMO). These features are more marked the closer are the energies of the initial orbitals and the greater their overlap or, more aptly, the greater the integral $<\sigma|V|\pi>$ (see the formula in Section II). The overlap depends comparatively little (±30%) on the type of heteroatom Z, but depends greatly on the conformation, being a maximum for the *gauche*-conformers. In planar forms, the mixing is minimal and the sets of frontier molecular orbitals of the compounds $AllZR_n$ can be regarded, without stretching things too much, as a set of several modified molecular orbitals of propene (π and π*) and the compounds ZR_m (σ orbitals, including the C–Z bond, the *n* orbitals of the Z atom, etc.).

Several examples in Fig. 8 provide a qualitative idea about the possibilities in the mixing of the orbitals of fragments adjoining the methylene bridge and combination of various substituent groups ZR_n and the simplest π-subsystems. Each column indicates the corresponding Z atom. The continuous sections of the horizontal straight lines represent the position on the energy scale of the π molecular orbitals of propene and $R_3C-CO-R$ and the σ molecular orbitals of the ZR_m molecules, which simulate the molecular fragments of $All-ZR_n$ and $R_3C-CO-CH_2-ZR_n$ in the absence of conjugation. The divided sections correspond to the orbitals of some of the compounds $R-ZH_3$; their positions explain the causes of the possible differences between the conjugation conditions in the $AllZR_n$ and $AllZH_n$ molecules. The divided sections of the horizontal straight lines correspond to tentative estimates. The dotted lines join isotypical molecular orbitals. The wavy lines correspond to orbitals of the model in which the contribution of the relativistic effects is not included.[57]

In setting up a molecular orbital scheme, photoelectron and electron-transmission spectroscopic data[72,77,90–92] as well as the results of MNDO calculations[57,175,176] were resorted to. Unfortunately, this method does not take into account the Rydberg atomic orbitals and yields incomplete and insufficiently reliable data for the unoccupied orbitals. Nevertheless the major role of Rydberg transitions has been noted in the UV spectra of many organic compounds;[73,98,100,147] thus the long-wavelength electronic transition in SnR_4 is associated with the involvement of the 6*s* and 6*p* atomic orbitals of tin.

The vertical arrows in Fig. 8 show in relation to Si, Sn, P, and As compounds how the positions of the molecular orbitals change on passing from non-interacting fragments to the *gauche*-conformers of C=C–C–Z and O=C–C–Z. To a first approximation, these changes can be identified with the shift in the *trans* → *gauche* transition induced mainly by conjugation (although delocalisation of the orbitals and small shifts on the energy scale occur also in planar

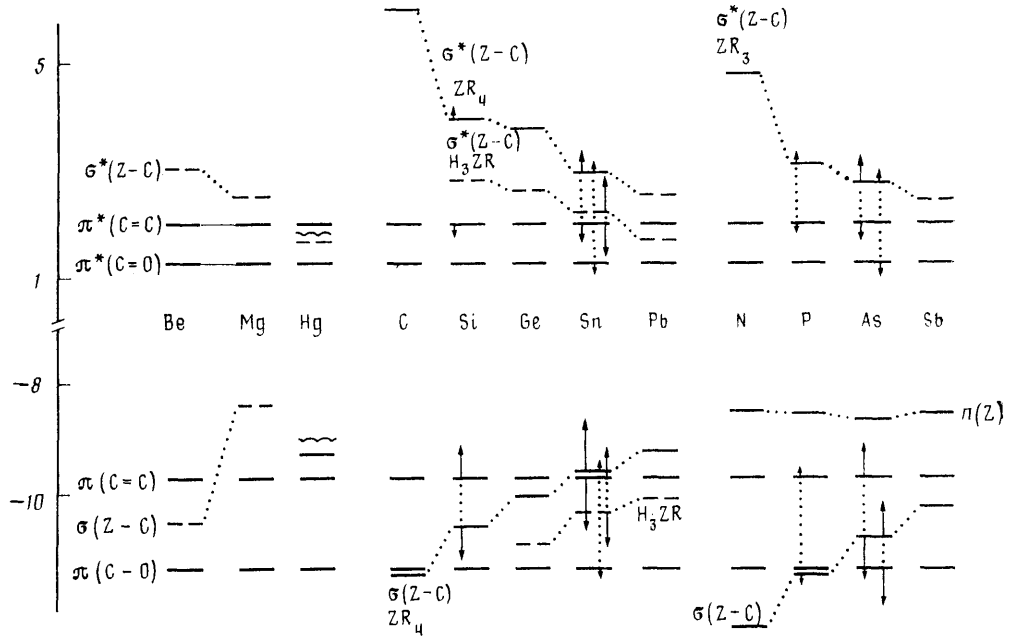


Figure 8. Schematic arrangement of the C=C and C=O π orbitals as well as orbitals associated primarily with the Z−C bonds in the ZR_m molecules; the proximity of the σ and π orbitals favours their mixing in the *gauche*-conformers of the $\Pi-CH_2-ZR_n$ molecules.

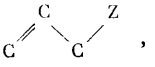
conformers). Changes of this kind in the B, C, N, and O compounds are slight but in allylic compounds of heavy elements, where the $E_\pi - E_\sigma$ energy gap is smaller, they become more significant.[57,107,175] They are accompanied by explicit changes in the UV absorption spectra;[160,164] the delocalisation of the occupied molecular orbitals in the non-planar conformers is then responsible for the intensification and the mutual approach of the frontier orbitals gives rise to the bathochromic shift of the absorption bands conventionally designated as $\pi \rightarrow \sigma^*$ bands, which can thus come to the fore.

More comprehensive information about allylic compounds is provided by Table 4. The figures quoted there show how much the following quantities *diminish* on passing from propene and ZR_m to the compounds $All-ZR_n$: (1) the first ionisation potential P_1 (which refers in addition to the lone pair of the Z atom):[39,72,77] (2) the wavelength λ of the first intense UV absorption band of the solutions in heptane (bold type):[32,73,92,164] (3) the stretching vibration frequency $\omega_{C=C}$.[32,78,160] The initial data for propene are as follows: $P_1 = 9.8$ eV, $\Delta P_1 = 0$, $\lambda = 180$ nm, $\Delta\lambda = 0$, $\omega = 1645$ cm^{-1}, and $\Delta\omega = 0$. Under the experimental conditions, the *gauche*-conformer predominated in most cases, which intensified the signs of conjugation. Approximate estimates based on analogies or on approximate quantum-chemical calculations, which are suitable only for qualitative inferences, are given in Table 4 in brackets; they correspond to the *gauche*-conformations.

The decrease in the ionisation potential (ΔP_1) characterises the destabilisation of the HOMO on passing from non-interacting fragments (simulated by the ZR_m and propene molecules) to the real $C=C-C-ZR_n$ system with orbitals of the mixed π/σ type. In those cases where the σ molecular orbital of ZR_m lies above the π molecular orbital of propene and makes a dominant contribution to the HOMO of $AllZR_n$, the ΔP_1 readings are begun from this orbital; the corresponding numbers in Table 4 are designated by the letter σ. In one way or another, the quantity ΔP_1 reflects the dominant influence of conjugation; in the majority of compounds, it is very close to the value which would have been observed in the conformational *trans* → *gauche* transition. The latter has been confirmed indirectly by the approximate constancy of E_π for the *trans*-conformer. However, among the compounds of certain elements (especially Li, F, and Cl), there is no such constancy; here the influence of the differences between the potential fields in the region of the heteroatom, which is usually regarded as the inductive effect, operates.

The shift of the UV band ($\Delta\lambda$) is in all cases determined relative to propene. In compounds of the Second Period *p* elements, this is a $\pi \rightarrow \pi^*$ transition, while in compounds of heavy elements it is a transition with participation of a molecular orbital to which the atomic orbitals of the heteroatom make an appreciable contribution; the involvement of the Rydberg states is then entirely probable (see above).

In interpreting the values of $\Delta\omega$ quoted above, one should bear in mind that in other structures, where the subsystem



is coplanar and there is no conjugation-induced decrease in the rigidity of the double bond but the influence of the greater mass of the heteroatom remains, the difference $\Delta\omega$ proved to be smaller by a factor of 2−3,[165] i.e. is relatively insignificant.

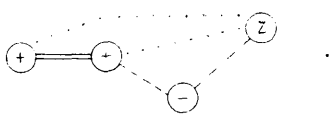
Table 4. The decrease in the first ionisation potential (ΔP_1, eV), the wavelength of the UV absorption band ($\Delta\lambda$, nm), and the C=C stretching vibration frequency ($\Delta\omega_{C=C}$, cm^{-1}) on transition from C=C−C to C=C−C−ZR_n.*

				Be (0.5) — —	B 0.1 5 9	C 0.2 0 0	N −0.2 2 3	O −0.2 5 2	F −0.7 0 −6
				Mg (0.4σ) — (60)	Al (1.0σ) — 15	Si 0.8 15 13	P 0.2 — 8	S −0.2 20 5	Cl −0.6 6 2
Ti (0.9σ) — 47	V — — —	Mn — — 25	Ni — — (40)	Zn 0.9σ — 25	Ga (1.0σ) — (20)	Ge 0.9 20 13	As 0.5 25 10	Se −0.1 20 8	Br −0.4 12 7
Zr — — 50	Nb — — (37)	Tc — — —	Pd — — (50)	Cd — — (30)	In (0.4σ) — —	Sn 1.2σ 30 18	Sb (0.7) — 15	Te 0 40 17	I 0 20 15
Hf 1.1σ — 42	Ta^V — — (30)	Re — — 27	Pt — — (32)	Hg 0.9σ 50 20	Tl — — —	Pb (0.8σ) — —			

* Under the symbol of each element, the first, second, and third rows indicate ΔP_1, $\Delta\lambda$, and $\Delta\omega_{C=C}$ respectively.

It is seen from Tables 1 and 4 and Fig. 8 that there is some correspondence between the spectra of the compounds ZR_m and $AllZR_n$; when Z is varied along the Periodic System from above downwards and from right to left, the above signs of conjugation in allylic compounds in general become more marked (cf. the data in Section V). In compounds of the heaviest elements, this tendency becomes less marked partly owing to the contribution of the relativistic effects.[57,177] The energy of the σ orbitals is then very important. Fig. 8 shows that, when Z varies within one subgroup of the elements from above downwards, the σ molecular orbitals of the compounds ZR_m are located in an increasingly higher position and thus the energy gap $E_\pi - E_\sigma$ narrows (which favours the π/σ mixing), but subsequently, when the σ molecular orbital lies above the π molecular orbital and the gap actually begins to widen, the π/σ mixing should weaken (but with a further increase in the bathochromic shift of the UV absorption band). Such changes in the occupied and unoccupied molecular orbitals are by no means "synchronous". The mixing of the *n* and π orbitals is in this case very slight (in contrast to the $\Pi-ZR_n$ system where there is no bridging group).

The mechanism of conjugation in σ-allylic compounds can be elucidated by using a scheme simplified to the maximum extent:

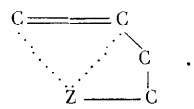


Here the four carbon atoms of the main chain $C_\gamma=C_\beta-C_\alpha-Z$ are represented by circles; the lines between the circles symbolise the interaction of the atomic orbitals in pairs. The symbols (+) and (−) denote the signs of the contribution of the $2p_x$ atomic orbitals of the three carbon atoms to the HOMO, whose structure is close to the π orbital of ethylene§ but which includes in addition a small contribution by the $2p_x$ atomic orbital of the bridging C_α atom. If this atomic orbital has in addition a non-zero population of the overlap with the orbitals of the heteroatom Z (which happens in non-planar conformers), then conditions are created for the formation of delocalised molecular orbitals incorporating the entire C=C−C−Z system. One may say that the conformation of the system determines the overlap population mentioned above and transition to compounds of heavy elements implies a higher (and close to the π orbital) position on the energy scale of the σ orbital of the C−Z type, which favours the π/σ mixing. In conformity with the above (by no means complete) scheme, the atomic orbitals of the heteroatom Z can, at least in non-planar conformers, become mixed with the π molecular orbital as a result of overlap (1) with the $2p_x$ atomic orbitals of C_β and C_γ (interaction through space denoted by dotted lines) and (2) with the $2p_x$ atomic orbital of C_α (interaction through a bridge or, in other words, there is a bond between the fragments formed as a result of the simultaneous overlap of the $2p_x$ atomic orbitals of the bridging C_α atom with the orbitals of X and C=C). Generally speaking, each of these two channels separately might promote the destabilisation of the HOMO and a decrease in the first ionisation potential; in the case considered, the contributions of these channels have different signs and one cannot therefore rule out the possibility of their "annihilation" (as in certain dienes[178]). Which of these two channels predominates depends, generally speaking, on the nature of the heteroatom, the bridging group, and the π- bond and also on the molecular conformation and on the structure of specific orbitals. The mixing of different orbitals of the two active centres can be determined by different channels; thus one cannot rule out the possibility that the highest occupied orbitals of the fragments are mixed via one channel, while the unoccupied one are mixed via another.

According to calculations,[57,107,176] the interaction through a bridge predominates markedly in the majority of σ-allylic compounds of *p* elements; it in fact determines the destabilisation of the HOMO (by as much as 1−1.5 eV). The specific features of the conformation then have an effect mainly through the overlap population of the $2p_x$ atomic orbital of the C_α atom and the orbitals of the Z atom (although the latter makes only a small contribution to the formation of the C−Z chemical bond). The interaction through space in such molecules is altogether insignificant. However, the more diffuse atomic orbitals of the heteroatom, for example, the *s* atomic orbitals of the alkali metals can, like the *d* orbitals of transition metals, overlap effectively with the atomic orbitals of all three carbon atoms; under these conditions, π complexes are formed readily and in relation to such complexes it is more appropriate to speak not of interaction through space but of chemical bonds with the heteroatom. The involvement of the $d-\pi$ overlap the σ-allylic compound of rhenium is represented in Fig. 9 after Bodner et al.[179] In any case, the presence of two−three methylene groups instead of one weakens the interaction through the bridge system and facilitates the mutual approach of the heteroatom

§ The cartesian *x* axis is perpendicular to the  plane; the Z atom lies outside this plane.

and the double bond in space, creating additional possibilities for interaction through space:



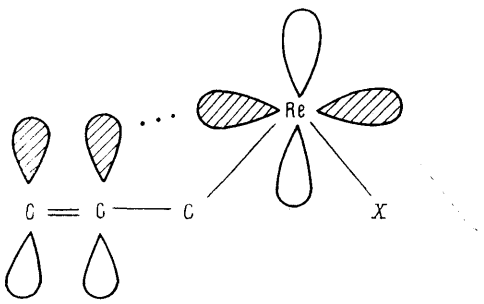


Figure 9. Involvement of the *d* atomic orbitals of rhenium in conjugation.[179]

The question arises of the correspondence between the above conclusions concerning the conjugation mechanism, based on the consideration of delocalised molecular orbitals, and the known ideas about $\sigma-\pi$ conjugation as a consequence of the overlap of the C=C π orbital and the C–Z σ orbital constructed from hybridised atomic orbitals and located in bonds. The electron density on the localised σ orbital is generated by several delocalised σ molecular orbitals, but in our case only one of them (the highest occupied σ molecular orbital) interacts with the π orbital, since the energies of the remaining orbitals differ markedly from that of the π orbital. Thus "conjugation with the σ-bond" can be interpreted as the participation of this particular "component" (by no means localised in the one σ-bond considered and not playing the principal role in the formation of the $C_\alpha-Z$ chemical bond). On the other hand, one may say that, for the description of the influence of conjugation on the parameters of an individual chemical bond (for example, on the force constant), the system of localised orbitals is more or less suitable but for the description of the electronic absorption spectra and various "one-electron" properties it is more convenient to resort to delocalised molecular orbitals.

By virtue of the influence of steric factors and conjugation, the *gauche*-conformation is more favourable on energy grounds for the majority of σ-allylic compounds (in contrast to $\pi-\pi$ conjugation systems). The conjugation energy, which is related to the weak interaction of the frontier orbitals having markedly different energies, is then low in the electronic ground state (<3 kcal mol^{-1}).[166,180] It proves to be somewhat greater for compounds of heavy elements, although the changes in the energy of the electrons occupying the π and σ molecular orbitals occurring under these conditions in the *s-trans* → *gauche* transition to some extent cancel out; however, after the transition of the molecule to the first electronically excited ($\pi \rightarrow \sigma^*$) or ionised state, such cancelling does not occur and the dependence of the energy of the molecule on the conformation should be appreciable[174] (see Fig. 10 and also Fig. 3 in the paper of Shorygin et al.[164]). The results of changes in the energies of the HOMO and LUMO not only do not cancel out but are actually added together if one considers the shift of the long-wavelength absorption band. Thus conjugation has little effect on the energy of an unexcited neutral molecule, has a greater effect on the ionisation potentials and electron affinities, and has a strong effect on the UV absorption spectrum.

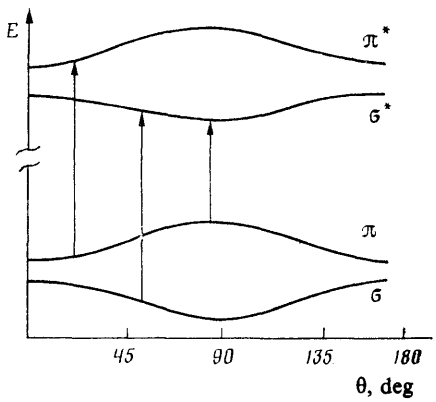


Figure 10. The energies of the σ and π orbitals of $XHg-CH_2-CH=CH_2$ for different conformations;[175] the arrows denote the types of allowed electronic transitions.

According to calculations,[166,167,175,176] the redistribution of electron density between the heteroatom and the vinyl group in the allylic compounds of the majority of *p* elements is insignificant and is almost independent of the conformations; the influence of the heteroatom on the charge of the C_γ atom, which varies within the range ± 0.03 e, is more instructive in this instance.

The redistribution of electron density on the atoms of the main chain in allyl fluoride and the hypothetical model of σ-allyl-lithium is more appreciable and can be represented by the following symbolic scheme for the *gauche*-conformers:[57,176]

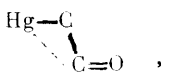
$$\overset{0.05}{C}=\overset{0.25}{C}-C-F, \quad \overset{0.1}{C}=\overset{0.4}{C}-C-Li \;(0.1), \quad \overset{0.2}{C}=\overset{0.1}{C}-\overset{0.5}{C}-Li.$$

In precisely these two extreme cases, the results resemble the situation which may be expected on the basis of ideas concerning the inductive influence of strongly polar C–Z bonds. However, the inclusion in the scheme of two equally important variants (out of the multiplicity of the possible ones) for allyl-lithium is sufficient to draw ones attention to the ambiguity of the treatment. The latter appears even less satisfactory in view of the considerable decrease in the redistribution of charges in the planar conformers of both compounds. In any case, the estimation of the involvement of individual molecular orbitals and of the distribution of electron density in space in different conformers leads to a completely valid description of the entire picture.

On considering a wider range of allylic compounds, one may say that the low electronegativity of the $-ZR_n$ group in general favours the transfer of electron density—predominantly to the bridging carbon atom in the σ-allylic forms and to the terminal carbon atoms in π-complexes. If such a group is called a σ-donor, then the $-CH_2-ZR_n$ group can be regarded as a π-donor. Accordingly, the σ_{para} Hammett constant, for example of the $-CH_2-SnR_3$ group, is −0.35 whereas that for the $-SnR_3$ group is close to zero;[127] the data are even more striking for the mercury and lead compounds.

Most of the conclusions about allylic compounds can be extended by benzyl, indenyl, and other systems of a similar type. The question arises whether they can be extended also to the compounds R_nZ-CH_2-A incorporating a π-acceptor A, for example, CN, COR, and NO_2. The data for the amines R_2N-CH_2-A have already been considered in Section X. Heavy atoms Z with a low electronegativity promote in this instance to a somewhat greater extent than in allylic compounds a decrease in the rigidity of the π-bond, the enhancement of other signs of σ−π conjugation, and the "metal atom → terminal atom of the π-bond" charge transfer (see the spectra of carbonyl compounds[44,124,158,160,164,165,181] and nitriles[124,157,182]).

We shall consider as an example the XHg−C−C=O bond system. According to approximate quantum-chemical calculations,[183] the Hg → O charge transfer in the planar conformer should be approximately 0.02; when coplanarity breaks down, an additional conjugation-related change in the atomic charges (up to 0.02) and bond orders (up to 1−2%) and very weak bonding



(designated by dashed lines) are observed. However, the description of these small changes as a certain trend towards the structure $X-\overset{+}{H}gC=C-\overline{O}$ (similar to that in the paper of Guerrero et al.[44]) can be resorted to only in a qualitative consideration. Conjugation favours in this instance the predominance of the *gauche*-conformers and accordingly a more explicit non-additivity in the generation of the UV absorption spectrum (Fig. 11) and a decrease in the C=O frequency.[181]

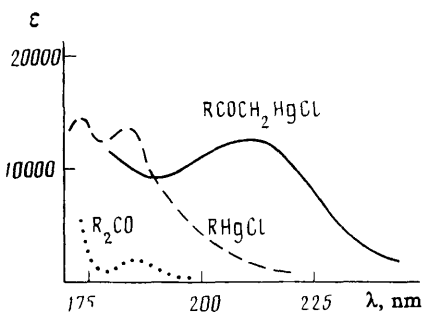


Figure 11. Signs of non-additivity in the UV absorption spectrum of $RCOCH_2HgCl$; the absorption band type is close to $\pi \rightarrow \sigma^*$.[180]

In compounds with the oxygen bridge, X−O−COR, the C=O frequency is much more sensitive to changes in the structure of X than in compounds with the CH_2, NH, S, and Φ bridges. Thus in the series of compounds $R_nZ-O-COR$ it varies within the range from 1785 cm^{-1} for Z = O to 1645 for Z = Sb^{III}, 1620 cm^{-1} for Z = Pb, and 1560 cm^{-1} for the anion $(OCOR)^-$.[181] Here we have a combination of $n-\pi$ conjugation in the O−COR subsystem, which is promoted by coplanarity, and σ−π conjugation, which is promoted by the breakdown of coplanarity. The correspondence between the electronegativity of the group ZR_n and the influence of the latter on ω_{C-O} is by no means always complete under these conditions.[184] It has also not been noted on comparing the A−M−Sb^{III} and A−M−Sb^V subsystems: judging from the data of Epstein et al.,[185] the M−Sb^V fragment is much more active as part of the conjugation system and a π-donor (while the −M−Au subsystem is more active than −M−Hg [186]). Interesting data for aromatic compounds with −O− and −NH− bridges can also be found in the communications of Chuvashev et al.[187] and Pozdnyakov et al.[188]

As already noted in Sections X and XI, the entire set of data obtained creates a basis for the interpretation of the characteristic features and the mechanism of the mutual influence of atomic groups separated by a bridging group (X−M−Y); it gives rise to additional possibilities for inferences about conjugation in electronically excited ionised states and the relative stabilities of σ-structures and π-complexes. The influence of substituents through a bridging group is of primary importance for the physical and chemical properties of many organic compounds; in many cases, it proves to be even greater than in the X−Y systems.

XII. Conclusion

The determination of the mechanism and of the characteristic features of the mutual influence of atomic groups forms part of the range of fundamental problems of organic chemistry. It leads ultimately to a more compact description of the enormous, almost unencompassable experimental data and hence to an improvement of its employment and to an increase in the productivity of the work of investigators endeavouring to obtain compounds with the required properties.

The mutual influence of functional groups is manifested by a complex set of heterogeneous signs of non-additivity; these signs are not linked by simple and universal correlations; it is sufficient to say that a change in the structure of the interface sometimes enhances and sometimes weakens other signs of conjugation. Under these conditions, the determination of at least the general trends, wherever this is possible, is already a useful step and facilitates further research.

The schemes for the differentiation of different forms of intramolecular interaction, including conjugation and the inductive effect, used in the literature are conventional in character and at the same time far from uniform, which very greatly complicates comparison of the conclusions of different workers. Calculations of the contribution by the inductive effect in the study of the interaction of the active centres of molecules is frequently based on estimates of the dielectric constant ε of the intervening medium, which is regarded as a kind of "black box". The adjustment or selection of ε in the range from 1 to ∞ and the use of the simple Coulomb law reveal the lack of validity of the method.

Almost all the most important features of the physical, chemical, and technical properties of organic compounds, including the possibility of the evolution of the state of the molecule in time (migration of the excitation energy or of the electron along the chain of chemical bonds) are associated directly or indirectly with conjugation and other forms of the mutual influence of atomic groups.

All forms of conjugation merit constant attention. The signs of the conjugation of σ-bonds are not an exception in this respect. They are significant even in the molecules of n-alkanes and in certain systems they actually prove more appreciable than in molecules with conjugated π-bonds. However, in view of the exceptionally great variety of the practical applications of organic compounds, it is not surprising that in some cases a strong interaction between the active centres plays an important or decisive role, while in others a weak interaction between such centres assumes this role. The latter factor has come to attract increasing attention in connection with the development of certain new types of study, including the study of the possibilities of using "submicroelectronic" systems for the transformation of information with an exceptionally high packing density, because in this instance one molecule with several active centres can in principle perform the function of a whole unit.

Advances in the experimental technique and in quantum-chemical calculations, the synthesis and study of new previously inaccessible model compounds, and the experience gained in logical analysis and generalisations, have made possible an appreciable advance in the understanding of the most important problems of theoretical organic chemistry, in particular, they have made it possible to characterise the principal aspects of conjugation with participation of heteroatoms from all the Groups of the Periodic System and to estimate at the same time the role of relativistic effects. Despite certain disappointments and a series of difficulties which have arisen at this new level of research, one can undoubtedly count on further rapid progress and the transformation of the science of molecular structure into an active research instrument designed to solve problems in practical chemistry.

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Translated from *Uspekhi Khimii* 60 45–68 (1991) U.D.C. 536.653:547

Thermochemistry of the solvation of organic non-electrolytes

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ABSTRACT. This review surveys experimental data on the thermochemistry of the solvation of organic non-electrolytes. An analysis of the enthalpy of solvation as the sum of the enthalpies of non-specific solvation and of specific interaction is presented. The various methods for isolating the contribution of the enthalpies of the complex formation reactions between the solute and the solvent are examined. The role of the dipole moment of the solute molecule in solvation is analysed in detail.

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I. Introduction

The problem of the thermodynamics of the dissolution and solvation of organic compounds has always aroused the interest of investigators working in various fields of science where the problems of the behaviour of species in a liquid medium were raised. At the present time, the study of this problem is prosecuted in two directions. On the one hand, the "purely solution" problems are solved—for example liquid–vapour and extraction equilibria have been investigated, which is a subject of classical physical chemistry. Extensive experimental and theoretical data have accumulated in this field and generalisations have been made. These have already been reflected in the monographs of Morachevskii and co-workers.[1,2]

The quantitative features relating the thermodynamic parameters of the dissolution and solvation of organic compounds to their structural characteristics as well as the macroscopic properties of the solvents have been studied within the framework of the second aspect of the chemistry of solutions. Studies on these lines have been associated as a rule with the solution of the problem of the influence of the medium on various physicochemical processes.

Abraham and co-workers[3] have worked fruitfully on the analysis of the activity coefficients within the framework of multiparameter correlations with the properties of the medium. As a result of the efforts by Fuchs, Arnett, Krestov, the authors of the present review, as well as other investigators, extensive data have accumulated during the last two decades on the enthalpies of solution and solvation of organic non-electrolytes. It is therefore necessary to survey the existing data and to examine them from a single standpoint. In the present review, this has been done within the framework of the empirical approach developed previously.[4,5]

Problems of the solvation of compounds in binary solvents as well as problems of the thermochemistry of the hydration of organic non-electrolytes are not discussed in the present review. They have been dealt with in the monographs of Krestov and co-workers[6] and Belorusov and Panov.[7] Nor does the present review deal with the theoretical approaches to the analysis of the thermodynamic parameters of solvation, because these problems have already been described in monographs.[8,9]

II. Phenomenological description

The stability of a solute molecule A_i depends on its interaction with the molecules of the surrounding medium, i.e. with solvent molecules and with other solute molecules. Henceforth, we shall discuss only the situation where the interactions between the molecules of the solute A_i in solution have been ruled out. The thermodynamic transfer functions are used to characterise such infinitely dilute solutions. Thus the enthalpy of the transfer of the substance A_i to an infinitely dilute solution ($\Delta H_t^{A_i}$) is equal to the difference between the partial molar enthalpy of the solute A_i in the infinitely dilute solution ($\overline{H}^{A_i}$) and the partial molar enthalpy of A_i in the standard state ($\overline{H}_{st}^{A_i}$):

$$\Delta H_t^{A_i} = \overline{H}_{\infty}^{A_i} - \overline{H}_{st}^{A_i}. \quad (1)$$

If one uses the pure substance (p.s.) A_i at a temperature T and a pressure of 1 atm as the standard state [$H_{st}^{A_i}$ (p.s.)], then the enthalpy of the transfer of A_i to the infinitely dilute solution from this state represents the enthalpy of solution of compound A_i in the solvent S ($\Delta H_s^{A_i/S}$):

$$\Delta H_s^{A_i/S} = \overline{H}_{\infty}^{A_i} - \overline{H}_{st}^{A_i}\,(\text{p.s.}). \quad (2)$$

When the vapour of the pure non-electrolyte, which has the properties of an ideal gas and is at a temperature T and a pressure of 1 atm, is adopted as the standard state [$\overline{H}_{st}^{A_i}$(G)], the enthalpy of transfer represents the enthalpy of solvation of compound A_i in the solvent S ($\Delta H_{solv}^{A_i/S}$) and can be defined as follows:

$$\Delta H_{solv}^{A_i/S} = \overline{H}_{\infty}^{A_i} - \overline{H}_{st}^{A_i}\,(\text{G}). \quad (3)$$

According to Eqns. (2) and (3), the difference between the enthalpies of solution and solvation of compound A_i in the two standard states is in its turn equal to the enthalpy of evaporation of A_i ($\Delta H_{vap}^{A_i}$):

$$\Delta H_s^{A_i/S} - \Delta H_{solv}^{A_i/S} = \overline{H}_{st}^{A_i}(G) - \overline{H}_{st}^{A_i}(p.s.) = \Delta H_{vap}^{A_i}. \quad (4)$$

The enthalpy of transfer from one solvent to another $\{\delta H_s^{A_i}\}_{S_0}^{S}$, with the enthalpy of solution of A_i in the solvent S_0 adopted as the standard state, is also used in studies on the thermochemistry of dissolution and solvation:

$$\{\delta H_s^{A_i}\}_{S_0}^{S} = \Delta H_s^{A_i/S} - \Delta H_s^{A_i/S_0} = \Delta H_{solv}^{A_i/S} - \Delta H_{solv}^{A_i/S_0}. \quad (5)$$

In most cases the enthalpies of solvation of substances are determined from the differences between two experimentally measured quantities: the enthalpy of solution and the enthalpy of evaporation. Recommendations concerning the determination of the enthalpies of solution may be found in original communications, for example that of Izaat et al.[10] The methods used for the measurement, the estimation of errors, and the analysis of the enthalpy of evaporation data have been described in the monograph of Lebedev and Miroshnichenko.[11]

III. Enthalpies of solvation of alkanes in various media

Systems where the solute is an alkane (Y) are relatively simple from the standpoint of the study of the nature of the forces of the intermolecular interaction which determines the solvation of alkanes. Frequent attempts have been made to calculate the enthalpies of solvation of alkanes in different, media representing it in the form of dispersion and induction interactions.[12]

The problem of the study of the thermodynamics of the solvation of alkanes usually reduces in essence to seeking the increment per $-CH_2-$ group.[12–14] This increment is found by determining the slope of the linear relation between the enthalpies of solvation of alkanes in a solvent S and the number of carbon atoms n_C in the molecule of the dissolved alkane.

The influence of the branching of the alkane on the enthalpy of its solvation has been investigated[15] and it has been shown that the enthalpy of solvation of a normal hydrocarbon is greater in absolute magnitude than that of a branched hydrocarbon with the same number of carbon atoms in the molecule. The authors[15] explained this effect by the fact that steric hindrance arises in the interaction of the quaternary carbon atom with solvent molecules.

The dependence of the enthalpies of solution and evaporation of alkanes on their molar volumes [$V_M^{Y_i}$] and molecular refractions

$$[MR^{Y_i} = V_M^{Y}(n^2-1)/(n^2+2)],$$

has been investigated[4,5] and correlations have been established for the enthalpies of solution:

$$\Delta H_s^{Y_i/S} = k_S^{V_M} V_M^{Y_i}, \quad (6)$$

$$\Delta H_s^{Y_i/S} = k^{MR} MR^{Y_i}. \quad (7)$$

The proportionality coefficients $k_S^{V_M}$ and k^{MR} in Eqns. (6) and (7) represent individual characteristics of the solvent and their significance will be revealed below. It is noteworthy that Eqns. (6) and (7) are applicable to liquid alkanes. If the enthalpies of solution of solid alkanes are analysed, then, according to Eqns. (6) and (7), the ratio of the enthalpies of transfer of alkanes is equal to the ratio of their molar volumes and molecular refractions, because the contribution of the enthalpy of fusion of the same substance to the enthalpy of its solution in a series of solvents is constant.

In contrast to the enthalpies of solution, the enthalpies of evaporation of alkanes $\Delta H_{vap}^{Y_i}$ depend significantly on the degree of branching of the carbon skeleton, groups of hydrocarbons with the same degree of branching giving rise to several almost parallel lines on the plot of $\Delta H_{vap}^{Y_i}$ against MR^{Y_i}:[4]

$$\Delta H_{vap}^{Y_i} = a_Y + bMR^{Y_i}, \quad (8)$$

where a_Y is a constant term which depends on the structure of the alkane (kJ mol^{-1}) and b = 1.05 kJ cm^{-3}. For linear alkanes, a_Y = 0.91 ± 0.94 kJ mol^{-1} and for monocyclic hydrocarbons, a_Y = 4.39 ± 0.62 kJ mol^{-1}. the appearance in the alkane molecule of one tertiary or one quaternary carbon atom leads to a decrease in the enthalpy of evaporation by 1.31 ± 0.41 or 4.60 ± 0.93 kJ mol^{-1} respectively compared with the value for the unbranched hydrocarbon with the same number of carbon atoms. Here one should bear in mind that the degree of branching of hydrocarbons hardly alters their molecular refraction.

If Eqns. (4) and (8) are valid, then the enthalpy of solvation of an alkane Y_i in a solvent S is linearly related to the molar refraction of the dissolved hydrocarbon:

$$-\Delta H_{solv}^{Y_i/S} = a_Y + k_S^i MR^{Y_i}. \quad (9)$$

An example of such relations is presented in Fig. 1. The constant term a_Y in Eqn. (9) is almost independent of the type of solvent and is determined solely by the structural characteristics of the dissolved hydrocarbon. The coefficient k_S^i depends on the properties of the solvent and can be estimated from the equation

$$k_S^i = b - k_S^{MR(V_M)}. \quad (10)$$

Fuchs and Stephenson[14] found an empirical relation between the enthalpies of solvation of the methylene group in various solvents and solvent parameters such as the Taft–Kamlert π^* constant and a polarisability [function] $(n^2-1)/(2n^2+1)$:

$$\Delta H_{solv}^{-CH_2-} = -3.68 + 1.61(\pi^*)^2 - 5.99(n^2-1)/(2n^2+1). \quad (11)$$

By adding together several empirical correlations,[7,9,11] it is possible to obtain an expression which permits the estimation of the enthalpy of solvation of any alkane from its molar refraction, structural characteristics (A_Y), and the empirical parameters of the solvents:

$$\Delta H_{solv}^{Y_i/S} = a_Y + \left\{0.79 + 0.347(\pi^*)^2 + 1.29\frac{(n^2-1)}{(2n^2+1)}\right\} MR^{Y_i}. \quad (12)$$

The results presented in Table 1 show that there is agreement between the enthalpies of solvation calculated by Eqn. (12) and the experimental values.

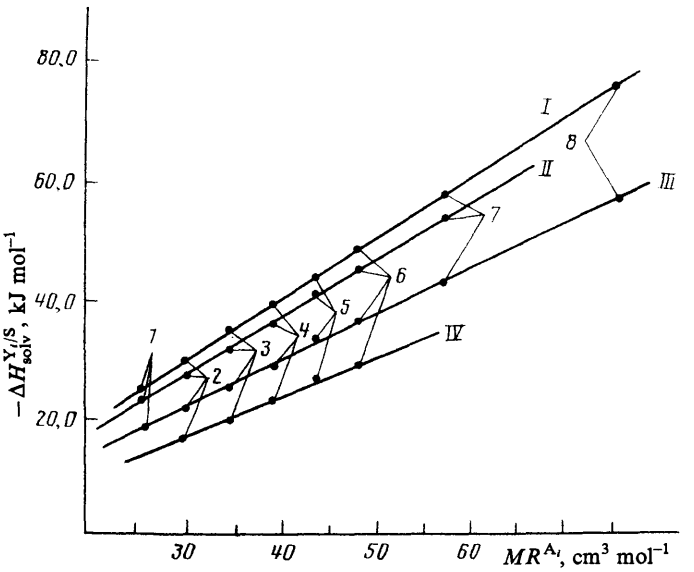


Figure 1. Relation between the enthalpies of solvation of alkanes and their molecular refractions in various solvents; (I) n-heptane; (II) n-butyl chloride; (III) dimethylformamide (DMF); (IV) dimethyl sulphoxide (DMSO). The numbers of the points correspond to the following compounds: *1*, n-pentane; *2*, n-hexane; *3*, n-heptane; *4*, n-octane; *5*, n-nonane; *6*, n-decane; *7*, n-dodecane; *8*, n-hexadecane. The enthalpies of solvation were taken from Fuchs and Stephenson.[14]

The relation obtained by Fuchs and Stephenson[14] is important also for the development of ideas about the solvation of organic compounds of different classes, because many organic compounds contain alkyl groups, the enthalpies of solvation of which enter additively into the enthalpy of solvation of the entire molecule.

The alkane solvation process can be subdivided arbitrarily into two stages:

(1) the creation in the solvent of a cavity whose size corresponds to the dimensions of the dissolved alkane molecule;

(2) the accommodation in this cavity of a molecule of the dissolved alkane and its interaction with solvent molecules.

Hence the enthalpy of solvation of an alkane can be represented by the sum of the enthalpies of formation of the cavity ($\Delta H_{cav}^{Y_i/S}$) and the enthalpy of the interaction of the alkane with the solvent ($\Delta H_{int}^{Y_i/S}$);

$$\Delta H_{solv}^{Y_i/S} = \Delta H_{cav}^{Y_i/S} + \Delta H_{int}^{Y_i/S}. \quad (13)$$

The problem of the subdivision of the solvation energy into the energy of formation of the cavity in the solvent and the energy of the interaction of the solute with the solvent has begun to be studied particularly vigorously during the last decade,[16–23] although this question had been raised already in the 1930's.[24,25] At the present time, there are two methods for calculating the energy of formation of the cavity. One of them is associated with the use of the theory of scaled particles (SPT) developed by Riess et al.[26] Another method for the calculation of the energy of formation of the cavity, based on the use of the concept of surface tension, was proposed by Sinanoglu.[27] It is noteworthy that the application of these methods to the calculation of the energy of the cavity leads to markedly divergent results.[18,19]

Table 1. Experimental enthalpies of solvation (kJ mol^{-1}) of cyclohexane and n-hexane in a series of solvents (298 K) and their values calculated by Eqn. (12).

Solvent	$-\Delta H_{solv}^{C_6H_{12}/S}$		$-\Delta H_{solv}^{C_6H_{14}/S}$	
	experiment	calculation	experiment	calculation
Hexane	32.42	33.06	31.55	30.73
Triethylamine	—	—	31.20	31.14
Dibutyl ether	32.30	32.91	31.22	30.55
Cyclohexane	33.05	33.76	30.43	31.51
1-Octanol	—	—	30.34	30.36
Mesitylene	—	—	30.29	30.64
Carbon tetrachloride	32.34	33.25	29.92	30.93
1-Chlorobutane	—	—	29.54	29.59
2-Propanol	31.05	30.94	29.77	28.46
1,1,1-Trichloroethylene	—	—	29.04	29.17
Toluene	30.75	31.75	29.00	29.33
Chlorobenzene	30.59	30.00	29.04	27.49
Tetrahydrofuran	30.12	30.25	28.24	27.71
1,1,1-Trifluorotoluene	—	—	28.20	27.11
Fluorobenzene	30.00	30.57	28.43	28.06
Cyclohexanone	29.70	28.43	27.16	25.79
1-Butanol	—	—	27.07	29.26
Benzene	29.53	30.39	26.91	28.82
Benzonitrile	28.57	27.06	—	—
Anisole	28.16	29.64	—	—
Methanol	28.11	29.05	25.86	26.42
Acetophenone	27.99	27.13	26.53	24.38
Ethyl acetate	27.94	30.17	26.68	27.63
Nitrobenzene	27.15	25.34	—	—
1,2-Dichloroethane	26.73	27.66	24.20	24.93
1,4-Dioxane	26.48	30.77	24.04	28.54
Dimethylformamide	25.65	26.35	23.64	23.54
Acetonitrile	24.03	25.70	21.13	22.84
Dimethyl sulphoxide	21.67	24.68	18.24	21.74
Nitromethane	20.25	26.24	17.79	23.41

Note. The enthalpies of solvation of the alkanes were taken from Refs.14, 15, and 29.

Attempts have been made to estimate experimentally the energy of formation of the cavity.[15,28–30] This was done most logically in the studies of the present authors and their co-workers.[28,29] The method proposed[28,29] was based on the following assertions: (1) the energy of formation of the cavity depends only on the energy of the solvent–solvent interaction and on the size of the solute molecules; (2) the energy of the interaction of the alkane with the solvent per unit volume of the latter is constant. The validity of the second postulate has been demonstrated in a series of studies.[31–34]

The enthalpy of solution of an alkane Y_i in a solvent S is described by the expression

$$\Delta H_s^{Y_i/S} = \Delta H_{vap}^{Y_i} + \Delta H_{cav}^{Y_i/S} + \Delta H_{int}^{Y_i/S}. \quad (14)$$

Taking into account the postulate that the energy of the interaction of the alkane with different organic non-electrolytic solvents is

constant, the differences between the enthalpies of solution of alkanes in a series of solvents are then determined by the differences between the enthalpies of formation of the cavity in these solvents:

$$(\delta H_s^{Y_i})_{S_h}^{S} = (\delta H_{cav}^{Y_i})_{S_h}^{S}, \quad (15)$$

where S_h is a hypothetical solvent in which the heats of solution of all saturated hydrocarbons are zero. It has been suggested[28,29] that each solvent be characterised by the specific relative enthalpy of formation of the cavity (δh_{cav}^{S}), which is equal to the proportionality coefficient k_S in Eqns. (6) and (7). Knowing k_S and the molecular refraction or molar volume of the substance A_i, it is possible to calculate the relative enthalpy of formation of the cavity generated by A_i in the solvent and to determine the enthalpy of the interaction of the solute with the solvent by an equation analogous to Eqn. (15).

The solvation energy has been represented[35] by three terms; the energy of formation of the cavity, the energy of the interaction of the solute with the solvent, and the energy of the reorganisation of the solvent molecules around the cavity in the solvent. The last term can be regarded as the "response" of the solvent to the replacement in the latter of a hypothetical molecule, not interacting with the solvent, by the real molecule which is capable of entering into various intermolecular interactions of the solvent–solute type.

Kiselev et al.[36] proposed a rigorous axiomatic approach to the consideration of the solvation process, which make it possible to justify theoretically the existing ideas in the literature concerning solvation as a multistage process and to estimate the limits of its applicability.

IV. Enthalpies of solvation of various compounds in alkanes

The thermochemistry of solvation of various compounds in alkanes has been studied in a number of investigations.[31,32,37–49] A universal relation between the enthalpies of solvation of compounds in cyclohexane and their molecular refractions was obtained on the basis of the results. It holds for most varied classes of compounds (Fig. 2). It is noteworthy that Fig. 2 presents data for compounds whose molecules contain an unbranched hydrocarbon skeleton. For cases where the solute molecule has a branched hydrocarbon skeleton, regularities have been found in the deviations from the linear relation between $\Delta H_{solv}^{A_i/S}$ and MR^{A_i}. An attempt has been made[5] to explain the universal relation between the enthalpies of solvation of compounds in cyclohexane and their molecular refractions on the basis of existing ideas about intermolecular interaction. It was verified if the molecular refraction is the only parameter of a substance to which its enthalpy of solvation in an alkane is linked by such a simple relation. For this purpose, correlations were drawn between $\Delta H_{solv}^{A_i/C_6H_{12}}$ and the molar volume ($V_M^{A_i}$), the molar magnetic susceptibility ($\chi_M^{A_i}$), and the surface area (A_W) calculated by Bondi's method:[50]

$$-\Delta H_{solv}^{A_i/C_6H_{12}} = 13.13 + 0.207 V_M^{A_i},$$
$$n = 72,\ r = 0.92,\ S_0 = 26.6;$$

$$-\Delta H_{solv}^{A_i/C_6H_{12}} = 15.21 + 1.995 \chi_M^{A_i},$$
$$n = 41,\ r = 0.95,\ S_0 = 16.4;$$

$$-\Delta H_{solv}^{A_i/C_6H_{12}} = 6.4 + 3.51 A_W,$$
$$n = 74,\ r = 0.80,\ S_0 = 7.99.$$

Comparison of the correlation parameters of the equation shows that the best description of the enthalpies of solvation in an alkane can be obtained with the aid of molecular refraction:

$$-\Delta H_{solv}^{A_i/C_6H_{12}} = 5.09 + 1.03 MR^{A_i}, \quad (16)$$
$$n = 102,\ r = 0.994,\ S_0 = 1.56.$$

Molecular refraction is known to be a thermodynamically invariant quantity.[51] Furthermore, the solvent exerts only a weak influence on it.[52] Molecular refraction and polarisability are sometimes regarded as measures of the "intrinsic volume" of molecules[53] or as the factors responsible for dispersion interactions. In the thermodynamics of solutions, the volume properties of the solute molecules are expressed in terms of the limiting values of the partial molar volumes ($\overline{V}_M^{A_i}$). It is believed that $\overline{V}_M^{A_i}$ is mainly made up of two quantities: the intrinsic volume of the molecule and the change in the volume of the solution as a result of the influence of the dissolved molecule on the packing of the solvent molecules in the perturbed part of the solution.[54]

The concept of the "intrinsic volume" of the molecule in a liquid is highly indefinite. The molecular size is sometimes expressed in terms of the molar volume, the van der Waals volume, the parachor, or the molar refraction. The interpretation of the observed relation between $\Delta H_{solv}^{A_i/C_6H_{12}}$ and MR^{A_i} would be greatly simplified if there were a relation between MR^{A_i} and $\overline{V}_M^{A_i}$. However, there are too few data for the partial molar volumes of different compounds in alkanes to reach any serious conclusions and the small amount of information available indicates the absence of a general relation between MR^{A_i} and $\overline{V}_M^{A_i}$.[5]

The interaction of alkanes with organic compounds has been discussed[12,38] within the framework of not only dispersion but also induction interactions. The existence of a relation between $\Delta H_{solv}^{A_i/C_6H_{12}}$ and MR^{A_i} in cyclohexane shows that, when solvation phenomena involving alkanes are considered, the induction interactions can be neglected, since, if it were the case that the contribution of these interactions plays a significant role, then for compounds having the same MR^{A_i} but different dipole moments, for example, for cyclooctane (μ = 0 D, MR^{A_i} = 36.5 cm^3 mol^{-1}) and acetophenone (μ = 3 D, MR^{A_i} = 36.5 cm^3 mol^{-1}), the enthalpies of solvation would not be the same, as indicated by experimental data. The molecular dipole moments of compounds dissolved in cyclohexane (Fig. 2) differ by several units. Since there is no general relation between molecular refraction and the dipole moment, the linear relation between $\Delta H_{solv}^{A_i/C_6H_{12}}$ and MR^{A_i} implies that, within the limits of experimental error, the enthalpies of solvation of compounds in alkanes are determined by forces related to the polarisability of molecules. It is believed that these forces are induced by dispersion interactions. Experimental enthalpies of solvation of compounds in cyclohexane have been compared[5] with the energies of dispersion interactions calculated in different ways. It has been shown that only the Kirkwood–Muller equation[16] reproduces the observed relation between $\Delta H_{solv}^{A_i/C_6H_{12}}$ and MR^{A_i} to an adequate degree of approximation.

The universal relation discovered[31,32] between the enthalpies of solvation of compounds in cyclohexane and their refractions created new possibilities for the determination of the enthalpies of solvation of compounds in other solvents. The point is that, in the present stage of the experimental determination of enthalpies of solvation, this is primarily the problem of measuring the enthalpy of evaporation of the solute. The problem consists not only in the fact that it is extremely difficult to measure $\Delta H_{vap}^{A_i}$ but also in the

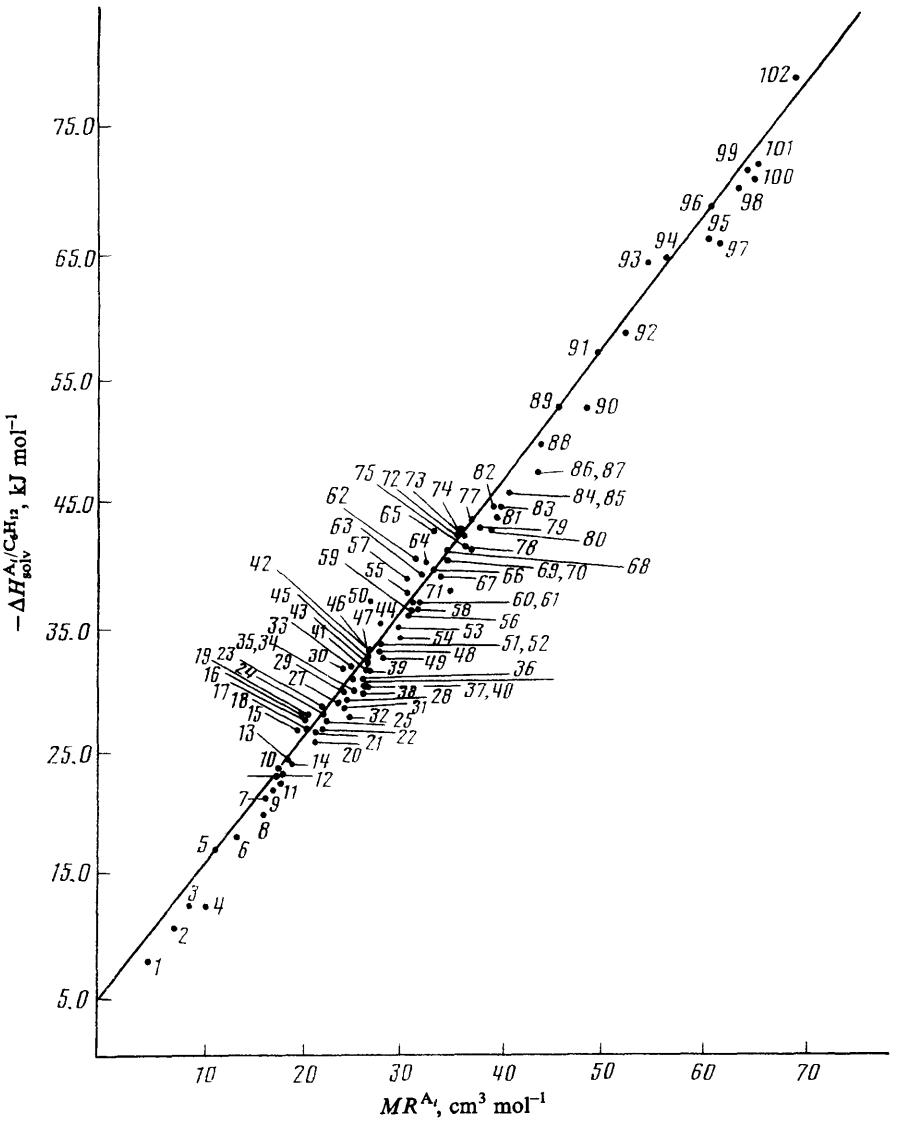


Figure 2. Relation between the enthalpies of solvation of compounds in cyclohexane and their molar refractions. The numbers of the points correspond to the following compounds: *1*, water; *2*, hydrogen chloride; *3*, methanol; *4*, hydrogen bromide; *5*, propionitrile; *6*, ethanol; *7*, propanal; *8*, propanone; *9*, 1-cyano-2-propene; *10*, 2-propen-1-ol; *11*, 1-propanol; *12*, methyl acetate; 13, 1-amino-2-propene; *14*, iodomethane; *15*, ethyl nitrate; *16*, tetrahydrofuran; *17*, chloroform; *18*, *cis*-1,2-dichloroethylene; *19*, *trans*-1,2-dichloroethylene; *20*, butanone; *21*, carbon disulphide; *22*, 1-butanol; *23*, methyl propionate; *24*, ethyl acetate; *25*, dimethyl sulphite; *26*, 1,4-dioxane; *27*, propane-1-thiol; *28*, 1-aminobutane; *29*, 1,2-dimethoxyethane; *30*, pyridine; *31*, thiophen; *32*, hexafluorobenzene; *33*, cyclopropyl methyl ketone; *34*, 2-pentanone; *35*, 3-pentanone; *36*, trichloroethylene; *37*, 1-chlorobutane; *38*, 1,4-difluorobenzene; *39*, fluorobenzene; *40*, benzene; *41*, carbon tetrachloride; *42*, piperidine; *43*, 1-pentanol; *44*, ethyl chloroacetate; *45*, methyl butyrate; *46*, n-propyl acetate; *47*, cyclohexane; *48*, 1-bromobutane; *49*, iodine; *50*, phenol; *51*, butane-1-thiol; *52*, 1-iodopropane; *53*, 2-hexanone; *54*, 3-hexanone; *55*, aniline; *56*, 1,1-dichlorobutane; *57*, 1,1,2,2-tetrachloroethane; *58*, 1-hexanol; *59*, chlorobenzene; *60*, n-butyl acetate; *61*, methyl valerate; *62*, benzonitrile; *63*, benzaldehyde; *64*, methyl trichloroacetate; *65*, nitrobenzene; *66*, methyl phenyl ether; *67*, bromobenzene; *68*, thiophenol; *69*, 2-heptanone; *70*, 4-heptanone; *71*, phenylacetylene; *72*, 1,4-dichlorobenzene; *73*, 1,2-dichlorobenzene; *74*, heptanol; *75*, vinylbenzene; *76*, acetophenone; *77*, ethyl trichloroacetate; *78*, phenyl acetate; *79*, methyl benzoate; *80*, 2-octanone; *81*, iodobenzene; *82*, 1,3-dinitrobenzene; *83*, methyl phenyl sulphide; *84*, 1-octanol; *85*, *N*,*N*-di-methylaniline; *86*, 2-nonanone; *87*, 5-nonanone; *88*, naphthalene; *89*, 1,2,4,5-tetrachlorobenzene; *90*, 2-decanone; *91*, 1-decanol; *92*, biphenyl; *93*, hexachlorobenzene; *94*, benzophenone; *95*, *cis*-azobenzene; *96*, phenanthrene; *97*, benzil; *98*, *trans*-azobenzene; *99*, anthracene; *100*, 1-bromodecane; *101*, 1,2-diphenylethylene; *102*, diphenylmercury. The enthalpies of solution and solvation were taken from Refs. 5, 31, 32, and 37–49.

fact that traditionally this problem is dealt with by specialists who use the values of $\Delta H_{vap}^{A_i}$ to determine the enthalpy of formation of a substance in the gas phase. It is quite natural that the set of experimental enthalpies of evaporation produced by them is suitable in the first place for the solution of problems in this field. Among the investigators known to us only Fuchs[47] and Suvorov and Kondrat'ev[55] measured enthalpies of evaporation in order to study solvation phenomena.

We proposed[4,31,32] a version of what is in our view an extremely convenient method for the determination of $\Delta H_{vap}^{A_i}$, which for many compounds is not inferior to dissolution calorimetry as regards its productivity and simplicity of its application. It is based on the use of the observed relation between the enthalpies of solvation of compounds in cyclohexane and their molar refractions. The determination of the enthalpy of evaporation in this method reduces to measurements of the enthalpy of solution of the given compound in cyclohexane and of its molecular refraction:

$$\Delta H_{vap}^{A_i} = \Delta H_s^{A_i/C_6H_{12}} + 4.39 + 1.05MR^{A_i}. \quad (17)$$

For compounds with a branched hydrocarbon skeleton, it is necessary to introduce the appropriate corrections.[32] Unfortunately, it is difficult to determine the error of the measurement of $\Delta H_{vap}^{A_i}$ by the method described,[31,32] because the existing significant discrepancies with literature data may be caused either by the limited applicability of Eqn. (17) or by the not always correct measurement of $\Delta H_{vap}^{A_i}$ by direct methods (the errors in the measurement of the enthalpies of solution of compounds in cyclohexane are not so great).

We shall now discuss the advantages of the method based on Eqn. (17). Firstly, in this method the molecular weight and the state of aggregation of the substance do not have such a significant influence on the accuracy of the measurement of $\Delta H_{vap}^{A_i}$ because the enthalpy of solution in alkane does not depend greatly on these parameters. An increase in the molecular weight of the substance leads in essence to a decrease in the relative error in the determination of the enthalpy of evaporation. Secondly, the determination of $\Delta H_{vap}^{A_i}$ for involatile compounds by classical methods requires fairly high temperatures. Many organic and organoelement compounds tend to decompose at these temperatures. Therefore, for compounds of this kind our method[31,32] may prove to be virtually the only one suitable at the present time.

There is no doubt that the direct experimental measurement of the enthalpy of evaporation is more promising from the standpoint of the accuracy of its determination. However, bearing in mind the difficulties in the determination of the enthalpy of formation at the present stage, the method based on the use of Eqn. (17) is, in our view, an essential instrument for the investigation of the thermochemistry of solvation over a wide range of organic compounds. Fuchs et al.[56] recently improved the equation relating the enthalpy of solvation and the molar refraction and put forward the following two parameter equation:

$$-\Delta H_{solv}^{A_i/S} = a + bMMR^{A_i} + cV_M^{A_i}, \quad (18)$$

where

$$MMR^{A_i} = V_M^{A_i} \quad (n^2-1)/(n^2+2),$$

is a function of polarisability. It was shown[56] that, for the range of compounds investigated (carbon tetrachloride, perfluoroheptane, diiodomethane, benzene, hexane, decane, hexadecane, cyclohexane, toluene, and mesitylene), Eqn. (18) describes the enthalpy of solvation better than Eqn. (17).

V. The influence of the polarity of the medium on the enthalpy of the non-specific solvation of organic non-electrolytes

Before proceeding to the description of this problem, it appears to be necessary to discuss the concept of the polarity of a non-electrolyte. The dipole moment of a molecule is the most widely used measure of the polarity of a non-electrolyte when solvation phenomena are considered. However, there exists also another viewpoint on the determination of the polarity of solute molecules which has been most fully formulated by Claessens et al.[57] These authors believe that the postulate that any polar molecule should possess a dipole moment is incorrect. Thus a molecule may have no dipole moment owing to the complete compensation of two systems of the distribution of charge density in the molecule, each of which is characterised by a dipole moment. The molecules having such a charge distribution have a quadrupole moment and are polar. The same considerations can be applied when oppositely directed quadrupoles are considered, etc. The authors[57] therefore suggest that the expression "polar molecule" be replaced by the expressions "dipolar molecule", "quadrupolar molecule", etc. The energies of electrostatic interactions for such molecules can be calculated by the equation[57]

$$\Delta G_{int} = -N_{A_i}\left[\frac{1}{2}\frac{2(\varepsilon_S-1)}{2\varepsilon_S+1}\frac{\mu_\alpha^2}{a^3} + \frac{1}{6}\frac{6(\varepsilon_S+1)}{3\varepsilon_S+2}\frac{\theta_{\alpha\beta}}{a^5} + \frac{1}{30}\frac{24(\varepsilon_S-1)}{4\varepsilon_S+3}\frac{\Omega_{\alpha\beta\gamma}}{a^7} + \ldots\right], \quad (19)$$

where ε_S is the dielectric constant of the solvent, μ_α a component of the dipole moment, a the radius of the cavity in which the molecule has been placed, $\theta_{\alpha\beta}$ a component of the quadrupole moment, and $\Omega_{\alpha\beta\gamma}$ a component of the octupole moment.

The idea of the polarity of the substance as a combination of the properties of dipolarity and polarisability appears less definite.[58] We adopt the dipole moment of the solute molecule as a measure of its polarity. The dielectric constant is adopted as a measure of the solvent polarity. Hence the problem of polarity reduces to the elucidation of the influence of these parameters on the energy of non-specific solvation.

The contribution of polar interaction is usually estimated by applying the homomorph principle, according to which the enthalpy of non-specific solvation, determined by dispersion forces for a compound capable of specific $[\Delta H_{int}^{A_i/S}(sp)]$ or polar $[\Delta H_{int}^{A_i/S}(or)]$ interactions is set equal to the enthalpy of solvation of a compound incapable of such interactions. An alkane Y_i with a molar volume equal to that of the solute A_i is usually selected as the homomorph:

$$\Delta H_{solv}^{A_i/S} - \Delta H_{solv}^{Y_i/S} = \Delta H_{int}^{A_i/S}(sp) + \Delta H_{int}^{A_i/S}(or). \quad (20)$$

If the polar molecule does not enter into a complex formation reaction with the solvent, the difference on the left-hand side of Eqn. (20) represents in this case the enthalpy of orientation interaction.

As can be seen from Eqn. (20), the homomorph method is based on the hypothesis that the dispersion interactions are determined

solely by the size of the solute molecules. However, it has been shown[4,59] that this hypothesis is incorrect, and the contributions of orientation interaction to the enthalpy of solvation, calculated by Eqn. (20), therefore represent overall quantities.

In this section, we shall attempt to show, using both our own and literature data, that the molecular dipole moment of the solute does not exert a significant influence on the enthalpy of solvation. The existence of a relation between the enthalpies of solvation of compounds of different polarity in cyclohexane (Fig. 2) and their molar refraction shows that the dipole–induction interactions do not make a significant contribution to the enthalpy of solvation.

The enthalpies of solvation of benzene and its halo-derivatives in cyclohexane and dimethyl sulphoxide are compared in Table 2. As can be seen from the results presented in Table 2, the difference between the enthalpies of solvation of chlorobenzene and benzene in cyclohexane and dimethyl sulphoxide ($\varepsilon_{C_6H_{12}}$ = 2.02, $\varepsilon_{(CH_3)_2SO}$ = 46.6) is approximately the same despite the fact that the polarities of the two solutes differ ($\mu_{C_6H_5Cl}$ = 1.7 D, $\mu_{C_6H_6}$ = 0 D). The enthalpies of solvation of these compounds are determined by dispersion forces. Relatively small differences between the $\Delta H_{solv}^{A_i/S}$ for halobenzenes in the two solvents can therefore be attributed, in principle, to their orientation interaction with dimethyl sulphoxide. However, the small size of the postulated orientation interaction of halobenzenes with the polar dimethyl sulphoxide is a major embarrassment. The results of Krichnan and Friedman[35] and Fuchs et al.[45] therefore stimulated our interest in the problem of solvation of aromatic hydrocarbons and their halo-derivatives.[59–61] It was found that, despite the difference between the polarities ($\Delta\mu$ = 2.5 D) of the solutes and solvents ($\Delta\varepsilon_S$ = 59), in all the cases investigated there is an excellent linear relation between $\Delta H_{solv}^{A_i/S}$ and the molar refraction of the solute:

$$-\Delta H_{solv}^{A_i/S} = a_S + b_S MR^{A_i}. \qquad (21)$$

Table 2. Enthalpies of solvation (kJ mol^{-1}) of benzene and fluoro-, chloro-, and bromo-benzenes in dimethyl sulphoxide and cyclohexane (298 K).

Solvent	$-\Delta H_{solv}^{C_6H_5X/S}$				Refs.
	X=H	X=F	X=Cl	X=Br	
Dimethyl sulphoxide	31.1	34.2	38.1	41.6	[35]
Cyclohexane	29.9	30.9	36.5	39.3	[45]

These results imply that the contribution of orientation interactions to the enthalpies of solvation of the test compounds is insignificant.

Another method of estimating the contribution of orientation interactions to the enthalpy of solvation has also been used[59–61] — comparison of the enthalpies of solution and solvation of compounds differing only in dipole moment. Such compounds are, in particular, the *o*-, *m*-, and *p*-isomers of disubstituted benzenes and the *cis*- and *trans*-isomers of disubstituted ethylenes. Pairwise comparison of the enthalpies of solution of these compounds in a series of solvents yielded a straight line with a slope close to unity.[59–61] The solvent polarity was varied within wide limits (from carbon tetrachloride to dimethyl sulphoxide). According to Eqn. (5), the difference between the enthalpies of solvation of compounds is equal to the difference between their enthalpies of solution. Hence it follows that the relative enthalpy of solvation is independent of the dipole moment ($\Delta\mu$ = 6.0 D) of the solute molecule.

The absence of an influence of the molecular dipole moment of the solute on the enthalpies of solvation of the organic non-electrolytes investigated may be due to several causes. Firstly, it is possible that not the dipole moment of the molecule as a whole but the dipole moments of individual groups or bonds in the molecule are important for solvation. This hypothesis makes it possible to explain the identical enthalpies of solvation of isomers. Secondly, the molecules investigated in the studies mentioned above [35,45,59–61] are fairly large and the continuous theory with the aid of which the contribution of electrostatic interactions to the solvation energy is estimated requires allowance not only for the dipole moment of the molecule but also for the size of the latter,[62] which was not done. Thirdly, it is possible that the contributions of polar interactions to the enthalpy of solvation are compensated by the energy of reorganisation of the solvent.[4,59] A detailed analysis of the causes which induced such an unusual phenomenon is therefore necessary.

The version which states that, for the analysis of the factors determining the solvation energy one must take into account not the dipole moment of the molecule as a whole but the dipole moments of its individual groups, appeared many years ago and was based on the study of different physicochemical characteristics of halobenzenes.[63]

The influence of the dipole moment of the $C_{Ar}-Hal$ bond on the enthalpies of solvation of halobenzenes was tested.[4,59] Since the dipole moment of the $H-C_{Ar}$ bond (0.7 D [64]) is approximately equal in absolute magnitude to the dipole moment of the $C_{Ar}-Hal$ bond (1.0 D [65]), the substitution of hydrogen atoms by halogen atoms in the molecule should not alter significantly the "polarity" of the latter. From this standpoint, the "polarities" of halobenzenes and benzene are the same. On the other hand, naphthalene, diphenyl, and anthracene are more "polar" than benzene, because they contain a larger number of polar bonds. If there is a linear relation between $\Delta H_{solv}^{A_i/S}$ for aromatic hydrocarbons and polyhalobenzenes and their MR^{A_i} while the dipole moments of individual bonds in the solute molecule influence its enthalpy of solvation, then at least a parallel variation should be observed between the characteristic of the "polarity" of the solute

$$n\sum_{i=1}^{n}\mu_i(C_{Ar}-H) \quad \text{or} \quad n\sum_{i=1}^{n}\mu_i(C_{Ar}-Hal),$$

and its molecular refraction. However, it has been shown[4,59] that such parallel variation is not observed. This means that the dipole moment of the $C_{Ar}-H$ or $C_{Ar}-Hal$ bond does not influence significantly the enthalpies of solvation of halobenzenes.

VI. Enthalpy of complex formation as a component of the enthalpy of solvation

The enthalpy of solvation of a substance can be represented by the sum of the enthalpies of non-specific solvation $\Delta H_{solv}^{A_i/S}$ and specific interaction $\Delta H_{int}^{A_i/S}$ (sp):

$$\Delta H_{solv}^{A_i/S} = \Delta H_{solv}^{A_i/S}(\text{non-sp}) + \Delta H_{int}^{A_i/S}(\text{sp}). \qquad (22)$$

The enthalpy of the specific interaction of the solute with the solvent represents the enthalpy of the complex formation reaction ($\Delta H_c^{A_i/S}$) (of the type of reaction involving the formation of hydrogen or donor–acceptor bonds between the solute and solvent molecules) per mole of the solute.

There are conflicting points of view in the literature on the relative contributions of the enthalpies of non-specific solvation and specific interaction to the enthalpy of solvation. Before proceeding to the discussion of the question of the subdivision of the enthalpy of solvation into components [Eqn. (22)], we shall demonstrate that these relative contributions may be different (Table 3).

Table 3. Relation between the enthalpies of non-specific solvation and the enthalpies of specific solvation (kJ mol^{-1}) for a series of compounds (at 298 K).[66]

Solute A_i in a solvent S	$-\Delta H_{solv}^{A_i/S}$(non-sp)	$-\Delta H_{int}^{A_i/S}$(sp)
Phenol in benzene	44.3	4.6
Iodine in chlorobenzene	37.7	4.6
Pyrrole in dimethylformamide	37.2	13.4
Phenol in pyridine	44.1	30.4
Water in tetrahydrofuran*	18.3	20.2
Water in dimethyl sulphoxide*	16.4	32.6

*Data taken from Somonov et al.[67] are quoted.

The development of a method for the subdivision of $\Delta H_{solv}^{A_i/S}$ into components consists in finding general principles of some kind which govern the determination of the enthalpy of non-specific solvation. Thus, from the difference between the enthalpies of solvation and non-specific solvation, we obtain the enthalpy of specific interaction, which may be compared with the enthalpy of complex formation, determined, for example, by spectroscopic methods. The agreement between the latter quantities may be a test of the validity of the method of subdivision of the enthalpy of solvation. Naturally, the most general principles governing the determination of the enthalpy of non-specific solvation can be deduced only when the principal quantitative relations involving the variation of the enthalpy as a function of the structural characteristics of the solute have become clear. Apparently the above problem cannot be fully solved at the present time but the search for ways of solving the problem of the subdivision of $\Delta H_{solv}^{A_i/S}$ into components by deducing the general principles governing the determination of the enthalpy of non-specific solvation nevertheless appears more progressive than the search for partial solutions.[44,68,69]

The simplest method of estimating the enthalpy of specific interaction consists in determining the difference between the enthalpies of solution in a solvent S and in a solvent I (usually carbon tetrachloride or an alkane) which is inert from the standpoint of the possibility of the formation of specific bonds with the solute:

$$\Delta H_{int}^{A_i/S}(sp) = \Delta H_s^{A_i/S} - \Delta H_s^{A_i/I} = \Delta H_{solv}^{A_i/S} - \Delta H_{solv}^{A_i/I}. \quad (23)$$

The disadvantages of this method as well as its modified version[70] have been discussed.[66] The method for the determination of $\Delta H_{int}^{A_i/S}$ (sp) according to which the enthalpy of specific interaction is determined from the difference between the enthalpies of solvation in a solvent S of the test compound A_i and of a compound M_i, which resembles A_i as regards molecular size, structure, and the parameters responsible for the non-specific interaction but is incapable of entering into specific interactions with the solvent S is free from fundamental disadvantages:

$$\Delta H_{int}^{A_i/S}(sp) = \Delta H_{solv}^{A_i/S} - \Delta H_{solv}^{M_i/S}. \quad (24)$$

Since the enthalpy of solvation of the compound M_i models the enthalpy of the non-specific solvation of compound A_i, M_i is referred to as a model compound.

The method based on Eqn. (24) has been used to determine the enthalpies of formation of hydrogen bonds between the molecules of pyridine, water, and methanol,[71] diazines, water, and methanol,[72] and oct-1-yne and a series of proton-accepting solvents.[73]

In order to obviate the difficulty involving the determination of $\Delta H_{vap}^{A_i}$, Arnett and co-workers[44,68,69] suggested that the enthalpy of specific interaction be determined from the equation

$$\Delta H_{int}^{A_i/S}(sp) = [\Delta H_s^{A_i/S} - \Delta H_s^{A_i/CCl_4}] - [\Delta H_s^{M_i/S} - \Delta H_s^{M_i/CCl_4}]. \quad (25)$$

This method, known as the "pure base method", has been used in numerous investigations.[74–80]

Spencer et al.[78] proposed an equation which makes it possible to calculate the enthalpy of specific interaction from the enthalpies of the transfer of compounds from one solvent to another.

Two further new methods for isolating the contribution of the enthalpy of specific interaction have been developed recently.[4,66,67,81–85] One of them[4,66,67,81] is based on the study of the dependence of the enthalpies of solvation of compounds in carbon tetrachloride on the molecular refraction, which makes it possible to classify the solutes in terms of the type of non-specific solvation: for example, aromatic hydrocarbons and their halo-derivatives; monofunctional aromatic compounds containing the nitrile, carbonyl, nitro-, amino-, and hydroxy-groups. This classification makes it possible to find the enthalpies of non-specific solvation of various compounds from the relation between $\Delta H_{solv}^{A_i/S}$ and MR^{A_i} established for compounds of the same type but incapable of specific interaction with the solvent.

Fig. 3 presents the relation between the enthalpies of solvation of some of the compounds investigated in the above studies[4,66,67,81] and their molecular refractions in carbon tetrachloride and in acetonitrile. The enthalpies of solvation of compounds in carbon tetrachloride are non-specific. In acetonitrile the picture is somewhat different: the points corresponding to compounds capable of specific interaction with the solvent deviate from the general relation. The magnitudes of the deviation of these points, determined from the plot of $\Delta H_{solv}^{A_i/S}$ and MR^{A_i} (Fig. 3*a*), is virtually equal to the enthalpy of complex formation between the solute† and the solvent determined in an inert solvent.

†The data for water are an exception, because the water molecule contains two hydrogen atoms capable of complex formation with the solvent.[67]

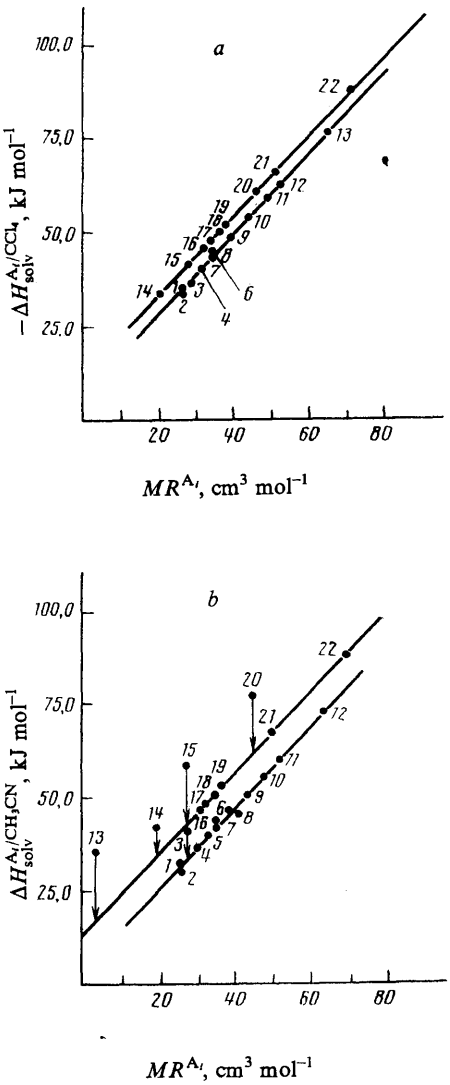


Figure 3. Relation between the enthalpies of solvation of compounds in carbon tetrachloride (*a*) and acetonitrile (*b*) and their molar refractions. The numbers of the points correspond to the following compounds: *1*, fluorobenzene; *2*, benzene; *3*, iodine; *4*, chlorobenzene; *5*, bromobenzene; *6*, *o*-dichlorobenzene; *7*, *p*-dichlorobenzene; *8*, iodobenzene; *9*, naphthalene; 10, 1-chloronaphthalene; *11*, biphenyl; *12*, anthracene; *13*, water; *14*, pyrrole; *15*, phenol; *16*, benzaldehyde; *17*, nitrobenzene; *18*, *p*-chlorobenzaldehyde; *19*, *p*-chloronitrobenzene; *20*, 1-naphthol; *21*, 1-nitronaphthalene; *22*, 9-anthraldehyde. The enthalpies of solvation were taken from Refs. 59, 66, and 67.

Fuchs and Stephenson[82–85] suggested that the "base line" method be used for the determination of the energies of hydrogen bonds. Its essential feature involves the comparison of the difference between the enthalpies of solvation of compounds A_i and M_i in a series of solvents with the Taft–Kamlert π^* constants. A "base line" is drawn through the points corresponding to inert solvents (n-heptane, cyclohexane, carbon tetrachloride, α,α,α-trifluorotoluene, and 1,2-dichloroethane). It takes into account the discrepancy between the enthalpies of solvation of the solute A_i and the model compound M_i, which models the non-specific solvation of A_i on passing from one solvent to another:

$$\Delta H_{solv}^{A_i/S} - \Delta H_{solv}^{M_i/S} = m\pi^* + d, \qquad (26)$$

where m and d are the parameters of the correlation. If the complex formation reaction takes place between the solute and the solvent, then the plot of the relation between the relative enthalpy of solvation $\Delta H_{solv}^{A_i/S} - \Delta H_{solv}^{M_i/S}$ and the π^* constant shows deviations of the points for the corresponding solvents which are equal to the enthalpies of specific interaction.

It is noteworthy that the methods for the determination of $\Delta H_{int}^{A_i/S}$ (sp) described in the studies quoted[4,66,67,81–85] reflect, in essence, two approaches to the study of the thermochemistry of solvation of organic non-electrolytes. In one of them,[4] emphasis is laid on the study of the solvation of structurally different solutes in one solvent of some kind. In the other approach,[82–85] the structure of the solutes is fixed and the properties of the solvent are varied. In contrast to the method based on the study of the relation between $\Delta H_{solv}^{A_i/S}$ and MR^{A_i}, the "base line" method reproduces the variation of the difference $\Delta H_{solv}^{A_i/S}$ (non-sp) – $\Delta H_{solv}^{M_i/S}$ in a series of solvents. In this case, it is necessary to solve a further two problems; to plot a reliable "base line" and to select the model compound.

In order to plot the "base line", it is essential to have data for several inert solvents which have different π^* constants, and this is not always possible. For example, it is difficult to determine the enthalpies of solution of carboxylic acids in cyclohexane, carbon tetrachloride, or benzene. One must be sure that the solvents employed are indeed inert. Since usually few such solvents are available, even a weak complex formation reaction with the solute can greatly distort the calculated results. If only two inert solvents are suitable for the test system, for example, cyclohexane and carbon tetrachloride, the probability of error increases.

The disadvantages of the existing methods for the determination of the enthalpy of specific interaction have been subjected to a thorough analysis.[66,86] This made it possible to formulate a series of measures whose application would permit the optimum determination of $\Delta H_{int}^{A_i/S}$ (sp). The essential features of these measures reduce to the following. In the initial stage, it is necessary to determine the enthalpy of the transfer of a molecule of compound A_i from an inert solvent to a solvent S [see Eqn (22)]. This permits a rough estimate of $\Delta H_{int}^{A_i/S}$ (sp). Here one must bear in mind that carbon tetrachloride and not an alkane must be used as the inert solvent.

In the case where the solute A_i contains an alkyl group the enthalpy of solvation of which varies significantly from solvent to solvent, the following equation has been proposed:

$$\Delta H_{int}^{A_i/S}(sp) = [\Delta H_s^{A_i/S} - \Delta H_s^{A_i/Y}] - [\Delta H_s^{M_i/S} - \Delta H_s^{M_i/S}] + \\ + MR^Y(\delta h_{cav}^S - \delta h_{cav}^Y). \qquad (27)$$

$\Delta H_{int}^{A_i/S}$ (sp) for proton donors not containing alkyl substituents can be determined by the "pure base" method having replaced the active hydrogen atom by the methyl group. It has been shown[74] that carbon tetrachloride, chloroform, or 1,2-dichloroethane can be used as the inert solvent. If none of the inert solvents can be used

but there is a possibility of determining the enthalpies of solvation of the proton donor and a model compound in which the active hydrogen can be replaced by the methyl group, then the enthalpy of specific interaction can be determined from the equation

$$\Delta H_{int}^{A_i/S}(sp) = \Delta H_{solv}^{A_i/S} - \Delta H_{solv}^{M_i/S} + 4.65k'_S, \quad (28)$$

where k'_S is the slope of the relation between the enthalpies of solvation of alkanes and their molecular refractions in the solvent S.

If there is a possibility of determining the enthalpies of solvation of compounds in several inert solvents, then one may resort to the "base line" method. If the number of inert solvents is small, it is necessary in this case to select model compounds whose employment leads to a slope of the "base line" close to zero. This can be achieved by applying the method based on the study of the relation between $\Delta H_{solv}^{A_i/S}$ and MR^{A_i}.[4,86]

When the enthalpies of specific interaction of proton acceptors are determined, the choice of the inert solvent necessary for the construction of the "base line" is very wide and the requirements as regards the choice of the model compound are less stringent. This factor is important in the determination of $\Delta H_{int}^{A_i/S}$ (sp) in solvents associated via hydrogen bonds.[86]

It is noteworthy that the determination of the enthalpy of specific interaction in associated solvents occupies a special place in the thermochemistry of solvation of organic compounds, since in a solvent of this kind there are equilibria between different types of associated species and in the course of the solvation of the solute A_i there is therefore the possibility of forming complexes consisting of the molecules of A_i and of the associated species. This complex formation process may be accompanied by a shift of the association equilibria in the solvent, which influences the enthalpy of the specific interaction of the solute with the solvent and the enthalpy of solvation in conformity with Eqn. (22).

An approach to the estimation of the influence of the shift of association equilibria in solution on the enthalpy of solvation has been developed.[87–89] Comparison of the enthalpies of the specific interaction of compounds such as phenols, alcohols, acids, ketones, aromatic and aliphatic amines, and pyridines with solvents associated via hydrogen bonding with the enthalpies of formation of complexes $\Delta H_c^{A_i/S}$ between A_i and S, measured in the absence of association of the molecules of the solvent S, showed that the relation between $\Delta H_{int}^{A_i/S}$ (sp) and $\Delta H_c^{A_i/S}$ depends on whether the solute is an "acid" (proton donor or electron acceptor) or a "base" (proton acceptor or electron donor). There is a possibility of two situations (1) $\Delta H_{int}^{A_i/S}$ (sp) is almost identical with $\Delta H_c^{A_i/S}$ ("acids" in aliphatic alcohols and acetic acids); (2) $\Delta H_{int}^{A_i/S}$ (sp) is appreciably smaller in absolute magnitude than $\Delta H_c^{A_i/S}$ and may be zero or positive ("bases" in aliphatic alcohols, acetic acids, formamide, and water; "acids" in water and formamide).

The results led to the development of ideas according to which the appearance of the reorganisation effect may be predicted from the nature of the solute—"acid" or "base"—and the ratio of the numbers of lone pairs and active hydrogen atoms in the solvent molecule.

VII. The dipole moment and the enthalpy of solvation. Additional arguments

If the reduced dipole moment of the molecule (the ratio of the square of the dipole moment of the molecule to the cube of its radius is adopted as a measure of the polarity of the solute, then one of the most polar non-electrolytes is water.

Fig. 4 presents the relation between the enthalpies of non-specific solvation in a series of compounds (including water) and the molecular refractions in a polar solvent—acetonitrile. Similar relations can be obtained for the entire set of solvents used by Solomonov et al.[67] The enthalpy of non-specific solvation is determined from the difference between the enthalpy of solvation of the given compound and the enthalpy of its complex formation reaction with the solvent molecule.‡

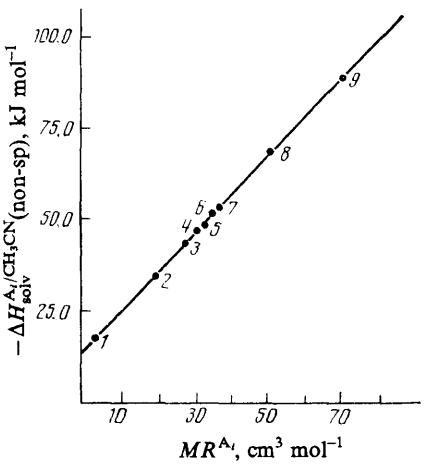


Figure 4. Relation between the enthalpies of non-specific solvation of a series of compounds in acetonitrile and their molar refractions. The numbers of the points correspond to the following compounds: *1*, water; *2*, pyrrole; *3*, phenol; *4*, benzaldehyde; *5*, nitrobenzene; *6*, *p*-chlorobenzaldehyde; *7*, *p*-chloronitrobenzene; *8*, 1-nitronaphthalene; *9*, 9-anthraldehyde.

Since the reduced dipole moments§ of molecules, presented in Fig. 4, differ significantly from one another, the existence of a relation between $\Delta H_{solv}^{A_i/S}$ and MR^{A_i} shows that this factor does not exert a significant influence on the enthalpy of non-specific solvation.

If benzaldehyde (μ = 2.6 D) or nitrobenzene (μ = 4.0 D) is adopted as the compound modelling the non-specific solvation of phenol (μ = 1.6 D) in the "pure base" method [Eqn. (25)], then, as shown by Solomonov and Konovalov[4] a correspondence is observed between the enthalpies of specific interaction and the enthalpies of complex formation determined in carbon tetrachloride for all the solvents investigated—proton acceptors, including highly polar ones (dimethyl formamide, dimethyl sulphoxide). This result also implies that the dipole moment of the solute molecule does not play a significant role.

Extensive experimental data on the thermochemistry of solvation of organic non-electrolytes show that the dipole moment of the

‡ In the case of water, twice the enthalpy of complex formation was adopted.

§ The ratio of the square of the dipole moment of the molecule to the electronic polarisability, which is proportional to the cube of the radius of the molecule, may be adopted as a measure of the reduced dipole moment.[90]

solute molecule does not influence significantly the enthalpy of solvation (at least for the compounds investigated).

Certain considerations have been put forward[4,59] concerning the possible compensation of the orientation interaction between solute and solvent molecules by the reorganisation of solvent molecules. However, if we accept that the energy of orientation interaction is compensated by the energy of the reorganisation of the solvent, then the next step must be taken — the recognition of the fact that in a physicochemical process occurring in solution, where the solvation shell "follows" reversibly (equilibrium process) the changes in the solute (for example, a chemical reaction), the contribution of the orientation interaction may not be observed because the experimental quantities reflect the overall solvent–solvent and solvent–solute interactions.

This view conflicts strongly with the existing ideas about the influence of the medium on various phyisochemical processes. Indeed, there exist a multiplicity of well established facts showing that the fraction of the more polar form of the solute increases in more polar solvents (for example, by virtue of tautomeric or conformational equilibria). Polar interactions are of decisive importance in the influence of the medium on the kinetics of reactions[91] and spectroscopic transitions.[92] The generally accepted Onsager–Böttcher model is in essence the only general physical model of the "test molecule–medium" system on the basis of which a large set of a wide variety of experimental data are analysed to this day.

Nevertheless, only the fact that, on passing from a less polar to a more polar solvent, certain parameters of the physicochemical process (reaction rate constants, activation energies, electronic transition energies, etc.) change has been reliably established experimentally. However, in the study of the influence of the medium on the thermodynamics of a process, the structure of the molecules of its final and initial states can be established and their dipole moments measured only in some cases. In the remaining instances, and these are in the vast majority, the polarity of the species (transition or excited state, non-isolatable complex) is unknown and is inferred from the influence of the solvent on the physicochemical process as a whole. It is therefore hardly possible to speak of the influence of the dipole moment on the solvation energy on the basis of "such" experimental data.

We shall now turn to the term "polarity of the medium". We shall not analyse the problem of which of the existing solvent polarity scales is best and shall only note that, on any of the solvent polarity scales known to us, acetonitrile, dimethyl formamide, and nitromethane are more polar than cyclohexane or carbon tetrachloride. It is also known that dimethyl formamide and dimethyl sulphoxide actually form the strongest hydrogen bonds with the solute, while acetonitrile and nitromethane are simultaneously proton donors and proton acceptors. These properties are absent from cyclohexane and carbon tetrachloride. The capacity of cyclohexane for dispersion interactions is also a minimum. Therefore an increase in the degree of interaction between the solvent and the solute may take place as a result of the increase in solvent "polarity". The parallel variation of the properties of the solvent has been frequently noted in the literature.[58,93] Hence it is entirely understandable that the observed changes in certain parameters of a physicochemical process on passing from a less polar to a more polar solvent are bound to be related to the change in the dipole moment of the species involved in this process.

The relative free energies of solvation of cryptate ion pairs have been investigated[94,95] in a series of solvents. Despite the large dipole moments of the solute molecules, the relative free energies of solvation of these compounds are comparable to the free energy of the transfer of polar neutral molecules in isodielectric solvents. Nevertheless, it has been shown[94,95] that the influence of the medium on the constants of the dissociation of the cryptate ion pairs into solvated ions and the absence of specific interactions with the solvent are due to polar forces. It may be that in this case the polar interaction plays a significant role only because the physicochemical processes are accompanied by the formation of ions.

The idea that the analysis of the solvation energy requires that account be taken of the contribution of quadrupole interactions together with that of dipole interactions has been developed in a number of studies.[57,96,97] This makes it possible to account for the enthalpies of solvation and solution of *cis*- and *trans*-dichloroethylenes,[96] dicyanoethylenes,[59] 1,3- and 1,4-dioxanes,[97] and *o*-, *m*-, and *p*-dinitrobenzenes.[59] Indeed, the absence of an effect of the dipole moment on the enthalpies of solvation of these compounds can be explained by approximately equal contributions of the dipole and quadrupole interactions to the enthalpy of solvation. The quadrupole moment is greater in the *trans*- and *para*-isomers, whereas the dipole moment is greater in the *cis*-, *meta*-, and *ortho*-isomers.

The importance of allowing for multipole interactions has been pointed out.[98] However, it has been shown[99] that the contribution of quadrupole and octupole interactions is negligible compared with the contribution of dipole interactions and the former should be regarded as corrections.

The experimental study of the influence of multipoles of a higher order than the dipole on the solvation energy is at present difficult, since the quadrupole and octupole moments are determined only with a very low accuracy.[57] Some doubts concerning a significant contribution of quadrupole interactions to the solvation energy have arisen from the relations obtained between $\Delta H_{solv}^{A_i/S}$ and MR^{A_i} for aromatic hydrocarbons and their halo-derivatives.[5]

VIII. Additivity in the enthalpies of the transfer and solvation of organic non-electrolytes

The question of the additivity of the solvation energies of organic compounds appears to be extremely important because, firstly, there is a prospect that the study of the solvation of complex organic compounds can be reduced to the study of simpler objects. Secondly, the possible deviations from the additivity of solvation energies may be caused by the mutual influence of atoms and groups in the solute molecule. The study of this question will help to improve our understanding of the inter-relation between the structure of the solute and its solvation energy.

The most significant argument in support of the additivity of the enthalpy of solvation of an alkyl group is the equality of the slopes of the relation between $\Delta H_{solv}^{A_i/S}$ and MR^{A_i} found for alkanes, ketones, and aliphatic alcohols. This equality implies identical solvation of the alkyl substituent at the carbonyl, hydroxy-, and aliphatic groups.[4]

An interesting observation was made by Fuchs and co-workers,[15] who showed that the enthalpy of solvation of benzene is approximately additive, corresponding to the enthalpies of solvation of the three double bonds. Unfortunately, no numerical data were

quoted in their communication. Apparently Fuchs based his treatment on the equation

$$\Delta H_{solv}^{C_6H_6/S} = 3\Delta H_{solv}^{C_6H_{10}/S} - 2\Delta H_{solv}^{C_6H_{12}/S}. \quad (29)$$

Table 4 lists the experimental enthalpies of solvation of benzene in various solvents and their values calculated by Eqn. (29). The enthalpies of solvation of benzene, cyclohexane, and cyclohexene were taken from Solomonov.[5]

Table 4. Experimental enthalpies of solvation (kJ mol^{-1}) of benzene in a series of solvents (298 K) and their values calculated by Eqn. (29).

Solvent	$-\Delta H_{solv}^{C_6H_6/S}$	
	experiment	calculation
Dimethylformamide	33.6	33.8
1,2-Dichloroethane	32.7	33.3
Methanol	32.4	32.5
Benzene	33.9	34.0
Carbon tetrachloride	32.7	33.0

Fuchs and Rodewald[100] determined the enthalpies of solution of 95 aromatic compounds in methanol and dimethyl formamide and showed that in the vast majority of cases the enthalpies of transfer of aromatic compounds are additive relative to the group composition regardless of the positions of the substituents in the aromatic ring. These findings were explained by the fact that not the dipole moment of the molecule as a whole but the dipole moments of its individual groups are important for solvation.

When there is a specific interaction between the molecule of an aromatic compound and the solvent, additivity is not observed in the enthalpies of transfer.[101]

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During the last 15 years, an enormous amount of experimental data have been obtained on the thermochemistry of the dissolution and solvation of organic or non-electrolytes. These can be analysed within the framework of simple empirical relations between the enthalpies of solvation of compounds and their polarisabilities. These relations made it possible to develop an approach to the estimation of the enthalpies of non-specific solvation of organic non-electrolytes in various media.

Methods for the thermochemical determination of the energies of hydrogen and donor–acceptor bonds have been developed on the basis of the enthalpies of solution and solvation.

However, the question of the applicability of general ideas must be considered in each specific case and the simplified approaches are not always correct in the interpretation of thermochemical solvation data.

The extensive experimental data and the empirical relations found in the thermochemistry of solvation undoubtedly require a theoretical interpretation. Studies on these lines have already begun.[9,102–104]

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Translated from *Uspekhi Khimii* **60** 69–102 (1991) U.D.C. 547.315.2'32–34+541.571.3

1,3-Alkadienes and their derivatives in reactions with electrophilic reagents

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ABSTRACT. **Literature data on the addition of electrophiles to 1,3-alkadienes and their derivatives have been reviewed. The chemo-, regio-, and stereo-selectivity of these reactions, mechanistic details, and their synthetic applications, are discussed.**

The bibliography contains 308 references.

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I. Introduction

The chemistry of 1,3-alkadienes has been a subject of close scrutiny during the last hundred years.[1–3] Work in this area has been stimulated in two ways: firstly by theoretical developments in organic chemistry, largely in connection with the ability of 1,3-alkadienes to participate in 1,4-conjugate addition; and, secondly, by the utilization of these compounds as monomers for the preparation of various forms of rubber and other synthetic materials.

The majority of the fundamental questions relating to the chemistry of 1,3-alkadienes were addressed within the first fifty years of this century. Experimentally, this has been achieved without the use of physical separation techniques or structure determination, and without attempting to gather authentic quantitative data. Therefore, in recent years, many reactions of 1,3-dienes, even well established ones, have been studied anew with the aid of chromatography, and IR- and NMR-spectroscopy. As a result, new data have been obtained for theoretical analysis.

Certain aspects of the chemistry of 1,3-alkadienes, for example halogenation, have been developed during the last ten years, notably for potential industrial application. The chlorination of 1,3-butadiene, and the subsequent dehydrochlorination of the resulting dichloride, has been known since the 1930's, and provides the basis of a new commercial route to chloroprene.[4]

As a result, a large amount of data on the chemistry of 1,3-alkadienes has been published, particularly in the last twenty years, and has not yet been reviewed in the literature or surveyed in monographs.

Reactions of 1,3-alkadienes with electrophiles are characteristic of this class of compound, which also undergo radical addition and participate in pericyclic processes, such as heterocyclisation (4+1), dimerisation and diene synthesis (4+2), and catalytic dimerisation (4+4).

Electrophilic addition to unsaturated compounds is a widely studied aspect of organic chemistry.[1–3] The majority of these reactions proceed by a two-step A_E2 mechanism. A carbenium or an onium ion is intermediate in the reaction depending on the nature of the substrate and electrophile. There is also reference in the literature to the possibility of there being other intermediates, notable uncharged species.[2,3] An alternative A_E3 mechanism has sometimes been invoked for this electrophilic addition.[1]

Electrophilic addition to 1,3-alkadienes follows the rules established for reactions of other alkenes. However, the presence of a further conjugated double bond has an effect on chemo-, regio- and stereo-selectivity.[5–9]

According to the general theory of electrophilic addition, the orientation of attack of the electrophile at the double bond should be such that the most stable intermediate is formed with delocalisation of the positive charge within an allylic system. The second stage, i.e. the addition of the nucleophilic residue, may proceed at one or other of the electrophilic centres depending on the electronic and steric environment of the conjugated system (inclusive of solvent and catalyst).

Electrophilic addition can be accompanied by substitution of hydrogen, usually at an unsaturated carbon atom, and in the case of 1,3-butadiene homologues there may be allylic substitution with rearrangement (Lvov–Tishchenko reaction). Although a detailed study of the mechanism of these reactions has not been undertaken, there is no doubt that an electrophilic mechanism is involved: the first stage is akin to aromatic substitution, and the second is a deprotonation characteristic of carbenium ions.

The information gathered and examined in earlier reviews and monographs has only been touched upon in this review. The bibliography contains references up to 1989. The chemistry of cycloalkadienes and carbon-functionalised alkadienes has not been included.

II. The addition of compounds with an electrophilic halogen atom

The following compounds contain an electrophilic halogen atom: halogens themselves, hypohalites (acids, esters and mixed anhydrides) and *N*-halides. All of these compounds can react with unsaturated compounds by a radical or electrophilic mechanism depending on their structure and the reaction conditions. In all cases, a direct indication of the mechanism of the reaction can be obtained from the chemo-, regio- and stereo-selectivity of the addition. All reported reactions of 1,3-dienes with *N*-halides proceed under conditions for radical addition,[10] and therefore have not been examined in this review.

1. Halogenation

Of all the electrophilic additions to 1,3-alkadienes, halogenation has been the most widely studied. It is normally carried out with free halogen (except fluorine) in an inert solvent (CH_2Cl_2, CCl_4 at -20 to 0 °C. Studies have been made of the interaction of 1,3-alkadienes with fluorine, chlorine, bromine and iodine, as well as with mixed halogens: FCl, FBr, ClBr and ClI. Detailed studies in this area have been carried out by V L Heasley et al. between 1970 and 1980.

The reaction of 1,3-butadiene with fluorine was reported for the first time in 1984.[11] The regioselectivity of the reaction depends on the nature of the fluorinating agent: with XeF_2 the 1,2-adduct predominates (87%), whereas with $PhIF_2$ the 1,4-adduct is favoured (64%). It is thought that reaction proceeds via a carbenium intermediate. Replacement of hydrogen by fluorine takes place as a side-reaction.

The interaction of 1,3-butadiene with chlorine was studied as long ago as 1886.[12] However, detailed information on the regioselectivity of the reaction was not available until 1930,[13] after which the reaction became the focus of numerous researchers.[14–27] Normally, 1,3-butadiene yields *trans*-1,4-dichloro-2-butene as the major product in preference to 3,4-dichloro-1-butene. However, if chlorination is conducted under non-radical conditions, the ratio of 3,4-dichloride to 1,4-dichloride is 2 : 1.[21] Both dichlorides undergo isomerisation on heating in the presence of $ZnCl_2$. At equilibrium, the mixture contains ~70%, 1,4-dichloro-2-butene.[18] In the presence of complex metal catalysts, e.g. copper naphthylate, the 1,4-dichloride isomerises to 3,4-dichloro-1-butene.[20]

By conventional chlorination of 1,3-butadiene the yield of dichlorides does not exceed 40% since significant amounts of tetrachloride are formed together with higher telomers. By adjusting the conditions of chlorination and using specific additives, in particular metal chlorides or various amines and phosphines, the yield of dichlorides can be raised to 97%.[23,24]

Several studies have been devoted to the kinetics of chlorination of 1,3-butadiene.[19,25–27] It has been shown that the formation of isomeric dichlorides follows a complex kinetic profile: 1,4-dichloro-2-butene by a second order process, and 3,4-dichloro-1-butene by a third order process. The activation parameters in the latter case would not suggest the formation of an ionic intermediate. From this it follows that the mechanism of addition of chlorine to 1,3-dienes is more complex than thought hitherto. It is possible that 1,4-addition proceeds to some extent by a radical pathway.[19,21]

Bromination of 1,3-butadiene is one of the most studied reactions of this compound.[14,28–41] The mechanism of addition of bromine depends on the dilution: at low concentrations (0.02 to 0.04 mol/l) it is electrophilic, while at high concentration a radical mechanism is involved.[36] Under conditions of electrophilic addition, 1,2-addition is observed to the extent of 57% in CCl_4 and 24% in CH_2Cl_2. *trans*-1,4-Dibromo-2-butene is formed predominantly (60%) under normal conditions. *cis*-1,4-Dibromo-2-butene has not been detected. 3,4-Dibromo-1-butene is converted slowly at room temperature, or rapidly on heating, to an equilibrium mixture containing ~80% *trans*-1,4-dibromo-2-butene. Thus, in contrast to the corresponding chlorides, the ratio of isomeric dibromides markedly depends on the conditions of bromination, notably the nature of the solvent.

In recent years, reference has been made to bromination of 1,3-butadiene with bromine complexes, e.g. dioxane dibromide,[39] pyridine dibromide, pyridinium tribromide,[40] and tetrabutylammonium tribromide.[41] In the first case, the ratio of addition products is approximately the same as that with molecular bromine. 3,4-Dibromo-1-butene is formed predominantly on bromination with pyridine dibromide, pyridinium tribromide and tetrabutylammonium tribromide. This indicates that the amine is involved in the transition state and/or the formation of an intermediate. The kinetics of bromination with Br_3^- has been studied in detail, and the distribution of electron density in the intermediate has been considered.[41]

Treatment of 1,3-butadiene with methyl hypochlorite and BF_3 in methylene chloride proceeds by 1,2- and 1,4-addition of FCl and methyl hypochlorite. The amounts of both types of adduct are approximately the same. In CCl_4 the yield of fluorochlorides, relative to methoxychlorides, rises significantly. The addition of FCl at the 1,2-position is strictly in accord with the Markovnikov rule, and is noticeably more dominant than 1,4-addition (with formation of *trans*-1-fluoro-4-chloro-2-butene). In CH_2Cl_2, the ratio of 1,2- to 1,4-addition is ~2 : 1, and in CCl_4 it is 3 : 1.[42]

Similarly, treatment of 1,3-butadiene with methyl hypobromite and BF_3 results in addition of FBr. The yield of fluorobromides in this case is less than that of bromoethers. The ratio of 1,2- and 1,4-adducts is 4 : 1.[42] It is thought that a complex, $BF_3Hal^+OR^-$, is formed during the reaction; this complexes with 1,3-butadiene to give an onium intermediate which then undergoes attack by both fluoride ion and methoxide.

The reaction of 1,3-butadiene with ClBr gives a mixture of 4-bromo-1-chlorobut-2-ene and 4-bromo-3-chloro-1-butene in 73 : 27 proportion.[43] With $Bu_4N^+BrCl_2^-$, only 1,2-addition of ClBr takes place; here, 84% of the product is formed according to the Markovnikov rule, and 16% contrary to this rule.[43,44] It is suggested that in this case reaction proceeds with formation of a three-centred intermediate with a delocalised positive charge; this is then attacked by chloride ion.

ICl adds to 1,3-butadiene with the formation of 1,4- and 1,2-adducts in 4 : 1 ratio. This is probably very close to the equilibrium product ratio.[45,46]

Iodination of 1,3-butadiene proceeds regioselectively with formation of *trans*-1,4-diiodo-2-butene.[47] Anionotropic systems with allylic iodine are extremely labile, and here reaction is clearly under thermodynamic control.

As a consequence, on passing from fluorine to iodine the amount of 1,4-adduct increases. Evidently, the determining factor here is the status of the system relative to that at equilibrium, i.e. the extent to which reaction is favoured by kinetic or thermodynamic control.[5]

The stereochemistry of addition of halogens to 1,3-alkadienes has been investigated with a view to assessing potential re-orientation and rotation in the transition state.[48] There is a possibility that addition of halogen results in formation of a non-ionic cyclic intermediate not requiring a significant degree of solvation. This accords with information gathered on the stereospecificity of this reaction.[35]

The regioselectivity of electrophilic chlorination of piperylene is markedly dependent on the geometry of the system and the polarity of the solvent. In CCl_4 *cis*-piperylene forms dichlorides (A), (B) and (C) in 29:20:46 proportion; in CH_2Cl_2 the proportion is 10:47:43. In CCl_4 *trans*-piperylene gives the same mixture of dichlorides in 4:47:49 proportion, while in CH_2Cl_2 the proportion is 2:66:32. Addition at the 3,4-position is stereospecific (89–95% *anti*).[48,49]

$$\underset{(A)}{MeCHCl{-}CHCl{-}CH{=}CH_2},$$

$$\underset{(B)}{MeCH{=}CH{-}CHCl{-}CH_2Cl},$$

$$\underset{(C)}{MeCHCl{-}CH{=}CH{-}CH_2Cl}.$$

Electrophilic bromination of piperylene proceeds predominantly with the formation of *trans*-1,4-dibromo-2-pentene.[50] 1,2-Addition at the disubstituted double bond (in the *anti*-mode) is much less, and minimal in the case of *trans*-piperylene. Thus, the halogen-onium complex at the terminal double bond, both on chlorination and bromination, is significantly more stable than the complex formed at the internal double bond.

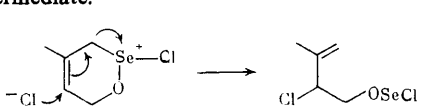
Chlorination of isoprene proceeds to a large extent by replacement of hydrogen by chlorine (Lvov–Tishchenko reaction) with the formation of 2-chloromethyl-1,3-butadiene.[21,51–55] Amongst the adducts which are also formed, 1,4-dichloro-2-methyl-2-butene (C) predominates.

$$\underset{\text{(A), 7\%}}{CH_2Cl{-}\overset{\overset{Me}{|}}{C}Cl{-}CH{=}CH_2}, \qquad \underset{\text{(B), 3\%}}{CH_2{=}\overset{\overset{Me}{|}}{C}{-}CHCl{-}CH_2Cl},$$

$$\underset{\text{(C), 49\%}}{CH_2Cl{-}\overset{\overset{Me}{|}}{C}{=}CH{-}CH_2Cl}, \qquad \underset{\text{(D), 49\%}}{CH_2{=}\overset{\overset{CH_2Cl}{|}}{C}{-}CH{=}CH_2}.$$

Other mono-chlorides are also reported to be formed on chlorination of isoprene. These may arise by dehydrochlorination of the dichloride adducts or may be products derived by 'aromatic' chlorination.[54] It is interesting to note that heating 1,4-dichloro-2-methyl-2-butene in the presence of a catalytic amount of copper(I) chloride and copper powder at 140 °C affords a mixture of comprising ~45% dichloride (B) and only ~3% dichloride (C).[53]

Chlorination of isoprene with $SeOCl_2$ in CH_2Cl_2 yields 1,4-dichloro-2-methyl-2-butene (in 39% yield) as a 2:1 mixture of *E*-and *Z*-isomers and 3-chloro-2-methyl-1-buten-4-ol (in 28% yield). The authors consider that the latter is formed by rearrangement of an intermediate:[55]



Bromination of isoprene has been reported extensively, as far back as 1898.[40,50,56–59] *trans*-1,4-Dibromo-2-methyl-2-butene is the major product, formed in 71% yield. The amount of 3,4-dibromo-3-methyl-1-butene in the mixture of dibromides is ~21%. *cis*-1,4-Dibromo-2-methyl-2-butene and 3,4-dibromo-2-methyl-1-butene are present in the mixture in small amounts (5 and 3%, respectively).

Bromination of isoprene with $SeOBr_2$ affords 1,4-dibromo-2-methyl-2-butene as a 2:1 mixture of *E*- and *Z*-isomers.[55]

ClBr adds to isoprene on treatment with $Bu_4N^+BrCl_2^-$ predominantly at the 1,2-position according to the Markovnikov rule.

$$\underset{78.6\%}{CH_2Br{-}\overset{\overset{Me}{|}}{C}Cl{-}CH{=}CH_2}; \qquad \underset{11\%}{CH_2{=}\overset{\overset{Me}{|}}{C}{-}CHCl{-}CH_2Br};$$

$$\underset{9.2\%}{CH_2Br{-}\overset{\overset{Me}{|}}{C}{=}CH{-}CH_2Cl}.$$

The addition of halogens to 2,4-hexadiene is of particular interest in relation to the stereochemistry of the reaction since this alkadiene exists as three geometric isomers. Their chlorination and bromination in a variety of solvents yields: *erythro*-4,5-dihalogeno-*cis*-2-hexenes, *threo*-4,5-dihalogeno-*cis*-2-hexenes, *dl*-2,5-dihalogeno-*trans*-3-hexenes, *meso*-2,5-dihalogeno-*trans*-3-hexenes, *threo*-4,5-dihalogeno-*trans*-2-hexenes and *erythro*-4,5-dihalogeno-*trans*-2-hexenes. The determination of the amount of each of these dihalides provides evidence in favour of the *syn*- or *anti*-character of the addition.[49,59]

In all cases, 1,4-addition is noticeably less on chlorination than on bromination. There is little information on solvent effects. These results are in accord with the findings of Farmer et al. more than 50 years ago,[31] and disprove a more recent report that the proportion of 1,2- and 1,4-adducts is independent of the polarity of the solvent.[35]

Chlorination and bromination of 2,3-dimethyl-1,3-butadiene[60–65] and 3-methyl-1,3-pentadiene[66] proceeds predominantly with the formation of *trans*-1,4-dihalides, and is associated with a significant degree of allylic substitution.

3,4-Addition takes place on chlorination and bromination of 1-aryl- and 1,4-diaryl-1,3-butadienes, while 1,4-addition is favoured on chlorination and bromination of 2-aryl-1,3-butadienes.[67,69]

Molecular-orbital calculations (LCAO approximation and others) have been carried out on several occasions with a view to examining the regioselectivity of addition to 1,3-butadiene and derivatives.[70,71]

All mono- and dichloro-1,3-butadienes, and notably polychloro-1,3-butadienes, undergo chlorination. Mkryan et al. have contributed most to this aspect. Data on reactions with other halogens is very limited.

Chlorination of 1-chloro-1,3-butadiene affords predominantly 3,4- and 1,4-adducts in addition to three of the possible substitution products:[72–74]

$$\underset{50.7\%}{CHCl{=}CH{-}CHCl{-}CH_2Cl}; \qquad \underset{5.9\%}{CHCl_2{-}CHCl{-}CH{=}CH_2};$$

$$\underset{12.1\%}{CHCl_2{-}CH{=}CH{-}CH_2Cl}; \qquad \underset{5.4\%}{CCl_2{=}CH{-}CH{=}CH_2};$$

$$\underset{1\%}{CHCl{=}CCl{-}CH{=}CH_2}; \qquad \underset{21.8\%}{CHCl{=}CH{-}CH{=}CHCl}.$$

According to another report, the proportion of 3,4- and 1,4-adducts is 1:1, which changes to 2:1 on addition of DMF to the solvent. In each case, 5–6% of the mixture comprises 3,4,4-trichloro-1-butene.[20]

A mixture of 3,4- and 1,4-adducts is formed on bromination of 1-chloro-1,3-butadiene.[73]

There are conflicting reports on the structure of the main product obtained by bromination of 1-bromo-1,3-butadiene. According to one reference the main product is 1,3,4-tribromo-1-butene,[45] and according to another it is 1,1,4-tribromo-2-butene.[75] In each case the structure of the product was assigned on the basis of ozonolytic data.

There are several publications on the chlorination of chloroprene.[76–81] All three of the possible trichlorobutenes are formed, but the 1,2- and 3,4-adducts are always in small amount:[79]

$$\underset{2.6\%}{CH_2Cl{-}CCl_2{-}CH{=}CH_2};\quad \underset{3.4\%}{CH_2{=}CCl{-}CHCl{-}CH_2Cl};$$
$$\underset{69.5\%}{CH_2Cl{-}CCl{=}CH{-}CH_2Cl};\quad \underset{20\%}{CHCl{=}CCl{-}CH{=}CH_2}.$$

The proportion of 1,2- and 3,4-adducts noticeably increases on addition of DMF to the solvent.[20] On chlorination in DMF the ratio of the three dichloride adducts shown above is 3 : 1 : 10.[80]

Bromination of chloroprene leads almost exclusively to 1,4-dibromo-2-chloro-2-butene. A trace of 3,4-dibromo-2-chloro-1-butene is also formed.[78]

ICl adds to chloroprene in an entirely different way: the 4,3-adduct, 2,3-dichloro-4-iodo-1-butene, is formed predominantly together with a trace of 4,1-adduct, 1,2-dichloro-4-iodo-2-butene:[78,81]

$$CH_2{=}CCl{-}CHCl{-}CH_2I;\quad CH_2Cl{-}CCl{=}CH{-}CH_2I.$$

Thus initial attack in this case is at the terminal C-atom of the non-chlorinated double bond. Below, it will be seen that bromination also takes place initially at the same carbon atom, while chlorination of chloroprene proceeds predominantly by attack at the terminal carbon atom of the chloro-substituted double bond.

Bromination of bromoprene takes place almost exclusively by 1,4-addition to give 1,2,4-tribromo-2-butene.[82]

Tables 1 and 2 summarise the results obtained by chlorination of all five dichloro-1,3-butadienes, two trichloro-1,3-butadienes, two tetrachloro-1,3-butadienes and one pentachloro-1,3-butadiene,[79–90] as well as a number of chloro-substituted isoprenes.[91–96] The preferential chlorination of the terminal, non-chlorinated, double bond is evident. Replacement of hydrogen by chlorine at the terminal methylene or methyl group takes place to a significant extent. There is no such substitution in the absence of terminal methyl or methylene groups.

3,4-Addition takes place on chlorination of 1-phenyl-4-chloro-1,3-butadiene, i.e. addition to the chlorine-substituted double bond.[96]

There is also reference in the literature to halogenation of certain halogeno-substituted 1,3-alkadienes, but without reliable information on the structure of the adducts (e.g. references[97,98]); these have been excluded from this review.

Halogenation of nitro-substituted 1,3-alkadienes has been rarely studied.[99] It is reported that bromine adds to 1-nitro-1,3-butadiene at the unfunctionalised double bond.[100] However, in more recent work it has been shown that 1-nitro- and 2,3-dimethyl-1-nitro-1,3-butadiene form 1,4-adducts with bromine.[101] Evidently, the latter can isomerise with rearrangement of the halogen to give the 3,4-adducts.

Dinitroalkadienes add bromine far more slowly than mono-nitro derivatives. 1,4-Dibromo-2,3-dimethyl-1,4-dinitro-2-butene is obtained by bromination of 2,3-dimethyl-1,4-dinitro-1,3-butadiene.[102]

Electrophilic halogenation is noticeably inhibited by phenyl substitution in the dinitroalkadienes. 1,4-Dinitro-1,4-diphenyl-1,3-butadiene does not give an adduct.

Bromination of 1-trimethylsilyl-1,3-butadiene gives a mixture of 3,4- and 1,4-adducts in equal amount.[103] The regioselectivity is the same as that observed on bromination of the all-carbon analogue, 4,4-dimethyl-1,3-pentadiene.

1,4-Dibromo-1-trimethylsilylbut-2-ene readily isomerises on heating with migration of bromine from the 1-position to the 3-position and from the 4-position to the 2-position. As a result, 3,4-dibromo-4-trimethylsilylbut-1-ene and 3,4-dibromo-1-trimethylsilylbut-1-ene are obtained.

Table 1. Chlorination of di- and poly-chlorobutadienes.

Chloro-substituted 1,3-butadiene	Products of chlorination	Content, %	Refs.
$CCl_2{=}CH{-}CH{=}CH_2$	$CCl_2{=}CH{-}CHCl{-}CH_2Cl$	69	[83]
	$CCl_2{=}CH{-}CH{=}CHCl$	31	
$CHCl{=}CCl{-}CH{=}CH_2$	$CHCl_2{-}CCl{=}CH{-}CH_2Cl$	*	[79]
$CHCl{=}CH{-}CCl{=}CH_2$	$CHCl{=}CH{-}CCl_2{-}CH_2Cl$	36/40**	[83]
	$CHCl_2{-}CH{=}CCl{-}CH_2Cl$	1/26**	
	$CHCl{=}CH{-}CCl{=}CHCl$	63/84**	
$CHCl{=}CH{-}CH{=}CHCl$	$CHCl_2{-}CHCl{-}CH{=}CHCl$	*	[83, 86]
$CH_2{=}CCl{-}CCl{=}CH_2$	$CH_2Cl{-}CCl{=}CCl{-}CH_2Cl$	*	[84, 85]
$CHCl{=}CCl{-}CCl{=}CH_2$	$CHCl{=}CCl{-}CCl_2{-}CH_2Cl$	71.5/66.2**	[87]
	$CHCl{=}CCl{-}CCl{=}CHCl$	28.6/28.7**	
$CCl_2{=}CCl{-}CH{=}CH_2$	$CCl_2{=}CCl{-}CHCl{-}CH_2Cl$	82	[88]
	$CCl_2{=}CCl{-}CH{=}CHCl$	18	
$CHCl{=}CCl{-}CCl{=}CHCl$	$CHCl_2{-}CCl{=}CCl{-}CHCl_2$***	*	[89]
$CCl_2{=}CCl{-}CCl{=}CH_2$	$CCl_2{=}CCl{-}CCl_2{-}CH_2Cl$	55	[87]
	$CCl_2{=}CCl{-}CCl{=}CHCl$	38.5	
$CCl_2{=}CCl{-}CH{=}CCl_2$	$CCl_3{-}CHCl{-}CCl{=}CCl_2$	72.8	[90]
	$CCl_2{=}CH{-}CCl_2{-}CCl_3$	27.2	

*One product isolated; **for *Z*- and *E*-isomers (given as a fraction); *** mainly the *cis*-isomer.

Thus, isomerisation leads in part to the formation of a dibromide which cannot be obtained by direct addition of bromine.

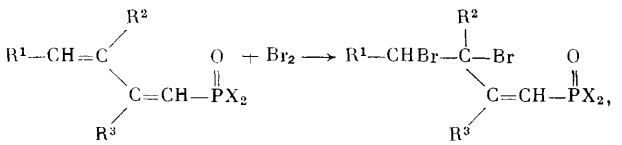
The isomeric ratio depends on the nature of the solvent and temperature: an increase in the solvent polarity and temperature favours the formation of the isomer having a silylated double bond.

The difference in the rate of bromination of 1-trimethylsilyl-1,3-butadiene and the all-carbon analogue suggests that the trimethylsilyl group exerts an electron-accepting activity relative to the tert-butyl group.[104]

Pudovik et al. established that chlorination of diethyl 1,3-butadiene-1-phosphonate takes place by attack at the non-phosphonated double bond.[105] More recently,[106] it was shown that bromination of both dialkyl 1,3-butadiene-1-phosphonates and the corresponding phosphonic acid chlorides also leads to the formation of the 3,4-adduct having the (*E*)-configuration.

Further studies on the interaction of 1,3-alkadiene-1-phosphonates with halogens has shown that various products result, depending on the preferred conformation of the 1,3-diene system. Thus, bromination of 1,3-alkadienephosphonates, prepared from PCl_5 and

the corresponding 1,3-alkadienes[107–109] and having, predominantly, the *S-trans*-conformation, proceeds with formation of 3,4-adducts:[110]



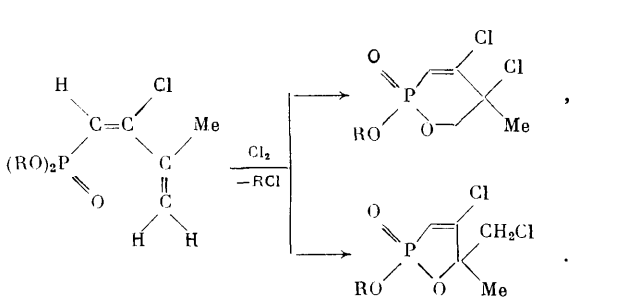
$R^1 = R^2 = R^3 = H$, Me; X = Cl, OMe, OEt.

Dehydrobromination with triethylamine leads to the corresponding 3-bromo-1,3-alkadienephosphonates.

Table 2. Chlorination of mono- and poly-chlorinated isoprenes.

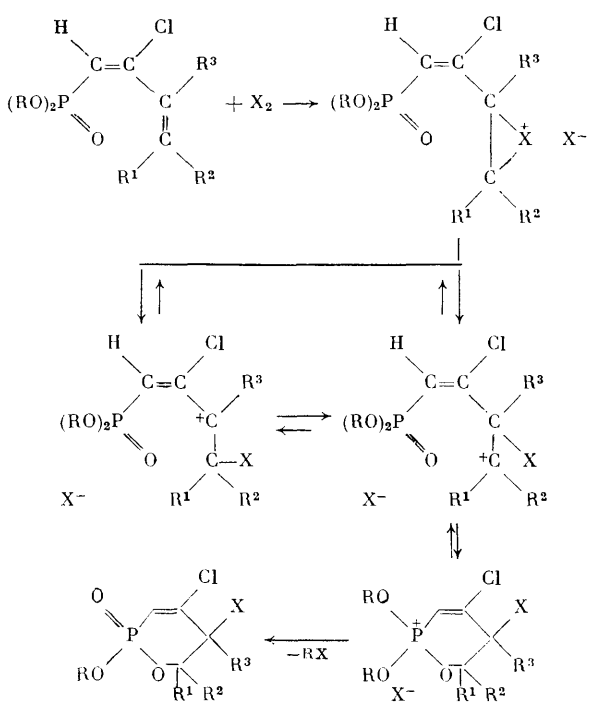
Chloro-substituted 2-methyl-chloro-1,3-butadiene	Chlorination products	Content, %	Refs.
$CHCl=C(Me)-CH=CH_2$	$CHCl=CMe-CHCl-CH_2Cl$	47	[91]
	$CHCl_2-CMe=CH-CH_2Cl$	33	
	$CHCl=CMe-CH=CHCl$	20	
$CH_2=C(Me)-CCl=CH_2$	$CH_2-C(Me)Cl-CCl=CH_2$	3.5	[92]
	$CH_2=CMe-CCl_2-CH_2Cl$	0.5	
	$CH_2Cl-CMe=CH-CH_2Cl$	55	
	$CH_2=C(CH_2Cl)-CCl=CH_2$	41	
$CH_2=C(Me)-CH=CHCl$	$CH_2Cl-C(Me)Cl-CH=CHCl$	38	[91, 93]
	$CH_2Cl-C(Me)=CH-CHCl_2$	30	
	$CH_2=C(CH_2Cl)-CH=CHCl$	12	
	$CHCl=C(Me)-CH=CHCl$	20	
$CH_2=C(Me)-CCl=CHCl$	$CH_2Cl-C(Me)Cl-CCl=CHCl$	19	[93, 94]
	$CH_2Cl-CMe=CCl-CH_2Cl$	24	
	$CH_2=C(CH_2Cl)-CCl=CHCl$	46	
$CH_2=C(Me)-CCl=CCl_2$	$CH_2Cl-C(Me)Cl-CCl=CCl_2$	36.8	[95]
	$CH_2=C(CH_2Cl)-CCl=CCl_2$	45.2	
	$CHCl=CMe-CCl=CCl_2$	18	
$Ph-CH=CH-CH=CHCl$	$Ph-CH=CH-CHCl-CHCl_2$	100	[96]

A mixture of 6- and 5-membered phosphorus-containing heterocyclics was obtained by chlorination of dialkyl 2-chloro-3-methyl-1,3-butadienephosphonates having predominantly the *S-cis*-conformation:[111–112]



The conversion to cyclic compounds is a consequence of a) the low energy of formation of such ring systems and b) the favourable transformation of the starting phosphonates into intermediates having a geometry which facilitates intramolecular nucleophilic attack by the phosphonyl group.[112,113] Chlorination of the corresponding 1,3-alkadienephosphonic dichloride does not effect cyclisation. Instead a complex mixture is obtained as a result of addition and dehydrochlorination of the adducts.[112]

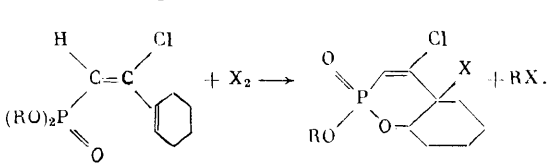
Halogenation of 2-chloro-3-alkyl-1,3-alkadienephosphonic acid esters having one or two substituents on the C_4 atom of the 1,3-diene system (which are obtainable via chlorination of the corresponding allenephosphonic acid dichlorides[114]) proceeds by heterocyclisation to yield 5,6-dihydro-2*H*-1,2-oxaphosphorins exclusively.[115,116] The highly selective interaction is due to the presence of an internal nucleophile (the phosphonyl group). This is attacked more readily by the electrophilic centre of the intermediate than by the anionic part of the reagent, thereby shifting the equilibrium towards formation of a stable six-membered phosphonium ion.[115]



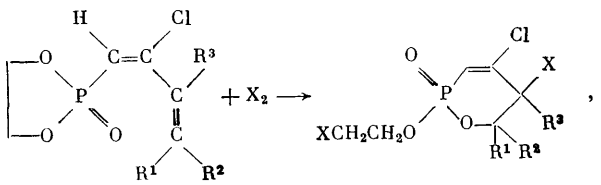
$R = Me, Et, Pr, Pr^i, Bu$; $R^1 = H, Me4$; $R^2 = Me, Et$; $R^3 = Me, Et, Pr, Pr^i$; $X = Cl, Br$.

Clearly, the preferential *S-cis*-conformation of the 1,3-diene system is particularly favourable for cyclisation.[117]

Halogenation[118,119] of dialkyl 2-chloro-2-(1-cyclohexenyl)-vinylphosphonates affords bicyclic *P,O*-containing heterocycles in which the C_3-C_4 double bond of the 1,3-diene system is incorporated in the ring.[118–120]

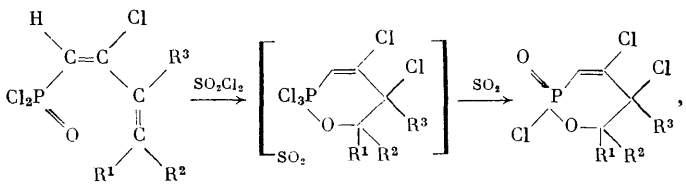


Halogenation of 2-(2-chloro-1,3-alkadienyl)-2-oxo-1,3,2-dioxaphospholanes proceeds in a similar way with associated cleavage of the dioxaphospholane ring and addition of halogen across the carbon-oxygen bond.[121]



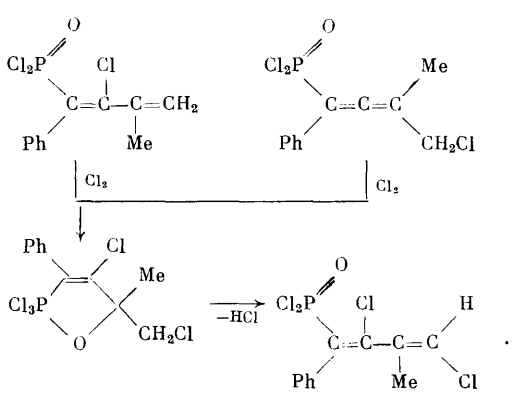
$R^1 = H$, Me; $R^2 = Me$; $R^3 = Me$, Et; X = Cl, Br.

Chlorination of 2-chloro-3-methyl-1,3-butadienylphosphonic acid dichloride with sulphuryl chloride yields a 3:1 mixture of the corresponding 5,6-dihydro-2*H*-1,2-oxaphosphorin and 2,5-dihydro-1,2-oxaphosphole.[122] However, 2-chloro-1,3-alkadienylphosphonic acid dichlorides with one or two substituents at the C_3 and C_4 positions give only a six-membered heterocycle under these conditions.[122]

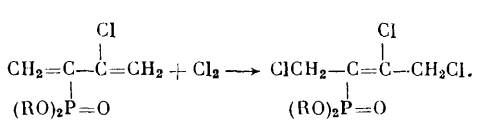


$R^1 = H$ or Me; $R^2 = H$ or Me, Et; $R^3 = CH_3$ or C_2H_5, C_3H_7.

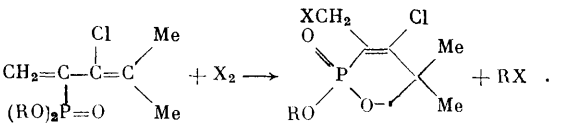
The interaction of 3-methyl-1-phenyl-2-chloro-1,3- and 3-methyl-1-phenyl-4-chloro-1,2-butadienylphosphonic acid dichloride with chlorine gives the same heterocycle, which eliminates HCl to give a dichloro-1,3-butadienylphosphonic acid dichloride.[123]



Halogenation of 3-chloro-1,3-alkadien-2-ylphosphonates gives a variety of products depending on the nature of the substituent at C_4 of the 1,3-diene system. Thus, interaction of dialkyl 3-chloro-1,3-butadien-2-ylphosphonates with chlorine leads to a 1,4-adduct.[124]



However, halogenation of 4-methyl-3-chloro-1,3-pentadien-2-ylphosphonic acid esters with two methyl groups at the 4-position yields 2,5-dihydro-1,2-oxophosphole derivatives.[124,125]



The geometry of the intermediate carbenium ion facilitates overlap of the unfilled orbital at the C_3-atom with the non-bonded orbitals of the phosphonyl group, leading to stabilisation of the entire system by ring closure.[124]

2. Addition of hypohalites

Hypohalites — hypohalous acids, their esters and mixed anhydrides — undergo addition to unsaturated compounds by a radical or ionic mechanism. In the latter case, reaction is conducted in dilute solution in the presence of radical inhibitors or in the presence of catalysts, such as BF_3, which facilitate electrophilic processes.

There is also the possibility of conjugate addition of hypochlorites to unsaturated compounds in hydroxylic solvents by using halogens, *N*-halogenamines and similar compounds with a positively polarised halogen atom. Under such conditions, the product obtained by addition of hypohalite contains a solvent molecule as well as halogen (solvo-adducts). Since the first step of the reaction (attack of the electrophile) is the same for both halogenation and conjugate hypohalogenation, the position of the halogen atom in the hypohalite adducts determines the direction of the initial attack in the first stage of halogenation. This reaction is important theoretically.

This reaction is also of significant synthetic value because it opens up a route to unsaturated epoxides, esters, carbonyl compounds, etc. The electrophilic addition of pre-formed hypohalites has only been studied in the hydrocarbon field. However, the products obtained by addition to 1,3-alkadienes are the same, irrespective of whether the hypohalite is pre-formed or formed *in situ*.

Conjugate addition of hypohalites to 1,3-alkadienes was studied systematically by A A Petrov et al. during the period 1935–1950.[126–129] 1,3-Butadiene, piperylene, isoprene and 2,4-hexadiene all undergo hypohalogenation. Various *N*-halogenamines and free halogen have been used as the halogenating agent. As a result of these studies, it has been established that hypohalites add predominantly at the 1,2-position, contrasting with addition of halogen and hydrogen halides. The proportion of 1,2- and 1,4-isomers is dependent on the method and the reaction conditions, as well as on the nature of the halogen.

Hydroxychlorination of 1,3-butadiene leads to the formation of the 1,2-adduct in 60–80% yield under various conditions.[126–131]

Alkoxyhalogenation of 1,3-butadiene also proceeds predominantly at the 1,2-position. As in the previously mentioned reaction, the regioselectivity depends on the method and temperature, the yield of 1,2-adduct being in the 80–90% range.[131–135] A 1,2-adduct is obtained in 62% yield by interaction of chlorine with a mixture of 1,3-butadiene and its mono-epoxide.[136]

Electrophilic addition of methyl hypochlorite to 1,3-butadiene in methanol affords 3-methoxy-4-chloro-1-butene in 70% yield. Approximately the same yield was obtained by treatment of methanolic 1,3-butadiene with chlorine, while radical addition of

methyl hypochlorite gives 4-methoxy-1-chloro-2-butene in 80% yield and the 1,2-adduct in 14% yield (contrary to the Markovnikov rule).[137]

Electrophilic addition of methyl hypochlorite to 1,3-butadiene in the presence of BF_3 gives a 37 : 17.5 mixture of chloroethers in CH_2Cl_2 and a 25 : 5.5 mixture in CCl_4. Fluorochlorobutenes are also formed, as has already been mentioned.[42]

Acoxychlorination of 1,3-butadiene with *N*-halogenamines in carboxylic acids gives a very small amount of ester, and the reaction has not been studied in detail.[126] Recently it was shown that the yield of acoxychlorides is significantly improved in the presence of $LiClO_4$; however, under these conditions the proportion of 1,4-adduct is increased markedly.[138]

Pre-formed acyl hypochlorites also add predominantly at the 1,2-position under electrophilic conditions.[21] The ratio of 1,2- and 1,4-adducts depends on the nature of the solvent: 2.8 : 1 in pentane, 2 : 1 in acetic acid, and 1.3 : 1 in acetonitrile.

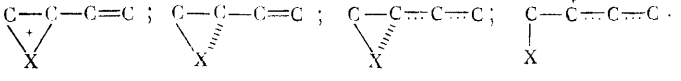
On hydroxy-, alkoxy- and acoxy-bromination of 1,3-butadiene with *N*-bromoamides, methyl hypobromite in the presence of BF_3, or with Br_2 in the appropriate hydroxylic solvent, the 1,4-adducts, if formed at all, are only obtained in small amounts; the corresponding bromoesters have not been isolated.[42,137,139,140]

The yield of 1,4-adduct is noticeably increased on acoxybromination with *N,N*-dibromobenzenesulfonamide in the presence of $LiClO_4$.[138] In contrast, alkyl hypobromites add exclusively at the 1,2-position in the presence of trimethyl borate.[141]

Only 1,2-adducts are obtained by hydroxy-, alkoxy- and acoxy-iodination of 1,3-butadiene with I_2/HgO in water or alcoholic media, or with iodoamides, e. g. NI_3, in acidic media.[142,143] The addition of pre-formed hypoiodites to alkadienes has not been studied.

The direction of the initial attack of halogen or hypohalite depends on the nature of the halogen atom; it is now thought that this directing influence is associated with the structure and stability of the intermediate onium ion.

It is conventional to represent the distribution of electron density in the intermediate by the following structures.[37]



The more the carbenium structure contributes to the intermediate ion, the more likely will reaction terminate by 1,4-addition. Kinetic and thermodynamic factors clearly play a leading role, being associated with the particular status of the system relative to that at equilibrium: on hypohalogenation under kinetic control, the less thermodynamically favourable 1,2-adduct is formed with a lower activation energy.[5]

Electrophilic addition of hypochlorous acid to piperylene leads to the formation of a mixture of 1,2-, 3,4- and 1,4-adducts in 47.1%, 39.7% and 13.2% yield respectively. The formation of the 3,4-adduct, which is contrary to the Markovnikov rule, requires further investigation.[144]

The interaction of piperylene with *N,N*-dichlorobenzenesulfonamide in methanol or ethanol proceeds by initial attack at the C_1-C_2 double bond to give, predominantly, a 5.6 : 4 mixture of 2-alkoxy-1-chloro-3-pentene and 4-alkoxy-1-chloro-2-pentene.[145]

The electrophilic interaction of piperylene with pre-formed hypochlorites (MeOCl) also provides a significant amount of 1,4-adduct. The yield of 1,2-, 1,4-, 4,1- and 4,3-adducts was 37–43%, 45–55%, 4–7% and 14–27%, respectively.[137]

It should be noted that the 3,4-adduct is formed in accordance with the Markovnikov rule, which is not the case for the addition of HOCl.[144]

2-Alkoxy-1-bromo-3-pentene and 4-alkoxy-1-bromo-2-pentene were obtained predominantly, in 5.6 : 4 proportion, by interaction of *N,N*-dibromobenzenesulfonamide with piperylene in alcoholic media (MeOH, EtOH).[146] Thus, as a general rule, alkyl hypobromites add to the 1,2-position to a greater extent than alkyl hypochlorites. However, in all cases piperylene forms much more of the 1,4-adduct. The reason for this is probably its rather high polarity.

Hypohalogenation of isoprene was first studied at the end of the last century.[56] More recently, reference has been made to the electrophilic addition of methyl and ethyl hypochlorite to isoprene in methanol and to the addition of tert-butyl hypochlorite in ethanol. A 3 : 2 mixture of 2-alkoxy-2-methyl-1-chloro-3-butene and 4-alkoxy-2-methyl-1-chloro-2-butene is formed in each case.[147] Other authors have reported slightly different ratios for these two products: 2 : 1 [148] and 3 : 1 [138] (with MeOCl), and 2.4 : 1 with EtOCl.[148] Small amounts of 3,4-adduct have also been reported.[148]

The interaction of isoprene with tert-butyl hypochlorite in acetic acid also leads primarily to the 1,2-adduct, which isomerises to the 1,4-adduct on treatment with acid.[147,149,150]

The 4,1-adduct is formed mainly if reaction is carried out in tert-butanol. This arises by radical addition of BuOCl to isoprene.

The addition of HOBr, alkyl hypobromites and alkyl hypoiodites to isoprene proceeds exclusively, or almost exclusively, at the 1,2-position.[148, 151, 152] This confirms that electrophilic bromination of isoprene is also initiated by attack at the C_1 atom.

The interaction of 1-tert-alkyl-substituted 1,3-butadienes with methyl hypoiodite (I_2, MeOH and HgO) leads to addition at the C_1-C_2 bond.[153]

Treatment of 1-phenyl-1,3-butadiene with dilute HOCl [154] and with HOBr [45] leads primarily to the 4,3-adduct. Later, the 1,2-adduct was also detected as one of the products.[155]

The study of reactions with halogeno-substituted alkadienes has revealed important mechanistic information on the addition of hypohalites to 1,3-dienes.

Hypohalites (HOBr, ROBr, ROI) add to 1-chloro- and 1-bromo-1,3-butadienes in the 4,3-mode.[14,156,157] Recently, an interesting reference was made to the conjugate chlorination of 1-chloro-1,3-butadiene in the presence of H_2O_2.[158] The reaction product is the hydroperoxide, $CHCl=CH-CH(OOH)CH_2Cl$.

Chloroprene and bromoprene add hypohalites in different ways depending on the nature of the halogen.

Contrasting with 1,3-butadiene, halogeno-1,3-alkadienes add HOCl and its esters predominantly at the 1,4-position; however 1,2-addition also takes place by attack at C_1 where the electron density is highest by virtue of the mesomeric effect of the halogen atom.[159] At the same time, reaction with HOBr or its esters and with HOI or its esters gives the 4,3-adduct almost exclusively with initial attack at C_4.[160–162] Clearly, these data would suggest that in the reactions of chloroprene and bromoprene with chlorine and iodine the direction of the initial attack is different.

Evidently, in both halogenation and hypohalogenation, the formation of an onium intermediate with participation of bromine and iodine is less facile in the presence of an electron-accepting C_1-C_2 bond. The intermediate is more stable if there is no halogen substitution of the double bond.

The recently reported conjugate addition of bromine and ethylene oxide to bromoprene is not in accord with the above. According to

the authors, reaction leads primarily to the formation of both types of 1,4-adduct as well as 3-bromethoxy-4-bromo-1-butene.[163]

1,2-Dichloro-1,3-butadiene adds methyl hypohalites at the unsubstituted double bond,[164] while 2,3-dichloro-1,3-butadiene gives both 1,2- and 1,4-adducts, the former predominating.[165]

1-Trialkylsilyl-1,3-alkadienes, just as the analogous all-carbon 1,3-alkadienes, add alkyl hypohalites only at the unsubstituted double bond (i.e. the non-silylated unsaturation) to give the 4,3-adduct.[166] The fact that the ratio of *cis*- and *trans*-isomers in the starting silyl-1,3-dienes and in the resulting 4,3-adducts is the same would suggest that an allyl-type carbenium ion is not formed in an intermediate step.

There is also reference in the literature to the formation of other solvo-adducts on halogenation of 1,3-butadiene. Thus, chlorination of 1,3-butadiene in DMF at −50 °C affords up to 70% of solvo-adducts as a mixture of two isomers which decompose at −10 °C:[167]

$$CH_2Cl{-}CH(OCH{=}N^+Me_2Cl^-){-}CH{=}CH_2;\quad CH_2Cl{-}CH{=}CH{-}CH_2OCH{=}N^+Me_2Cl^-.$$

III. The addition of compounds with an electrophilic hydrogen atom

Reagents in this category include hydrogen halides, hydroxylic compounds (water, alcohols, carboxylic acids) and mercapto compounds (hydrogen sulphide, thioalcohols, thioacids). Most of the data covering this aspect relates to the addition of hydrogen halides. Only the latter add to 1,3-dienes in the absence of catalyst, although in certain cases the use of a catalyst is necessary. An electrophilic mechanism is involved in the majority of reactions. Hydroxylic compounds add to 1,3-alkadienes only by an electrophilic mechanism in the presence of acid.

1. Hydrohalogenation

The hydrohalogenation of both 1,3-dienes and halogeno-1,3-dienes has been reported. There is reference to the addition of all four hydrogen halides to 1,3-alkadienes, but most of the data pertains to the reactions with HCl and HBr. A catalyst is required for the addition of HCl in non-aqueous media.

Table 3. Hydrochlorination of some chloro-substituted 1,3-alkadienes.

Chloro-substituted 1,3-alkadiene	Products of hydrochlorination	Content, %	Refs.
$CCl_2{=}CH{-}CH{=}CH_2$	$CCl_2{=}CH{-}CHCl{-}Me$	*	[196]
$CHCl{=}CCl{-}CH{=}CH_2$	$CCl_2{=}CCl{-}CHCl{-}Me$	*	[196]
$CH_2{=}CCl{-}CCl{=}CH_2$	$Me{-}CCl{=}CCl{-}CH_2Cl$	*	[84, 85]
$CH_2{=}C(Me){-}CH{=}CHCl$	$Me{-}C(Me)Cl{-}CH{=}CHCl$	74.6	[197]
	$CH_2{=}CMe{-}CHCl{-}CH_2Cl$	3.3	
	$CH_2Cl{-}CMe{=}CH{-}CH_2Cl$	8.6	
	$CHCl_2{-}CH{=}CMe_2$	13.5	
$CH_2{=}C(Me){-}CCl{=}CH_2$	$Me_2C{=}CCl{-}CH_2Cl$	49	[198]
	$CH_2Cl{-}CMe{=}CCl{-}Me$	33	
$CH_2{=}C(CH_2Cl){-}CCl{=}CH_2$	$(CH_2Cl)_2C{=}CCl{-}Me$	82	[92]
	$Me{-}C(CH_2Cl){=}CCl{-}CH_2Cl$	18	

* Only one product isolated.

1,3-Butadienes polymerise in the presence of HF.[168] Treatment with HCl in the presence of a catalyst (Cu_2Cl_2, $FeCl_2$, $FeCl_3$, $ZnCl_2$, $HgCl_2$) at room temperature in acetic acid, or without solvent at −80 °C, leads to a mixture of products containing 75−80% 3-chloro-1-butene and 20−25% 1-chloro-2-butene. The addition of peroxide has no effect on the course of the reaction. There is no interconversion of the two isomeric chlorides in the absence of catalyst, but on prolonged treatment with HCl or in the presence of catalyst (Cu_2Cl_2, $FeCl_3$) the mixture equilibrates to give ~25% 1,2-adduct.[169–171] Thus, on hydrochlorination the thermodynamically less stable isomer is present in far greater amount than in the equilibrated mixture. It is also reported that more than 96% of the 1,2-adduct is formed at low temperatures.[172]

The kinetics of the addition of HCl to 1,3-butadiene has been studied.[173] Electrophilic addition of HBr to 1,3-butadiene leads to the preferential formation of 1-bromo-2-butene. At equilibrium the mixture contains ~80% 1,2-adduct at −80 °C, and 80% 1-bromo-2-butene at 40 °C.[174,175] 1,2-Addition takes place to the extent of 65−90% in the absence of peroxide and at low temperatures.[175]

1-Iodo-2-butene is obtained by passing 1,3-butadiene through 57% HI at 20 °C.[169]

For the interaction of hydrogen halides with homologues of 1,3-butadiene, the direction of the initial electrophilic attack is in accord with the Markovnikov rule: the proton always adds to the terminal atom of the conjugated system since in this way the most stable (conjugated) carbenium ion is formed. For halogenation, there are a few exceptions to this rule. As seen in the tabulation above, small amounts of regioisomer may also be formed as a result of the two possible modes of cleavage of the halonium intermediate.

Because of the symmetry of the intermediate carbenium ion, hydrochlorination and hydrobromination of piperylene leads to the formation of only one halogenopentene isomer: 4-chloro- or 4-bromo-2-pentene. These may arise either by 1,2- or 1,4-addition of the hydrogen halide.[48,176,177] But, in fact, the 1,2-pathway is preferred. This is evident from a study of the interaction of *trans*-piperylene with DCl in a variety of solvents in the temperature range −78 to 25 °C. In all cases the 1,2-adduct is formed preferentially, i.e. 4-chloro-5-deuterio-2-pentene (62−78% of the mixture).[178]

The addition of HCl and HBr to isoprene has been studied by many authors.[179–183] Preferential 1,4-addition is reported, except in one instance[183] where 76−85% of the 1,2-adduct was isolated on hydrochlorination of isoprene at low temperatures under kinetic control.

Treatment of 2,4-hexadiene with HBr affords 90% of the 2,3-adduct,[179,184] while HCl and HBr react with 2,3-dimethyl-1,3-butadiene primarily by 1,4-addition.[46,179]

A special note should be made of the addition of HCl to the third isomer of dimethylbutadiene, namely 4-methyl-1,3-pentadiene.[88] Here, the product is reported to be 4-chloro-4-methyl-1-butene. Thus, if this information is correct, then it is the only example which is not in accord with the general rule mentioned above: that the proton adds only to the terminal carbon atom of the conjugated system. With 4-methyl-1,3-pentadiene, the intermediate carbenium atom is evidently stabilised by hyperconjugation with the C−H bonds of the two methyl groups.

Hydrochlorination and hydrobromination of 1-phenyl-1,3-butadiene leads to the 4,3-adducts, i.e. 1-phenyl-3-halogeno-2-butenes.[185,186]

1-Chloro-1,3-butadiene adds HCl at −10 to −15 °C in the presence of Cu_2Cl_2 to give primarily 1,3-dichloro-1-butene (73%

4,3-adduct) together with a mixture of 1,1-dichloro-2-butene and 1,4-dichloro-2-butene (in 15% yield).[187] A catalyst, e.g. $AlCl_3$ or $FeCl_3$, is necessary for this reaction in non-aqueous media.[188]

1,3-Dihalogeno-2-butenes are formed predominantly by interaction of chloroprene or bromoprene with HCl or HBr in the presence of copper halides.[189–194] The reaction of bromoprene with HCl, either in the presence or absence of Cu_2Cl_2, is accompanied by isomerisation and halogen exchange to give 3% of the 2,1-adduct.[195] The formation of a small amount of primary carbenium ion is possibly associated with the participation of the halogen atom in the conjugated system.

The hydrochlorination of a numbr of dichlorobutadienes and mono- and dichloro-isoprenes is summarised in Table 3.

It is clear from the tabulation that addition of HCl takes place preferentially at the unfunctionalised double bond.

The replacement of the hydrogen atoms of the methyl group by chlorine lowers its electron-donating properties in relation to the conjugated double bond system, and the mesomeric effect of a chlorine atom at the other double bond has a clear effect on the orientation of attack by the proton.

1,2-Dichloro-1,3-butadiene adds HBr at the unchlorinated double bond in accordance with the Markovnikov rule,[198] and 2,3-dichloro-1,3-butadiene affords the 1,4-adduct.[85]

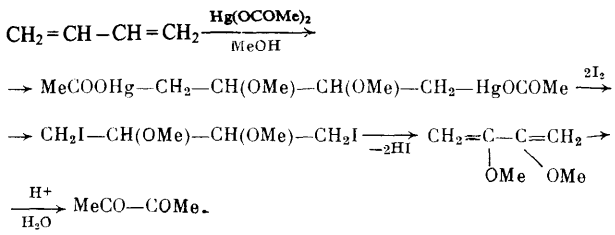
Hydrobromination of 1-phenyl-4-chloro-1,3-butadiene takes place at the 4,3-position, i.e. by attack of proton at the terminal carbon atom of the chlorinated double bond.[45]

2. Addition of water, alcohols and organic acids

The reactions of 1,3-alkadienes with hydroxyl-containing compounds have not been extensively studied, although they are of significant interest as methods of preparing unsaturated alcohols and ethers. Certain of the latter may serve as suitable synthons in, for example, the synthesis of natural products and their analogues.

Diacetyl has been obtained by addition of water to 1,3-butadiene in the presence of Hg^{2+} and acid.[199,200]

The initial stage of formation of diacetyl involves addition of methanolic mercuric acetate to 1,3-butadiene according to the following scheme.[201]

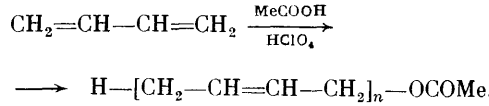


A mixture of 1,2- and 1,4-adducts was obtained by hydration of 2-alkyl-1,3-butadienes in the presence of mineral acid. Hydration of isoprene gives primarily 3-methyl-1-buten-3-ol.[202]

The addition of water to 1-phenyl-1,3-butadiene in the presence of acid, under kinetic control, proceeds with initial protonation of the C_4 atom and formation of a mixture of isomeric alcohols (4,3- and 4,1-adducts).[203]

A kinetic study has been made of acid-catalysed hydration of 1,3-butadiene, chloroprene, bromoprene, and 2-phenyl-1,3-butadiene.[202]

Addition of acetic and propionic acid to 1,3-butadiene in the presence of perchloric acid affords mainly the 1,4-adduct. Telomerisation takes place simultaneously with the formation of esters having two or more linearly bonded butene residues.[204]



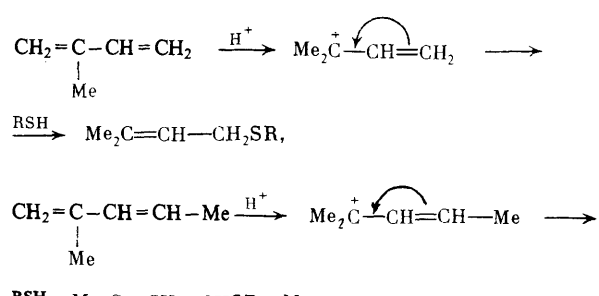
In the case of acetic acid, the yield of 1,4-adduct (n = 1) is ~15% and that of the telomer (n = 2) is ~35%. Isomeric esters were also isolated in trace amounts as a result of telomerisation of the corresponding isomeric carbenium ions. Several patents have been published on this process, e.g. Ref. 205.

The addition of acetic acid to isoprene in the presence of $HClO_4$ proceeds mainly by 1,4-addition and is accompanied by telomerisation.[206] This reaction has been applied to the synthesis of prenyl acetate, aliphatic terpenes, sesquiterpenes, etc., notably geranyl acetate and farnesyl acetate.

Hydration of chloroprene in the presence of acid proceeds predominantly by 1,4-addition with the formation of 3-chloro-2-buten-1-ol.[192] More recently, it has been shown that methyl vinyl ketone is formed as a by-product in small amounts, i.e. 1,2-addition also takes place.[202]

3. Addition of thiols

Thiols and mercapto-containing compounds in general add to unsaturated hydrocarbons and their derivatives primarily by radical and nucleophilic mechanisms. Electrophilic addition does not normally take place. However, reference has been made to the electrophilic addition of thiols to 1,3-dienes in the presence of catalytic amounts of $HClO_4$.[207] In this way, 1,4-adducts are formed preferentially (> 80% yield). With unsymmetrical alkadienes proton attack takes place at the terminus having the most nucleophilic carbon atom to give the corresponding carbenium ion.



Reaction with 2-methyl-1,3-pentadiene is more facile than with isoprene, as would be anticipated for electrophilic addition.

IV. Addition of compounds with an electrophilic carbon atom

Organic halides add to a multiple bond only in the presence of a Friedel-Crafts-type catalyst. Acyl halides and α-halogenoethers are the most reactive.

1. Addition of alkyl and alkenyl halides

The first reference to the addition of alkyl and alkenyl halides to 1,3-alkadienes was made in a French patent in 1938.[208] This reaction was studied in detail by Leets and A A Petrov et al., commencing in 1954.[209–213,215–223] In the addition to unsaturated halogeno derivatives, satisfactory yields were only obtained by reaction with tertiary alkyl halides. The latter add in the 1,4-position, reaction being accompanied by telomerisation, i.e. 1:1 adducts are formed together with 2:1, 3:1, etc. adducts. Most reactions have been carried out in the presence of $SnCl_4$ as catalyst, although improved yields may be obtained with $BiCl_3$.[214] The regioselectivity of addition to unsymmetrical alkadienes is the same as that with hydrogen halides. The products of these reactions have been widely used in the synthesis of unsaturated hydrocarbons, carbonyl compounds, carboxylic acids, and various heterocyclics.[211]

The reaction between 1,3-alkadienes and allylic halides is synthetically the most interesting, notably the reaction of isoprene with isoprene-HCl adducts.[215,216] In this case, a mixture of 1:1 adducts is obtained, comprising geranyl chloride (52–56%), linalyl chloride (7–8%), lavandulyl chloride (9–10%), α-terpenyl chloride (18–20%) and prenyl chloride dimers (9–10%).[217] Farnesyl chloride is one of the components of the fraction containing a 2:1 mixture of telomers.[218–200] This compound can also be obtained by reaction of isoprene with geranyl chloride.[221,222]

The above-mentioned reaction has been applied in recent years to the synthesis of various natural compounds and their analogues, including vitamins, hormones and insecticides.

Studies have also been made of the products formed by telomerisation of other alkadienes with various allylic chlorides. Thus, a number of homologues, isomers and analogues of natural terpenes have been obtained.

2-Chloro-1,3-butadiene adds alkyl and alkenyl halides in the 1,4-position, the regioselectivity being the same as with HCl.[223]

2. Addition of halogenoethers

The study of the reaction between 1,3-dienes and α-halogenoethers in the presence of Friedel–Crafts catalysts was undertaken much earlier than that with other organic halides.[224] This reaction was investigated in detail by Pudovik between 1945 and 1949.[225–227] Catalytic activity decreases in the following order: $ZnI_2 > ZnBr_2 > ZnCl_2 > HgCl_2 > Cu_2Br_2 > PdCl_2 > CoCl_2$. Ethers of the type ArCH(Hal)OMe react with alkadienes without a catalyst. A mixture of 1,2- and 1,4-adducts is obtained from 1,3-butadiene, the former comprising 75–80% if isomerisation is prevented. At equilibrium the mixture contains 75% of 1-methoxy-3-pentene.

Isoprene affords 1,4-adducts predominantly, i.e. 4-alkoxy-1-chloro-2-methyl-2-butenes.[227] The reaction of 1,3-alkadienes with α-chloroalkyl acetates leads to alcohols following 1,4-addition.[228] The reaction of alkadienes with cyclic α-chloroethers proceeded in the same manner.[229–231] 4-Alkoxy-1,3-dichloro-2-butenes were chiefly obtained by treatment of chloroprene with α-chloroethers, i.e. the regioselectivity of the reaction is the same as that with hydrogen halides.[232,233] Tetrahydropyran derivatives were mainly formed by reaction of alkadienes with α,α-dichloroalkyl ethers.[234] The products obtained by reaction with α-halogenoethers have been used synthetically in a variety of ways, e.g. in the synthesis of juvenile hormones and insecticides.[211,234–236]

3. Addition of acyl halides

The reactions of unsaturated compounds with acyl halides with Friedel–Crafts catalysts were first studied in the 1960s.[211,237,238]

It was not until several years later that Badanyan et al. reported the successful chloracylation of alkadienes, e.g. isoprene, chloroprene, isomeric dichlorobutadienes and other alkadienes.[239–243] Acyl halides add to alkadienes in the presence of $AlCl_3$ at −78 °C to give ethylenic ketones of the type $RCOCH_2CX=CHCH_2Cl$, which readily dehydrochlorinate with triethylamine to give primarily *cis*-2,4-dienones of the type (*E*)-$RCOCH=CX-CH=CH_2$.[240,241] Dehydrochlorination can take place during the reaction.

Unsaturated aromatic ketones are obtained by chloroacylation of 1,3-alkadienes and their halogen-containing derivatives in the presence of aromatic compounds:[243]

$$CH_2=CX-CX=CH_2 \xrightarrow[AlCl_3]{MeCOCl,\ PhR} Me-CO-CH_2-CX=CX-CH_2-C_6H_4R.$$

Dibasic dicarboxylic acid chlorides (derived from suberic, azelaic and sebacic acids) react similarly with 1,3-butadiene and chloroprene under the same conditions. The products formed by double addition readily dehydrohalogenate with triethylamine to give (*E,E*)-diketotetraenes of the type $[CH_2=CH-CX=CHCO(CH_2)_n]_2$.[242]

Acylation of 1,3-butadiene with acetyl fluoroborate in the presence of acetic anhydride (in 1:1 proportion) leads to the formation of 1,2- and 1,4-solvo-adducts, namely (*E*)-3-acetoxy-1-hexen-5-one (by 1,2-addition) and 1-acetoxy-2-hexen-5-one (by 1,4-addition), respectively, in 1:8 proportion.[244,245]

$$CH_2=CH-CH=CH_2 \xrightarrow[(MeCO)_2O]{MeCO^+,\ BF_4^-} \begin{cases} \rightarrow Me-CO-CH_2-CH(OCOMe)-CH=CH_2, \\ \rightarrow Me-CO-CH_2-CH=CH-CH_2OCOMe. \end{cases}$$

The addition of acetyl fluorosulfonate to alkadienes provides a potential synthetic route to acyl-1,3-alkadienes.[246] The latter are obtained by treatment of the adducts with triethylamine. If the dehydrohalogenation is carried out in methanol, the corresponding solvo-adducts are formed, i.e. β-alkoxy-γ,δ-ethyleneketones.

$$CH_2=CH-CH=CH_2 \xrightarrow{Me-CO-OSO_2F} Me-CO-CH_2-CH(OSO_2F)-CH=CH_2$$

$$\xrightarrow{Et_3N} Me-CO-CH=CH-CH=CH_2, \qquad \xrightarrow{Et_3N,\ MeOH} Me-CO-CH_2-CH(OMe)-CH=CH_2.$$

V. The addition of compounds with an electrophilic atom of sulphur or its analogues

Organosulphur compounds with the sulphur atom in all three valence states may participate in electrophilic addition or substitution of 1,3-alkadienes. Most of the data in this area relates to the reactions of 1,3-alkadienes with sulphenyl chlorides, RSCl. However, reactions with sulphinyl chlorides, sulphonyl chlorides and SO_3 are also known.

1. Addition of sulphenyl halides and their analogues

Reactions of unsaturated compounds with sulphenyl halides and their analogues have already been the subject of a review.[247] They all proceed by electrophilic attack with the intermediate formation of an episulphonium ion.[248,249] With unsymmetrical olefins, adducts may arise in accordance with, and contrary to, the Markovnikov rule, the Markovnikov products predominating under kinetic control. These reactions are more facile in polar media, and are characterised by *trans*-addition.

Studies have been made of the reactions of sulphenyl chlorides with 1,3-alkadienes, their halogeno- and trialkylsilyl-derivatives, and with 1,3-alkadienylphosphonates. 1,2-Addition or 3,4-addition takes place in all cases, either exclusively or predominantly.[250–257] As is evident from Table 4, sulphenyl ion initially attacks 1-alkyl- or 1-aryl-derivatives at the 4-position, 2-methyl-derivatives at the 1-position, and 2-phenyl-derivatives at the 4-position. The rate of addition can vary by factors of ten.[252]

The nature of the solvent has a pronounced effect on the regioselectivity of addition. Thus, in acetic acid, isoprene and *p*-chlorobenzenesulphenyl chloride give 1,2-, 4,3- and 4,1-adducts in 20:20:60 proportion, while in nitromethane the ratio is 61:18:21, in THF it is 33:27:40, and in CCl_4 it is 63:22:15.[253]

The 1,2-adducts readily isomerise, even at room temperature, to give the thermodynamically more stable 1,4-adducts. At equilibrium the mixture contains more than 90% of the 1,4-isomer. The rate of isomerisation increases on heating in the presence of sulphuric acid as catalyst. The nature of the substituent on the sulphur atom influences the rate of isomerisation. Thus, the products obtained by addition of PhSCl isomerise less than those obtained with MeSCl.[251]

Acetylthiosulphenyl chloride (MeCOSSCl) adds to 1,3-butadiene in the same manner at −20 °C in CH_2Cl_2. With piperylene, addition takes place preferentially (82%) at the mono-substituted double bond.[255]

Dimethyl and diphenyl disulphide undergo 1,4-addition with 1,3-butadiene in the presence of boron fluoride. Reaction also proceeds via an episulphonium intermediate, although in the presence of a catalyst rearrangement takes place.[256]

Diethoxyphosphorylsulphenyl chloride adds to 1,3-butadiene to give the 1,2-adduct in accordance with the Markovnikov rule.[257]

p-Chlorobenzenesulphenyl chloride adds to 1-chloro-1,3-butadiene at the unfunctionalised double bond.[253]

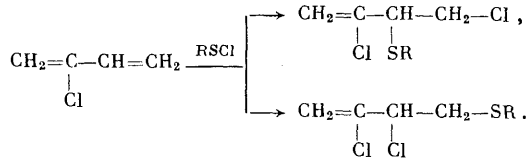
The reaction of methyl- and *p*-chlorobenzene-sulphenyl chloride with chloroprene proceeds chemo- and regio-selectively. Attack takes place at the more nucleophilic C_3-C_4 double bond with the

Table 4. Addition of *p*-chlorobenzenesulfenyl chloride to 1,3-alkadienes.

1,3-Alkadiene	Temperature, °C	Solvent	Reaction products	Content, %	Refs.
$CH_2=CH-CH=CH_2$	25	$C_2H_2Cl_4$	$ArS-CH_2-CHCl-CH=CH_2$	>95	[252]
$CH_2=CH-CH=CH-Me$	»	»	$ArS-CH_2-CHCl-CH=CH_2$	73/60*	[252]
			$CH_2=CH-CHCl-CH-SAr-Me$	24/35*	
$CH_2=C(Me)-CH=CH$	»	»	$ArS-CH_2-CMeCl-CH=CH_2$	72	[252]
			$CH_2=CMe-CHCl-CH_2SAr$	23	
$CH_2=C(Me)-C(Me)=CH_2$	»	»	$ArS-CH_2-CMeCl-CMe=CH_2$	см. 2*	[252]
$CH_2=CH-CH=CMe_2$	»	»	$ArS-CH_2-CHCl-CH=CMe_2$	см. 2*	[252]
$CH_2=CH-C(Me)=CH-Me$	»	»	$ArSCH_2-CHCl-CMe=CH-Me$	53 3*	[252]
			$CH_2=CH-CMeCl-CH(SAr)-Me$	45 3*	
$Me-CH=CH-CH=CH-Me$	»	»	$ArS-CHMe-CHCl-CH=CH-Me$	>95 4*	[252]
(*E*) $CH_2=C(Me)-CH=CH-Me$	»	»	$ArS-CH_2-CMeCl-CH=CH-Me$	73	[252]
			$CH_2=CMe-CHCl-CH(SAr)-Me$	22	
(*E*) $PhCH=CH-CH=CH_2$	20	CCl_4	$Ph-CH=CH-CHCl-CH_2SAr$	см. 2*	[253]
$CH_2=C(Ph)-CH=CH_2$	»	»	$CH_2=CPh-CHCl-CH_2SAr$	20	[253]
			$CH_2Cl-CPh-CH-CH_2SAr$	80	
$CH_2=C(Ph)-C(Ph)=CH_2$	»	»	$CH_2ClCPh-CPh-CH_2SAr$	см. 2*	[253]

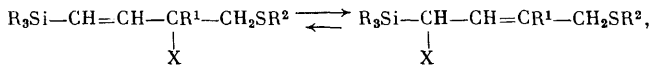
* The first number refers to the yield from the *Z*-isomer, and the second number from the *E*-isomer; 2* only one isomer isolated; 3* the yield was almost the same from either *E*- or *Z*-isomer; 4* the *Z*-adduct was formed from the *Z,Z*-isomer; the *Z*/*E* proportion was ≃28:67 from the *Z,E*-isomer, and ≃22:73 from the *E,E*-isomer.

predominant formation of the Markovnikov adduct (74–94%) and 6–26% of the anti-Markovnikov adduct.[255]



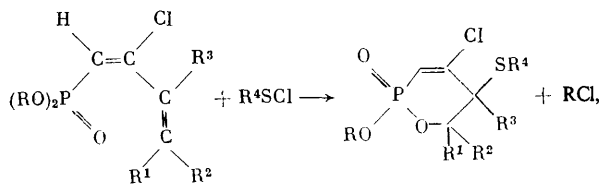
The addition of alkylsulphenyl halides (chlorides and bromides) to 1-trialkylsilyl-1,3-dienes takes place at the non-silyated double bond in accordance with the Markovnikov rule, i.e. formation of 4,3-adducts.[258]

The high regioselectivity is evidently a consequence of increased steric hindrance at the silylated double bond. It is also probable that the addition at the 4,3-position is facilitated by the increased stability of the episulphonium ion at the unfunctionalised double bond relative to that at the C_1-C_2 double bond due to $d_\pi-p_\pi$ interaction. The resulting 4,3-adducts undergo allyl rearrangement on heating (distillation) with migration of halogen from tertiary to primary carbon atom.[258]



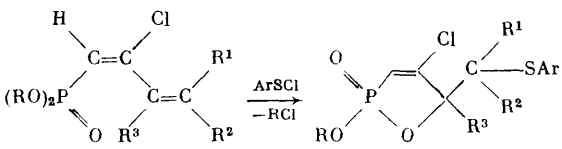
R = Me, Et; R^1 = H; Me; R^2 = Me, Et; X = Cl.

Sulphenyl chlorides react with phosphorylated 1,3-alkadienes at the C_3-C_4 double bond, as is the case with addition of halogens (as mentioned earlier). A 5- or 6-membered heterocycle is then formed depending on the nature of the sulphenyl chloride. This interaction is not regioselective since a number of conformers are involved in the reaction.[259] With alkylsulphenyl chlorides, the *cis*-conformer of the alkadienylphosphonate is involved.



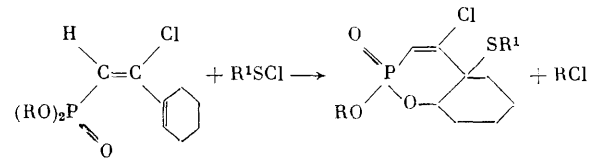
R^4 = Me, Pr^i.

Because of steric hindrance by substituents, the interaction with arylsulphenyl chlorides involves the *S-trans*-conformer, which leads to 2,5-dihydro-1,2-oxaphospholes:[259]



Ar = Ph, *p*-MeC_6H_4.

The interaction of 2-chloro-2-(1-cyclohexenyl)vinylphosphonates with sulphenyl chlorides affords hexahydrobenz-2*H*-1,2-oxaphosphorines, irrespective of the nature of the substituent on the sulphur atom.[260]



R^1 = Me, Pr^i, Ph, *p*-MeC_6H_4.

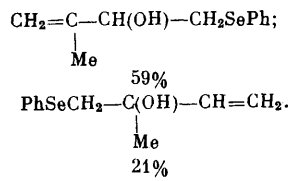
The fact that 6-membered bicyclic *P,O*-heterocyclics are formed predominantly, irrespective of the nature of the organic residue (on sulphur), can be explained, in part, by the stability of the *S-cis*-conformer of the starting dienephosphonate and, in part, by the probable increased stability of the intermediate involved in formation of the bicyclic compound relative to that of the spirocyclic intermediate which would arise if a 5-membered *P,O*-heterocycle were formed.

Phenylselenenyl chloride adds to isoprene both at the 1,2- and 4,3-positions. The ratio of the adducts is 1:1 at 0 °C and 5:2 at 60 °C.[261]

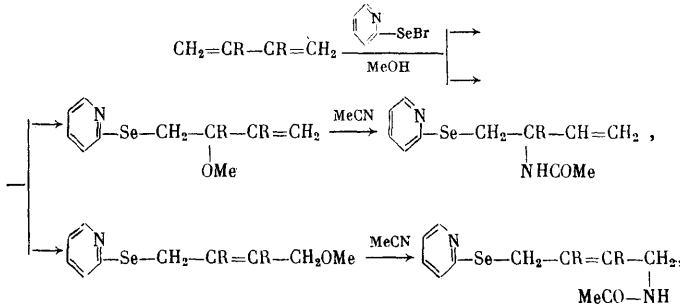
Alkylselenenyl chlorides add to *Si*-containing 1,3-alkadienes only at the unfunctionalised double bond, in the same manner as alkylsulphenyl chlorides. Here, the electrophile (RSe^+) attacks C_4 of the conjugated system to give the corresponding 4,3-adducts.[262]

The interaction of 1,3-alkadienes with selenenyl chlorides may also lead to solvo-adducts,[263] as is the case with halogenation (see earlier). Hydroxyl-containing selenoethers are obtained by reaction of PhSeCl with 1,3-butadiene, isoprene, and 2,3-dimethyl-1,3-butadiene in acetonitrile-THF in the presence of water.

With isoprene, addition takes place predominantly at the monosubstituted double bond. 1,4-Adducts are not formed.



The interaction of 1,3-butadiene and 2,3-dimethyl-1,3-butadiene with 2-pyridylselenenyl bromide in methanol and acetonitrile proceeds in a similar way in the presence of CF_3SO_3H, although here solvo-adducts of a different type are formed.[264] With 1,3-butadiene, the ratio of 1,2- and 1,4-adduct was 67:33, while 2,3-dimethyl-1,3-butadiene gave only the 1,4-adduct.



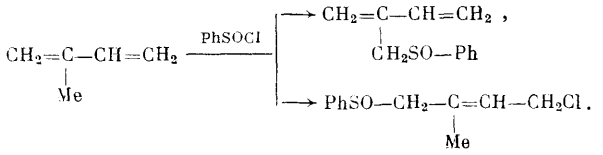
R = H or Me.

As 1,2-adducts readily isomerise into 1,4-adducts, the latter may arise via isomerisation of initially-formed 1,2-adducts.

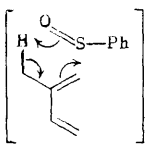
The interaction of 1,3-alkadienes with $PhSeCl_3$ has also been studied.[265] 1,3-Butadiene affords 2-chloro-3-butenyl(phenyl)selenide dichloride, which can be converted to chloroprene on hydrolytic removal of the selenium function. Isoprene gives a mixture of 1,2- and 4,3-adducts in 1 : 1 proportion.

2. Reactions with oxygen-containing sulphur compounds

The interaction of 1,3-alkadienes with benzenesulphinyl chloride has only been studied in the case of isoprene.[266,267] Reaction proceeds predominantly by sulphinylation, but the mechanism of the conversion has not yet been established with certainty.

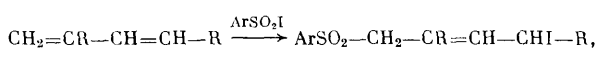


It is thought that sulphinylation takes place by an ene-type reaction through the following transition state:



Reactions of 1,3-alkadienes with aromatic sulphonyl halides has been studied widely. In the majority of cases, reaction proceeds in the presence of a catalyst, notably copper halides, by a radical-ion mechanism (Ascher–Vofsi reaction).[268,269] The same is true for the related sulphonylhalogenation based on the reaction between diazo compounds and SO_2.[270]

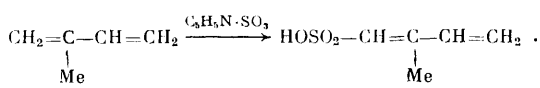
Sulfonylhalogenation by electrophilic addition in the absence of catalyst is rare. However, 1,4-addition does take place in the absence of catalyst by reaction of 1,3-butadiene, *trans*-piperylene, isoprene, and 2,3-dimethyl-1,3-butadiene with arenesulfonyl iodides.[271] The regioselectivity of the reaction with piperylene and isoprene is in accord with a mechanism involving electrophilic addition.



R = H, Me.

The amount of the lesser regioisomer, i.e. the 1,4-adduct, depends on the reaction conditions, but never exceeds 17%.

Direct sulfonylation of alkadienes with pyridine.SO_3 complex is of potential synthetic interest, but has not been greatly studied.[272] In all examples, replacement of hydrogen proceeds at the most nucleophilic carbon atom, being C_1 in the case of isoprene.



The mechanism of this reaction has not been studied. However, in all probability it is similar to aromatic electrophilic substitution. The authors of these investigations consider that reaction involves the intermediate formation of a 1 : 2 complex between the alkadiene and pyridine.SO_3.

VI. The addition of compounds with an electrophilic nitrogen atom

The addition of compounds with an electrophilic nitrogen atom to unsaturated compounds has not been studied extensively. The mechanism of such reactions has only been established in certain instances, but even here there is uncertainty in some respects. There is evidence to support electrophilic attack at the double bond by such reagents as nitrosyl chloride ($NO^{\delta+}Cl^{\delta-}$), N_2O_3, N_2O_4, nitryl halides ($NO_2^{\delta+}Hal^{\delta-}$), etc. However, one cannot exclude the possibility of addition of the reagents via a four-centred transition state, or by a free radical mechanism as a result of the weak polarisation.[2,273]

1. Addition of nitrogen oxides

NOCl adds to 1,3-butadiene at the 1,2-position in accordance with the Markovnikov rule, followed oxidation of the resulting nitroso compounds to nitro derivatives.[274] It is likely that this reaction proceeds through a four-centred transition state.[5]

Dinitro compounds and nitro(nitroso)alkenes are obtained by interaction of conjugated dienes with N_2O_3. Thus, 2,3-dimethyl-1,3-butadiene affords 2,3-dimethyl-1,4-dinitro-2-butene and 2,3-dimethyl-4-nitro-1-nitroso-2-butene dimer.[275,276]

1,3-Butadiene,[277,278] 2,3-dimethyl-1,3-butadiene,[279] 2,3-di-tert-butyl-1,3-butadiene[280] and 1,4-diphenyl-1,3-butadiene[281,282] yield 1,4-adducts with N_2O_4, while 2,3-diphenyl-1,3-butadiene[283] affords a mixture of 1,2- and 1,4-adducts.

The interaction of nitryl chloride with 1,3-butadiene, isoprene and piperylene in methylene chloride leads to a mixture of 1,4-adducts and products derived by isomerisation of the latter wherein the double bond migrates towards the nitro group.[284,285] Such isomerisation of unsaturated nitro compounds has been reported elsewhere in the literature.[286]

The addition of nitryl iodide (N_2O_4 + I_2) to 1,3-alkadienes leads to the formation of only 1,4-adducts.[287–289]

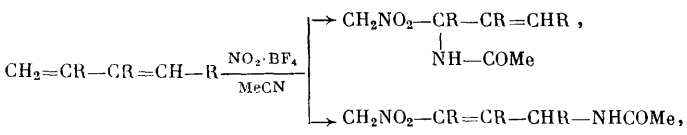
It is possible to nitrate 1,3-butadiene with concentrated nitric acid.[290,291] However, there are no details on this reaction, and it cannot be excluded that it proceeds with the participation of nitrogen oxides by a radical mechanism.

Recently, the reaction of 1,3-alkadienes with nitronium acetate [HNO_3 + $(MeCO)_2O$] was studied.[292] Thus, the reagent adds to isoprene to give a 3 : 7 mixture of 1,2- and 1,4-adducts, the latter containing 85% of the *trans*-isomer. In contrast to nitronium acetate, the corresponding trifluoroacetate (trifluoroacetic anhydride with added NH_4NO_3) adds to 1,3-alkadienes at the 1,2-position according to the Markovnikov rule.[293]

The adducts formed in the two reactions mentioned above readily eliminate acetic or trifluoroacetic acid to yield 1-nitro-1,3-alkadienes.

Nitronium fluoroborate has been used to prepare solvo-adducts.[294,295] In acetonitrile reaction with 1,3-alkadienes affords acetylaminonitro compounds. The ratio of 1,2- to 1,4-adducts is as follows: 48 : 51 for 1,3-butadiene, 39 : 50 for isoprene, 35 : 35 for

2,3-dimethyl-1,3-butadiene, 26:64 for piperylene, and 6:78 for 2,4-hexadiene.



R = H, Me.

Treatment of chloroprene with N_2O_4 leads to both 1,4- and 1,2-adduct, the former predominating.[296,297] The addition of NO_2Cl affords 1,4-adducts and products derived by their subsequent isomerisation (the double bond shifting towards the nitro group).

There are many reports on the nitration of polyhalogenated 1,3-alkadienes. Thus, nitration of 1,4-dichloro-1,3-butadiene with HNO_3 at 0–70 °C leads to *trans,trans*-1,4-dinitro-1,4-dichloro-1,3-butadiene, while treatment with $Cu(NO_3)_2$ at 20 °C leads to the formation of 1,4-dinitro-1-chloro-1,3-butadiene.[298]

The addition of N_2O_4 to polyhalogenated 1,3-butadienes proceeds mainly at the 1,4-position. Thus, a mixture of fluorinated 1,4-dinitro-2-butenes and 4-nitro-2-buten-1-ol nitrites was obtained on nitration of 1,1,4,4-tetrafluoro- and perfluoro-1,3-butadiene,[299] while the interaction of 1,2,3,4-tetrachloro-1,3-butadiene[89,300] and 1,1,2,4,4-pentachloro-1,3-butadiene[301] with N_2O_4 gives only 1,4-dinitro-adducts.

2. Reactions with aromatic diazo compounds

The reactions of 1,3-dienes with diazonium salts represent a special area of study. Recently, 1,4-halogenoarylation of 1,3-dienes in the presence of copper salts has been widely applied. Normally, reaction proceeds by a radical-ion mechanism,[302–305] but in certain cases an electrophilic mechanism is possible in the absence of copper ion.

1,3-Alkadienes participate in azo coupling with active diazonium salts in the same manner as aromatic compounds. The mechanism of this azo coupling has not been studied. However, one could invoke a mechanism similar to electrophilic aromatic azo coupling.

This reaction was discovered in 1919 by Meyer.[306] Terent'ev proposed an application of the method for the assay of 1,3-dienes in hydrocarbon mixtures.[307] It was studied more recently by Arbuzov and Rafikov, as exemplified by reactions with 1,3-butadiene and 2,4-hexadiene.[308] Brightly coloured crystalline azo compounds were isolated, and converted to the corresponding pyrazolines on reduction.

VII. Conclusion

From the data set out in this review, certain general conclusions can be drawn on electrophilic addition to 1,3-dienes.

The regioselectivity of electrophilic addition to 1,3-dienes is dependent on the nature of the electrophile, the structure and configuration of the 1,3-alkadiene, the nature of the solvent, the concentration of the reactants, and the temperature.

The reactions with hydrogen-containing electrophiles proceed with formation of carbenium ions, stabilised by allylic conjugation; in general, electrophilic attack takes place at the most nucleophilic atom of the conjugated system in accordance with the Markovnikov rule. The addition of HCl to 2-methyl-2,4-pentadiene is an exception: a tertiary carbenium ion, stabilised by hyperconjugation, is predominantly formed in this case.

Dilution favours electrophilic addition of halogens. Normally, the latter attack the terminal carbon atom of the conjugated system, but the nature of the halogen is an important factor. The position of attack by chlorine is determined by the electron density in the system, and evidently leads to that carbenium or ionium ion which is energetically most favoured. Attack by bromine and iodine need not take place at the most nucleophilic atom of the conjugated system since, being associated with formation of a cyclic onium salt, may be subject to steric factors.

The proportion of 1,2- and 1,4-adducts is determined first and foremost by the structure of the intermediate. The closer the intermediate is, in structure, to a carbenium ion, the more likely is 1,4-addition. Sulphenyl chlorides, which form stable episulphonium ions, add almost exclusively at the 1,2-position, in spite of the fact that such adducts tend to rearrange, even at room temperature, into the thermodynamically more stable 1,4-adducts.

The solvent has an effect on the regioselectivity of addition, either by virtue of its higher or lower polarity, or by its involvement in formation of the intermediate.

Both addition and replacement of hydrogen by halogen take place on treatment of 1,3-alkadienes with fluorine or chlorine.

1,3-Alkadienes participate in electrophilic substitution with nitronium salts, diazonium salts and pyridine.SO_3 complex, in the same manner as aromatic substrates.

Solvo-adducts may be formed on reaction of 1,3-alkadienes with halogens and with compounds containing electrophilic sulphur or nitrogen atoms; in the second stage of the addition process, a hydroxyl-containing nucleophile (e.g. water, alcohols, carboxylic acids, H_2O_2) or a nitrogen-containing nucleophile, such as a nitrile or a carboxylic acid amide, may participate.

The electrophilic addition to 1,3-alkadienylphosphonates is particularly interesting since, here, phosphorus-containing heterocyclics are formed as a result of intramolecular trapping of a nucleophilic centre.

All of these chemical properties of 1,3-alkadienes and their derivatives have been applied in organic synthesis, and the possibilities of broadening their synthetic value are by no means exhausted.

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Translated from *Uspekhi Khimii* **60** 103–133 (1991) U.D.C. 547.314+547.738+547.78

Synthetic aspects of the chemistry of *p*,π-unsaturated amines

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ABSTRACT. The review covers the electrophilic and nucleophilic addition of mono- and bi-functionalised reagents to ynaminocarbonyl compounds to 1,3-enynes possessing an enamine or ynamine group. Amines of this type are synthons for preparing five-, six-, seven- and eight-membered rings with two heteroatoms as well as condensed ring systems. The effect of the structure of the acetylenic compound on the mode of interaction has been analysed. Special features of the intra- and inter-molecularity of the reactions were discussed. Data are presented in 1,3-dipolar cycloaddition with all three types of amine.

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I. Introduction

Acetylenes and their nitogen-containing derivatives play an important role in modern organic chemistry, as indicated in a number of reviews[1–3] and monographs.[4–7]

Over the last ten years, acetylene chemistry has developed along non-classical lines, and there has been particular emphasis on the study of 1,3-enynes possessing an ynamine (I) or enamine groups (II) and of ynaminocarbonyl compounds of type (III).

$$\underset{(I)}{R_2NC{\equiv}CCH{=}CR_2'}, \quad \underset{(II)}{R_2NCH{=}CHC{\equiv}CR'}, \quad \underset{(III)}{R_2NC{\equiv}CCOX},$$

where X = H, R′, OR′.

The reactivity of such compounds is different from that of the corresponding 1,3-enynes and acetylenecarbonyl compounds, and the amino group reactivity differs from that of simple tertiary amines. Unsaturated nitrogen-containing systems of this type, which are obtainable from the commercially available diacetylene[1], vinylacetylene and propargyl alcohol, are valuable synthons for the preparation of five-, six-, seven- and eight-membered heterocyclics with two heteroatoms, as well as condensed systems. In addition, alkenylynamines and ynaminocarbonyl compounds are synthetically useful starting materials for the synthesis of novel types of polyfunctionalised compound.

The study of reactions of *p*,π-conjugated unsaturated amines with bifunctional compounds, and research into structural effects, the nature of the reagent and the factors affecting the course of the reaction, have provided the basis for new routes to synthetically important compounds. The chemistry of ynamines has particularly developed in this direction during recent years, and their participation in multi-step syntheses of terpenes, steroids[8], vitamin D_3 [9] and peptides[5] has been noted. Conjugated ynamines with acceptor groups are especially valuable in this respect. They are considerably more active than simple and vinylacetylenic ynamines; furthermore, they possess reaction centres which offer wider scope for synthetic applications.

In one of the recent reviews, Shrot[2] states that "in the synthesis of heterocycles the triple bond serves as a latent carbonyl function, participating in the usual carbonyl condensations as well as in heteronucleophilic addition, being equivalent to vinylation at a heteronucleophilic centre". Developing the concept of "alkynes as pseudo-carbonyl compounds", the author formulated an orientation principle which is governed largely by electronic effects; other factors are not considered.

In heterocyclic syntheses from *p*,π-unsaturated amines (I–III), the pattern of behaviour is more complex.

II. The interaction of *p*,π-unsaturated amines with mono-functionalised electrophiles and nucleophiles

1. Reactions of alkenylynamines

The first compounds with an ynamine structure (in the phenothiazine series) were obtained by chance in 1958. In 1961, while studying the nucleophilic replacement of halogen at sp^2- and *sp*-carbon atoms, Belgian chemists developed a number of methods of preparing this class of compound. Around the same time, further syntheses of ynamines were carried out by Viehe et al. (FRG), Ficini et al. (France), Arens et al. (Holland), A A Petrov et al. (USSR) and by a number of chemists in the United States.[5]

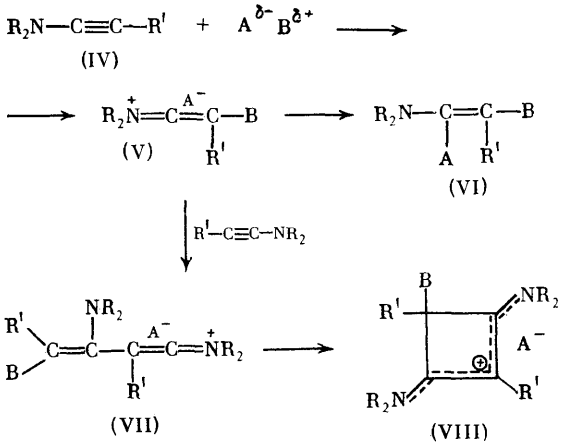
Contrasting with acetylenic hydrocarbons, conjugated *p*,π-unsaturated ynamines are strong nucleophiles.

By interaction of ynamines (IV) with a polar molecule, $A^{\delta-}B^{\delta+}$, reaction proceeds at the C_2-atom with formation of a ketenimminium salt (V) (Scheme 1).

It is quite probable that the mechanism involves addition of B^+ at the nitrogen atom. Such an interaction would not be unlike that of the corresponding enamines,[6] but in the case of ynamines no stable salts have been formed. In the meantime, Drenth[10] reported a kinetic study of the acid-catalysed hydration of ynamines by stopped flow technique, which confirmed the formation of N-protonated intermediates with subsequent charge transfer to the C_2-atom of the acetylene group. The rate constant for the hydration of ynamines is 2000 times greater than that for the hydration of enamines. This is because the process of transferring a proton from the nitrogen atom

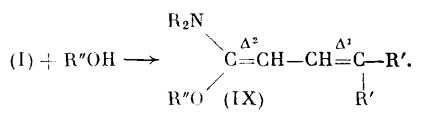
to the β-carbon of the ynamine is concerted, the separation and addition of the proton being accomplished in one step.

Scheme 1

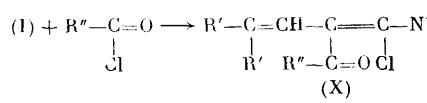


The pathway by which the ketenimminium salt is transformed is dependent on the reagent. Thus, on treatment with electrophilic reagents having a weakly nucleophilic anion, the salt (V) undergoes subsequent reaction with a second ynamine molecule rather than with the anion; in this way, an enamine-ketenimminium intermediate (VII) is formed, which subsequently undergoes intramolecular C-alkylation to form a π-cyclobutenyl cation (VIII) via addition of B^+ to the corresponding cyclobutadiene.[11]

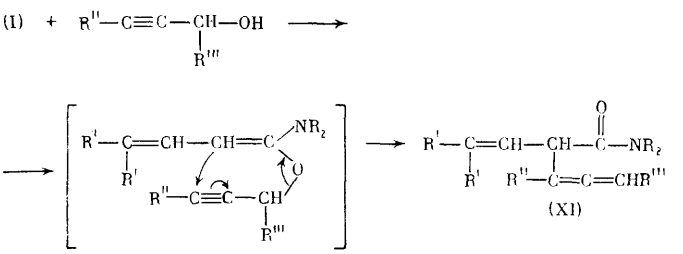
The reactivity of 1-dialkylaminoalk-3-en-1-ynes is noticeably less than that of simple ynamines. Thus, interaction with electrophilic reagents having a weakly nucleophilic anion, e.g. phenols, proceeds with the formation of vinylketene O,N-acetals, namely 1-dialkylamino-1-(aryloxy or alkoxy)-1,3-pentadienes, rather than cyclobutenium salts (VIII) as described above. Reaction proceeds regio- and stereo-specifically across the Δ^2-bond with formation of a *cis*-adduct.[12]



Ketenimminium salts (V) react with electrophilic reagents having strongly nucleophilic anions by addition of the anion A^-. Thus, treatment of 1-dialkylaminoalk-3-en-1-ynes with acetyl chloride or benzoyl chloride affords 1-dialkylamino-1-chloro-2-acetyl(benzoyl)-1,3-pentadienes (X) which are readily distillable.[13]

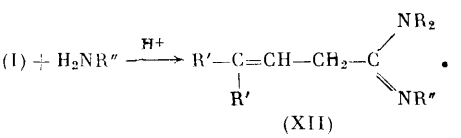


In certain cases, the ketenimminium salts (V) are sufficiently nucleophilic in themselves, and participate in Claisen rearrangement. Thus, branched dialkylamides of β-allenecarboxylic acids (XI) have been prepared by reaction of 1-dialkylamino-3-penten-1-ynes with propargyl alcohol.[14] Reaction with propargyl alcohol derivatives proceeds quite readily since the electron-accepting acetylene group increases the acidity of the alcohol.

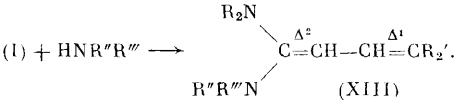


Reaction of vinylacetylenic ynamines with nucleophiles proceeds only by acid catalysis. Thus, for nitrogen-containing analogues of propargyl alcohol the amino-Claisen rearrangement does not take place.

In catalysed reactions of 4-alkyl-1-dialkylamino-3-penten-1-ynes with primary amines, the amino group attaches to the C_1-atom of the multiple bond, but the interaction is complicated by protropic rearrangement involving the participation of the second labile hydrogen of the amino group with the formation of per-N-substituted amidines of 4-alkyl-3-pentenoic acids (XII).[15]

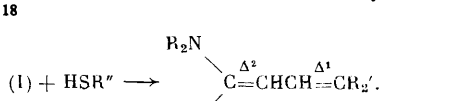


Reactions of 1-dialkylamino-4-methyl-3-penten-1-ynes with secondary aliphatic, aromatic and heterocyclic amines proceed regioselectively and with *cis*-stereospecificity across the acetylenic bond with formation of conjugated vinylketone aminals (XIII).[16,17]



From data on the reactivity of primary and secondary amines, it is clear that weakly basic amines are more reactive than highly basic amines since the latter inhibit acid catalysis. However, this is only true within a limited range of the basicity constant. Butylamine (pK_B = 3.2) and cyclohexylamine (pK_B = 3.34) are far less reactive than aniline (pK_B = 9.37). Secondary heterocyclic amines (piperidine, pK_B = 2.88) react far less than N-alkylaromatic amines (N-methylaniline, pK_B = 9.15) even though there is significant steric hindrance in the latter. *p*-Nitroaniline does not take part in the addition since its nucleophilic acitivity is low.

The addition of aliphatic and aromatic thiols proceeds across the acetylenic bond with the formation of vinylketone N,S-thioacetals (XIV).[18]



Reaction is not stereospecific. Reaction is regioselective and proceeds in the same manner as those described above, i.e. by attack of the nucleophile at the C_1-atom of the aminoenyne. However, mixtures of *Z*- and *E*-Δ^2-isomers are formed. The isomeric composition varies significantly and reproducible results cannot be achieved. This is because sulphur-functionalised ethylenes readily isomerise—a well-known observation in sulphur chemistry.

It cannot be excluded that a radical mechanism is involved in parallel with an electrophilic process. The interaction of (I) with RSH differs significantly from the reaction of simple ynamines. Thus, addition of propenethiol to the latter is accompanied by thio-Claisen rearrangement with formation of thioamides.[5]

The group $R_2NC{\equiv}C-$, is a masked carboxylic acid amide function. Thus, addition of compounds of the type H_2X (X = O, S, Se) to 1-dialkylamino-3-alken-1-ynes affords β,α-ethylenecarboxylic acid amides, thioamides and selenoamides, respectively (XV).[19,20]

$$(I) + H_2X \longrightarrow R'-C(R')=CH-CH_2-\overset{\overset{X}{\|}}{C}-NR_2. \quad (XV)$$

The thiol group displays significantly higher acidity and nucleophilicity than the hydroxyl group in similar compounds. Thus, reactions with H_2S and H_2Se proceed far more readily than reaction with water, the reactivity of the reagents increasing in the order O < S < Se.

In the case of thioamides, reaction can be reversed, i. e. synthesis of ynamines can be based on thioamides. The corresponding amides do not participate in the reverse reaction.[5]

$$C_6H_5-CH_2-\overset{\overset{S}{\|}}{C}-N(CH_3)_2 \xrightarrow{NaNH_2} C_6H_5-C{\equiv}C-N(CH_3)_2. \quad (XVI)$$

By comparison, the hydration of aminoenynes is not in itself of great interest. However, one should recall that this reaction has been applied in the dehydrative syntheses of functionalised carboxylic acid derivatives and in peptide synthesis.[5,20]

Thus, summarising the reactions of vinylacetylenic ynamines with simple nucleophiles, it should be noted that the nucleophile attacks the C_1-atom of the hetero-substituted acetylene bond, as is the case with the reactins of ynolethers, ynamines and enynolethers.

Alkenylynamines react with compounds containing polar multiple bonds, e. g. $>C=O$ (aldehydes, ketones, carboxylic acid esters) via intermediate formation of cycloaddition products, as is the case with simple ynamines.[26] Thus, substituted amides of unsaturated carboxylic acids (XVIII) are obtained in 60–65% by reaction of (I) with both aliphatic and aromatic aldehydes in the absence of catalyst.[21]

$$(I) + R''-CHO \rightarrow \left[R'-C(R')=CH-C(R''(H)-O)=C-NR_2\right] \rightarrow R'-C(R')=^{\Delta^1}CH-\overset{\overset{O}{\|}}{C}-CH_AR''-NR_2.$$

(XVII) (XVIII)

It is likely that reaction proceeds through an intermediate oxete, formed by the synchronous addition of the carbonyl atom group to the triple bond. Thus, for the reaction of 1-diethylamino-4-methyl-3-penten-1-yne with butanal, the ^1H NMR spectrum displays, in addition to signals from product (XVIII), a weak triplet (4.23 p. p. m.), which would correspond to the protons of the oxete ring in (XVII). This signal was absent when the spectrum was retaken after 2 days. Intermediates of type (XVII) have been isolated from the reaction of ynolethers with ketones.[22]

The ^1H NMR spectrum of (XVIII) (Table 1) confirms the formation of only one Δ^2-isomer. For structural confirmation, the experimental values of the chemical shifts of proton H_A were in agreement with those calculated according to the formula:[54]

$$\delta_H = 5.25 + Z_{gem} + Z_{cis} + Z_{trans}.$$

From the data presented, it is clear that the experimental values are close to the values for the *cis*-isomer, and noticeably different from those calculated for the *trans*-isomer. The *cis*-structure for (XVIII) is consistent with the proposal that reaction proceeds via a stereo-defined oxete ring. The isomeric composition at the Δ^1-unsaturation corresponds approximately with the proportion of double bond isomers in the starting ynamine — 30% *trans*-isomer and 70% *cis*-isomer. Thus, the double bond in the starting ynamine (I) does not take part in the reaction.

Table 1. Chemical shifts of vinylic protons

$$CH_3-C(CH_3)=CH-C(=O)-C(=CHR'')-NR_2,$$

where R″ = CH_3 (XVIIIa), C_2H_5 (XVIIIb), C_3H_7 (XVIIIc).

for *cis*- and *trans*-isomers at the Δ^2-bond.

Compound	δ_H (found) p.p.m.		δ_H(calculated), p.p.m.	
	cis	*trans*	*cis*	*trans*
(XVIIIa)	5.52	—	6.00	6.45
(XVIIIb)	6.36	—	6.74	7.42
(XVIIIc)	6.56	—	7.01	7.69

According to the literature,[23] alkylamines readily react with ketones. However, reaction of alkenylynamines with ketones, under the conditions of the aldehyde addition, was not possible, except in the case of alkenylynamines (II) with cyclohexanone. Here, the yield is only 50% and the amount of catalyst had to be doubled.

Acetone and acetophenone react with alkenylynamines in the presence of a stoichiometric amount of $MgBr_2$. The latter is known to activate the carbonyl group of ketones by complex formation which increases the δ^+ charge on the carbon atom.[21]

$$(I) + R''R'''CO \xrightarrow{MgBr_2} R'-C(R')=^{\Delta^1}CH-\overset{\overset{\Delta^2}{\|}}{C}(CR''R''')-CONR_2.$$

(XIX)

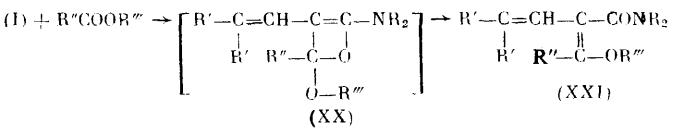
Reaction is regioselective, as with aldehydes; however, in the case of acetophenone stereospecificity is reduced with the formation of Δ^2-isomers in 67 : 33 proportion.

Thus, it has been shown, that alkenylynamines react with aldehydes regioselectively and stereospecifically at the triple bond in the presence of a catalytic amount of BF_3-etherate. Ketones only participate in the reaction in the presence of stoichiometric amount of $MgBr_2$ with the same regioselectivity, but reduced stereo-specificity.

The decrease in the electrophilic activity of the carbonyl group from ketones to carboxylic acid esters explains the lower activity of the latter in reactions with alkenylynamines. $MgBr_2$-ethereate serves as catalyst only with addition of ethyl acetate, and only on heating.

With carboxylic acid esters, there is a marked difference of reactivity between aliphatic and aromatic compounds. Methyl

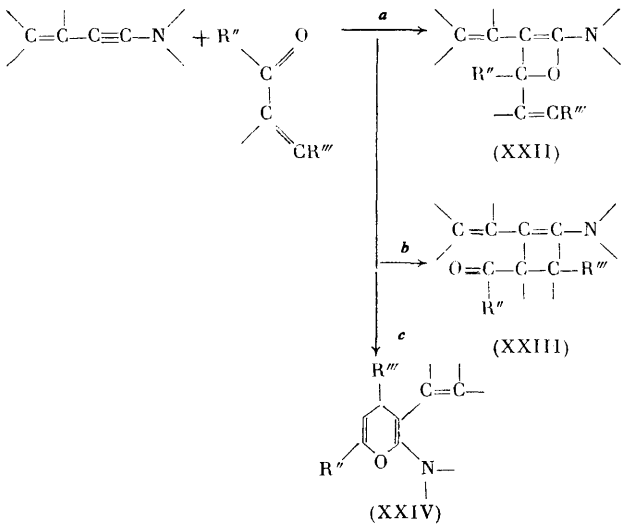
benzoate adds to alkenylynamines only in the presence of a stoichiometric amount of boron fluoride, the product yield being around 6–7%. The majority of unreacted methyl benzoate can be removed by distillation. The unconverted alkenylynamines polymerise, which evidently explains the low yield of adducts (XXI).[24]



(XX) (XXI)

Cycloaddition is strictly chemoselective, reaction taking place only at the triple bond of ynamine. A [2 + 2]-cycloaddition is involved. The intermediate oxete (XX) is unstable, and is immediately converted to the dialkylamides of the corresponding carboxylic acid.

For cycloaddition of α,β-unsaturated aldehydes and ketones to alkenylynamines, there are several possible pathways (*a*–*c*).[25]



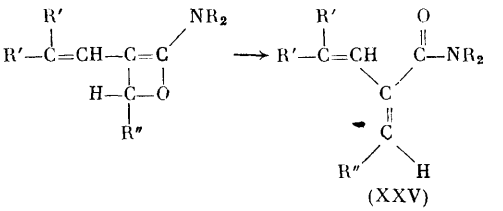
(XXII) (XXIII) (XXIV)

The more probable cisoid conformation should favour route *c* ([4 + 2]-cycloaddition), and the transoid conformation should favour route *b*. It has been shown, in fact, that [2 + 2]-cycloaddition of carbonyl compounds across the C=C bond (route *b*) is characteristic of cyclic ketones having a fixed transoid conformation.[26]

On the same theme, a study has been made of the reaction between alkenylynamines and α,β-unsaturated carbonyl compounds. Here is it assumed that rotation around the C–C bond is more rapid than the interconversion of the *cis*- and *trans*-conformers. For cinnamaldehyde one might anticipate reaction by all three pathways. It has been shown that, on reaction with 1-diethylamino-1-propyne, adducts are formed only by routes *a* and *c*.[27,28] In this particular example reaction takes place only on the carbonyl group (route *a*).

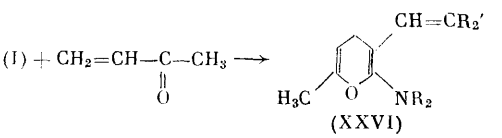
Phenylpropional might be expected to add with formation of products via a cyclobutadiene intermediate, as is characteristic of the reaction of alkenylynamines with activated acetylenes.[29,30] However, in the case of alkenylynamines, addition takes place only across the aldehyde group (route *a*) via an oxete intermediate.

^{1}H NMR spectral data confirms that only Δ^2-isomer is formed. The intermediate oxete undergoes electrocyclic ring opening by the most sterically favourable pathway. Thus, as with aliphatic and aromatic aldehydes[26], the *E*-isomer is formed.



(XXV)

Alkenylynamines react with methyl vinyl ketones by [4 + 2]-cycloaddition (route *c*) to give (XXVI).[25]



(XXVI)

Only scant reference to 4*H*-pyrans is given in the literature. Nevertheless, interest in this class of compound is great, primarily because 4*H*-pyrans are useful starting materials for the synthesis of pyrylium salts and unsaturated 1,5-diketones.[31] It is interesting to note that methyl vinyl ketone reacts with enamines either by heterocyclisation to give dihydro-4*H*-pyrans or by proton transfer to give unsaturated carboxamides.[32] Such proton transfer is not possible with ynamines since the system is fully unsaturated. As illustrated above, alkenylynamines can serve as valuable reagents for the synthesis of dialkylamino-4*H*-pyrans.

Summarising, the relative reactivity of the C=C and C=O group in α,β-unsaturated aldehydes and ketones determines the mode of addition to alkenylynamines.

2. Reactions of vinylacetylenic enamines, $R_2N-CH=CH-C\equiv CR'$, with mono-functionalised agents

In contrast with acetylenic hydrocarbons, en- and yn-amines readily participate in electrophilic reactions, and as a consequence the addition of nucleophilic reagents can take place, both in the presence and absence of mineral acid. However, with aminoenyne systems, the nature of the addition process is dependent on whether the amino group is attached to the ethylenic or acetylenic fragment.

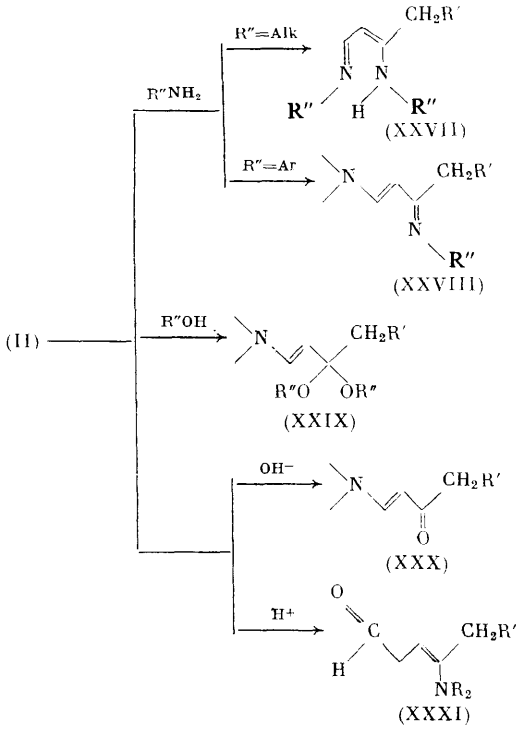
Thus, enamines $R_2N-CH=CH-C\equiv CR'$ (II) react with primary aliphatic amines to give vinylogous and potentially tautomeric aminocrotonaldimines (XXVII) via transamination; on the other hand, reaction with arylamines proceeds with formation of (XXVIII) (Scheme 2).[33,34]

Base-catalysed addition of alcohols leads to vinylogous amide acetals (XXIX).[35] Depending on reaction conditions, hydration of (II) can provide β-aminovinyl ketones or β-aminocrotonoaldehydes.[35,37]

It should be pointed out that compounds (XXVII) are of potential synthetic utility. Thus, subsequent C-alkylation and hydrogenation affords N-monosubstituted 1-aminoalkanes as synthons for the nucleophilic incorporation of the 4-aminobutyl group (R = H).[36]

It is interesting to note that the reaction of 1-alkoxy-1-butene-3-ynes with alcohols affords primarily the C_1-adducts, hydration of

Scheme 2



which leads to β-ketoacetals, thence β-alkoxyvinyl ketones by thermolysis.[4]

$$RO{-}CH{=}CH{-}C{\equiv}CH \xrightarrow{ROH,\ HOH(H^+)} \underset{RO}{\overset{RO}{\diagdown\!\!\diagup}}CH{-}CH_2{-}CO{-}CH_3 \longrightarrow$$
$$\longrightarrow RO{-}CH{=}CH{-}CO{-}CH_3.$$

According to Engelhardt[38], vinylacetylene undergoes 1,4-addition with secondary amines.

$$R_2NH + CH_2{=}CH{-}C{\equiv}CH \rightarrow R_2N{-}CH_2{-}CH{=}C{=}CH_2.$$

Badanyan reported the same mode of addition with tert-aminomethyl derivatives[39], i.e. the additional amino function has no effect on the reaction.

$$R_2N{-}CH_2{-}C{\equiv}C{-}CH{=}CH_2 + R_2'NH \rightarrow$$
$$\rightarrow R_2N{-}CH_2{-}CH{=}C{=}CH{-}CH_2{-}NR_2'.$$

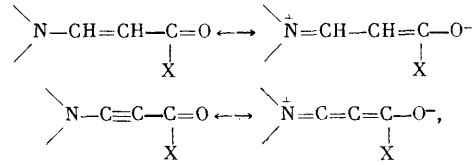
Because the chemistry of enamines (II) has already been the subject of a review[1] and a monograph[4], the present article covers only general trends in the reactions of this compound class in relation to other types of amine.

3. Reaction of ynaminocabonyl compounds, $R_2NC{\equiv}CCOX$ (III), with mono-functionalised reagents

The chemistry of enaminocarbonyl compounds has been well documented in a monograph[40] and in a number of review articles published in recent years[2,41]. Acetylene analogues of carbonyl compounds, first prepared some 100 years after the corresponding ethylenic derivatives, have been studied somewhat less. Data on their relative reactivity are few, and there have been no surveys in this area.

A study has been made of the electronic effects of donor and acceptor groups in ethylenic and acetylenic dialkylaminocarbonyl compounds on the electron density in the molecule by ^{13}C NMR spectroscopy. The constants for spin-spin interaction, $^{13}C-{}^{13}C(^1J_{CC})$, of the double and triple bonds in en- and yn-amines have been determined (Table 2) (pulse sequence inadequate with decoupling of the signals from ^{13}C-isomers[42]).

It has been shown that, in the case of en- and yn-aminocarbonyl compounds, the value is somewhat less than that calculated by the simple additive principle. This is a consequence of the delocalisation of the multiple bonds as a result of direct polar conjugation, through the double (triple) bond, involving the lone pair on the nitrogen atom and the π-system of the carbonyl fragment. This can be expressed by the following canonical forms:



X = H, R′, OR′.

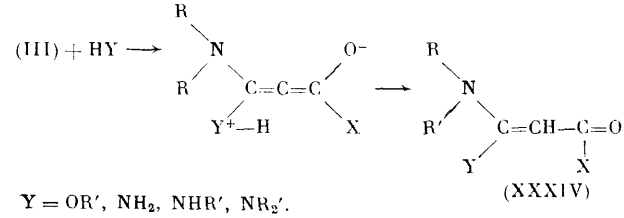
The contribution of the bipolar resonance forms was computed to be around 30% for enaminocarbonyl compounds and in excess of 50% for the acetylene analogues.

By analysis of the chemical shifts in the ^{13}C NMR spectra of the carbon atoms of the triple bond of substituted ynamines, relative to the corresponding values for ethylenic analogues, there is evidence of opposite polarisation of the orthogonal π-system of the triple bond in ynamines containing acceptor groups. This effect explains the unusually low value for the shielding contribution from the dialkylamino group adjacent to the C-atom of the multiple bond.

The data obtained on the structure of ynaminocarbonyl compounds confirms that the conjugation of donor and acceptor groups with the multiple bond has a profound effect on the distribution of electron density in the molecule, and, thereby, on the reactivity of this class of compound. Carbonyl-containing dialkylaminoacetylenes thus have unique properties, differing from those of both simple ynamines[5,26] and acetylenic ketones.[43]

While simple ynamines react with mono-functionalised compounds only after initial protonation,[44] ynaminocarbonyl compounds react with alcohols, ammonia and amines in the absence of catalyst even at room temperature (ynaminoaldehydes) or at 60–70 °C (ynamino-ketones and -carboxylic acid esters).[45,46]

A detailed study of the mechanism, stereochemistry and kinetics of addition[47] have shown that the limiting step in the process is the nucleophilic attack of the alcohol or amine at the C_3 carbon atom. The bipolar compound formed is stabilised by proton transfer, so that in polar aprotic solvents the (*E*)-isomer is formed (by intramolecular proton transfer) whereas in protic solvents the product is a mixture of *E*- and *Z*-isomers (possibly formed via intermolecular protonation). Interconversion of the *E*- and *Z*-forms takes place on increasing the temperature.



Y = OR′, NH_2, NHR′, NR_2'.

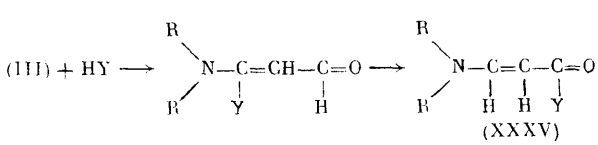
Table 2. ^{13}C Chemical shifts and $^{13}C-^{13}C$ spin-spin coupling constants of β-substituted enamines and ynamines[a].

No.	Formula	^{13}C NMR spectral data						
		C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	$^1J_{3,4}$
1	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}H=\overset{4}{C}H-\overset{5}{C}H_2-\overset{6}{C}H_3$	12.75	45.03	136.94	99.64	24.75	16.90	79.2
2	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}H=\overset{4}{C}H-\overset{5}{C}H=\overset{6}{C}H_2$	13.33	45.38	141.57	99.41	138.19	103.43	77.2
3	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}H=\overset{4}{C}H-\overset{5}{C}HO$[b]	11.54 14.74	42.74 50.22	159.14	100.99	188.21	—	71.8
4	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}H=\overset{4}{C}H-\overset{5}{C}O-\overset{6}{C}H_3$[b]	13.01	44.42	150.67	96.83	192.83	27.47	70.8
5	$\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}H=\overset{4}{C}H-\overset{5}{C}O-O\overset{6}{C}H_3$[b]	13.30	45.31	157.09	83.48	169.37	49.88	72.8
6	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}\equiv\overset{4}{C}-\overset{5}{C}H_3$	12.87	48.94	83.39	57.36	3.18	—	189.2
7	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}\equiv\overset{4}{C}-\overset{5}{C}H=\overset{6}{C}H-\overset{7}{C}H_3$[c]	13.17	48.85	99.73	63.19	112.15	128.30	174.1
8	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}\equiv\overset{4}{C}-\overset{5}{C}H=\overset{6}{C}H-\overset{7}{C}O-\overset{8}{C}H_3$[d]	13.15	48.22	110.89	70.86	126.79	126.79	175.6
9	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}\equiv\overset{4}{C}-\overset{5}{C}O-\overset{6}{C}H_3$	13.03	47.95	104.80	77.79	180.19	31.39	186.5
10	$(\overset{1}{C}H_3-\overset{2}{C}H_2)_2N-\overset{3}{C}\equiv\overset{4}{C}-\overset{5}{C}O-O\overset{6}{C}H_3$	12.94	47.66	98.76	65.44	155.70	50.98	177.0

[a] *trans*-Isomers: chemical shifts given in p.p.m. (TMS) with a precision of ±0.05 p.p.m.; $^{13}C-^{13}C$ spin-spin coupling constants given in Hz and with a precision of ±0.2 Hz. [b] In compound 3 the signals from atoms C(1) and C(2) are doublets, and in compounds 4 and 5 there is noticeable broadening due to restriction of internal rotation around the C–N bond. [c] C(7) 15.47 p.p.m. [d] C(7) 194.98 p.p.m.; C(8) 26.96 p.p.m.

The addition of mono-functionalised nucleophiles to activated acetylenes is a second order reaction. The rate of reaction increases in parallel with 1) the basicity of the reagents (amines add more easily than alcohols, and secondary amines more rapidly than primary amines and ammonia), 2) the electrophilicity of the reactive centre at C_3 (the rate of addition decreases in the order: ynamino-aldehydes > ynaminoketones > aminoacrylic acid esters), and 3) the polarity of the solvent (as a result of enhanced solvation of the bipolar transition state).

It has been shown that the products obtained by addition of simple alcohols to ynaminodehydes undergo rearrangement to the isomeric aminoacrylic acid esters on heating or on treatment with protic or Lewis acids. Formally, the alkoxy group migrates from C_3 to the carbonyl group. Ynamino-ketones and -esters do not undergo such a transformation.[45,48]



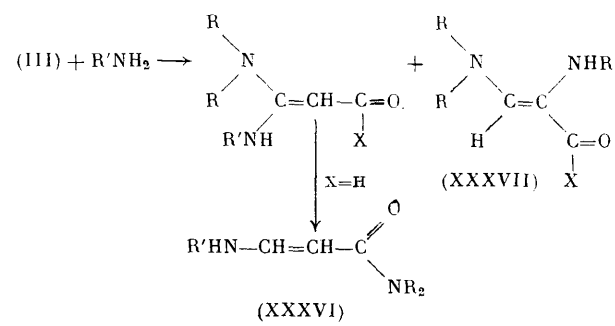
(III) + HY → N–C=CH–C=O → N–C=C–C=O, (XXXV)

X = H, Y = OCH_3, OC_2H_5.

3-Dimethylaminoacrylic acid esters are obtained in the *E*-configuration in 55–60% yield.

The rearrangement takes place via an oxete intermediate with migration of an oxygen atom and the dimethylamino group.[45]

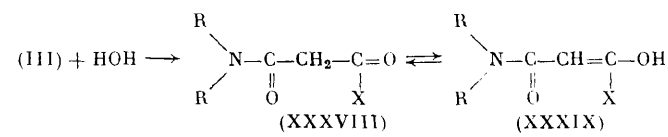
The products of addition of amines to ynaminoaldehydes underwent rearrangement far less smoothly, and a low yield of 3-aminoacrylic acid dimethylamide was obtined, i.e. a similar oxygen migration takes place with participation of an amino group.



(III) + R′NH₂ → N–C(R)(R′NH)–CH=C(X)–C=O + N–C(R)(H)–C=C(NHR′)–C=O (XXXVII); X=H → R′HN–CH=CH–C(=O)–NR₂ (XXXVI)

By addition of ammonia and amines to ynamino-aldehydes and -ketones, isomeric adducts are also formed by inverse attack of nitrogen at the C_2-atom of the multiple bond to give (XXXVII).[49]

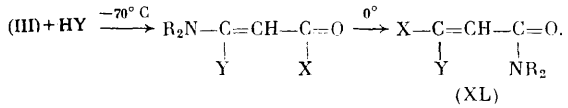
Hydration of ynaminocarbonyl compounds proceeds in neutral media at 20 °C (with ynaminoaldehydes) and at 60–70 °C (with ynamino-ketones and -esters).[45]



(III) + HOH → N–C(R)(R)–CH_2–C=O (XXXVIII) ⇌ N–C(R)(R)–CH=C(X)–OH. (XXXIX)

The β-ketoamides obtained exist as a mixture of keto and enol tautomers. According to ^{1}H NMR spectral data the proportion of the enol form in $CDCl_3$ varies from 4% (for esters, X = OMe) to 20% for ketones (X = Me). Acids readily add to the triple bond of ynaminocarbonyl compounds.[45,48] The geometry of the product is determined by the nature of the acceptor group. For aldehydes, the reaction is stereospecific, for ketones it is highly stereoselective in favour of the *trans*-adduct (*Z*-configuration), while esters afford both *cis*- and *trans*-adducts in approximately equal amount.

In the overwhelming majority of cases the initial adducts undergo facile rearrangement to the corresponding substituted α,β-ethylenic carboxylic acid dialkylamides (XL) (amino-, mercapto- and hydroxycarboxylic acid derivatives).

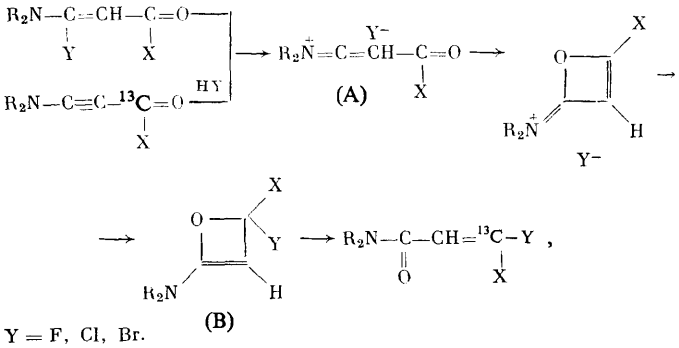


(XL)

Rearrangement does not take place, or proceeds to a small extent, only in the case of dimethylaminopropiolic acid esters (X = OMe) or on addition of HF (Y = F). The adducts formed in these reactions are stable, even on heating.

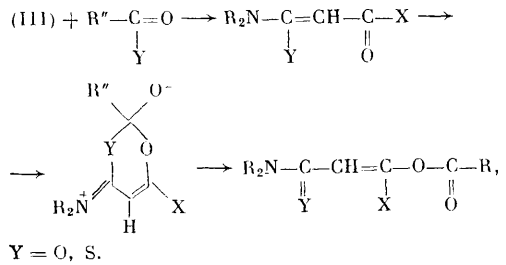
An oxete mechanism has been invoked only for the addition of hydrogen halides to ynaminocarbonyl compounds, as shown in Scheme 3.[45,50,51]

Scheme 3



Y = F, Cl, Br.

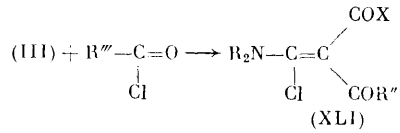
The mechanism of the rearrangement is quite different for the addition of carboxylic and thiocarboxylic acids. Here, there is intramolecular formation of an intermediate six-membered bipolar compound, which is subsequently cleaved stereospecifically.[50]



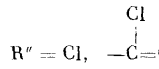
Y = O, S.

In such cases, the obtained *cis*-product isomerises to the thermodynamically more stable *trans*-product on heating to 60–70 °C.

Acylation of ynaminocarbonyl compounds has been examined by a study of the reaction with phosgene and oxalyl chloride.[52] It has been shown that these reagents add across the triple bond of activated ynamines to give (XLI), as would be anticipated from considerations of the electron density.

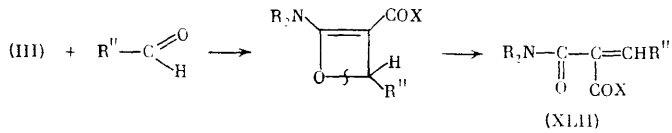


(XLI)



The products obtained are extremely reactive, participating in heterocyclisation with a number of bifunctional reagents.

The interaction of aldehydes with ynaminocarbonyl compounds proceeds in a totally different manner. Here, there is an analogy with the reactions of ynamines (I). Thus, [2 + 2]-cycloaddition of the carbonyl group to the triple bond of the activated acetylene takes place at 0–5 °C in methylene chloride with formation of an oxete intermediate.

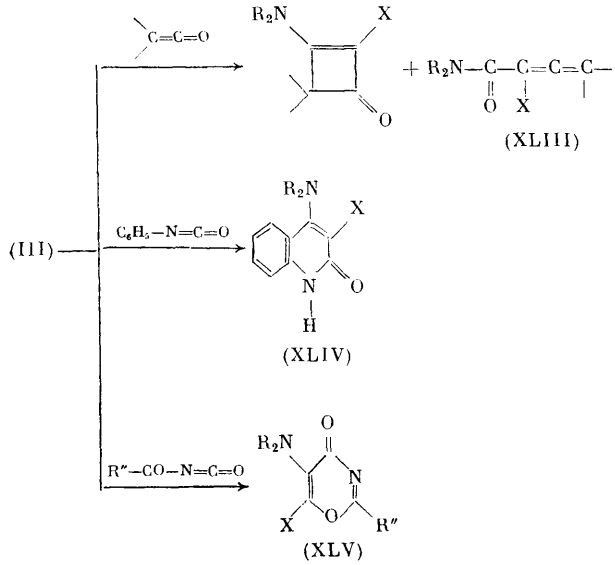


(XLII)

Stereospecific ring opening of the oxete leads to the corresponding unsaturated carboxylic acid amides (XLII), having a *cis*-configuration.[53]

The reaction of heterocumulenes with ynaminocarbonyl compounds affords cyclic products by [2 + 2]- [4 + 2]-cycloaddition[54,55] (Scheme 4)

Scheme 4



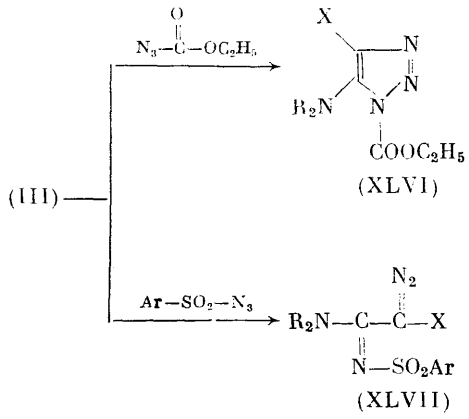
(XLIII)

(XLIV)

(XLV)

Ynaminocarbonyl compounds participate in reaction with 1,3-dipolar compounds in the same way as ynamines and acetylenecarbonyl compounds.[45] Thus, substituted triazoles are formed in high yields by interaction with ethyl azidoformate at 65 °C.

Arylsulphonyl azides, however, yield products derived primarily by triazole cleavage, the corresponding triazole analogues of (XLVI) being formed only in small amounts.[56]



III. Heterocyclisation involving *p*,π-unsaturated amines and bifunctionalised reagents

The reactions of enamines (II) with bifunctional compounds provide a general route to five- and six-membered heterocycles. In this capacity, enamines (II) have been described in reviews[1,2] as three-carbon synthons.

In acidic media, enamines (II) are protonated with the formation of a conjugated carbenium ion, ($R_2N-CH=CH-\overset{+}{C}=CH_2 \leftrightarrow R_2\overset{+}{N}=CH-CH=C=CH_2$), which, on further reaction, dictates the structure of the final product. Thus, reaction of the conjugated carbenium ion with reagents having adjacent functionality proceeds with participation of the C_1- and C_3-atoms, leading to the formation of 5-substituted isoxazoles and pyrazoles (XLVIII),[57,58] 2-substituted 4-alkylpyrimidines (XLIX), (L)[59–61] and 3-substituted 2,4-dialkylpyridines (LI)[57,62–65] (Scheme 5).

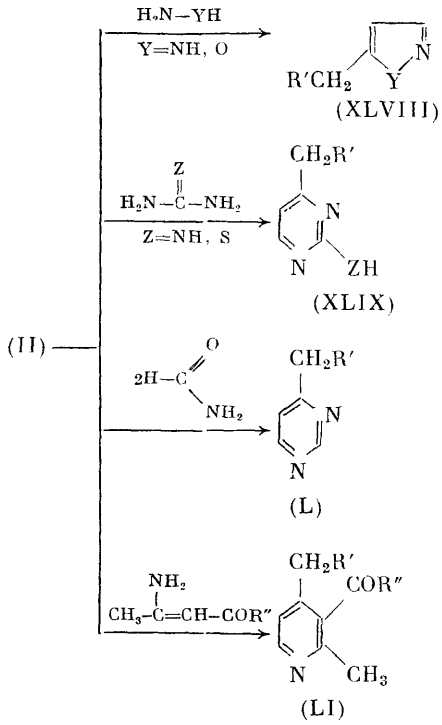
Since under acid catalysis the reaction of the carbocation with the nucleophile is the key step prior to cyclisation, the structure of the final product will, to a large extent, be determined by the activity of the electrophilic centres at C_1 and C_3 of the conjugated carbocation. For enamines (II), the electrophilic centre at C_1 has the greater effect, which accordingly determines the direction of the reaction.[66]

In this connection, one should especially emphasise the preparative value of the method since, by using β-dicarbonyl compounds or 1-alkoxy-1-alken-3-ynes as starting material in such ring syntheses, one obtains a mixture of 3- and 5-substituted isoxazoles and pyrazoles and a mixture of 2,4- and 2,6-dialkyl-substituted pyridines.[66]

Ring syntheses with enamines (II) take place via direct nucleophilic attack. Thus, 4-alkylpyrimidines (L) are obtained in high yield by treatment of (II) with formamide. Evidently, reaction proceeds by transamination of the dialkylamino group with the formation of a foramido compound which decarbonylates to give an imine; the latter then reacts with a second molecule of formamide to give the 4-methylpyrimidine (L).[61]

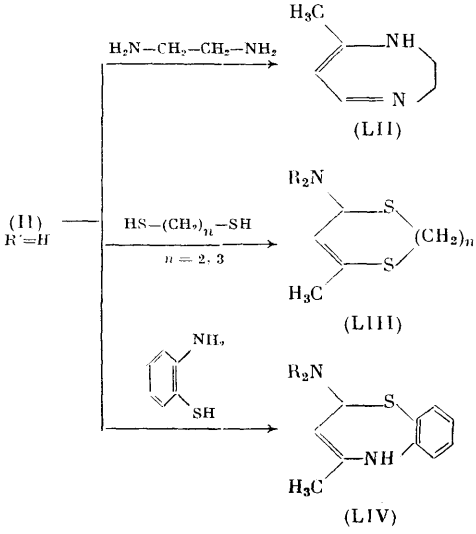
The same is true for the reaction of β-amino-α,β-ethyleneketones which afford 3-functionalised 4-alkylpyridines (LI).[64] Of the several possible routes by which reaction takes place, the most likely involves transamination of the function at the C_1 electrophilic centre with the primary amine group; this would be accompanied by intramolecular cyclisation via attack of the methine function at C_3, leading to the formation of the 2,4-disubstituted pyridine. The isolation of transamination products and literature data on the configuration of enaminoketones and enaminonitriles would support this pathway.[66]

Scheme 5



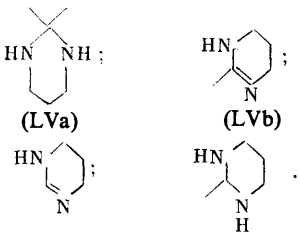
The formation of 2,3-dihydro-1,4-diazepines (LII) by reaction of enamines (II) with 1,2-diaminoethane is in accord with the above-described cyclisation via transamination (Scheme 6).[67–69]

Scheme 6



The interaction of 1-dialkylamino-1-buten-3-ynes with 1,2-ethanedithiol 1,3-propanedithiol also proceeds with involvement of the reactive C_1- and C_3-atoms of the conjugated system with the formation of 7-dialkylamino-5-methyl-7*H*-2,3-dihydro-1,4-dithiepines and 2-alkylamino-4-methyl-8*H*-6,7-dihydro-1,5-dithiocins, respectively (LIII).[70,71] In contrast with the reaction of 2-aminothiophenol with alkenylynamines, interaction with enamines (II) proceeds by 1,3-attack of the conjugated system to give the corresponding 2-dialkylamino-4-methyl-5*H*-1,5-benzothiazepines (LIV).[70,72]

Normally, the reaction of enamines (II) with 1,3-difunctionalised reagents would be expected to give heterocyclics with a large ring size. However, this is not always the case. Thus, the reaction of 1,3-butadiyne with 1,3-diaminopropane leads to the formation of a bis-adduct of the type XXVII, rather than an 8-membered ring; C-cleavage of these adducts affords the corresponding tetrahydro- and hexahydro-pyrimidines (LV):[35]



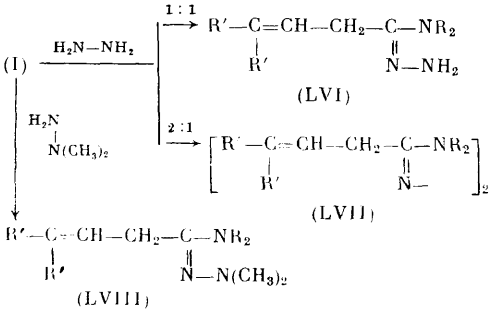
(LVa) (LVb) (LVc) (LVd)

Pyrroles with a variety of substitution patterns are obtainable by other routes, notably via 1,4-addition. Here, the synthesis can be achieved with butadiyne and ammonia or primary amines in the presence of copper salts.[1,4,73]

Since the starting enamines (II) can be obtained by direct interaction of diacetylene with secondary amines, the syntheses described above are potentially interesting from an industrial viewpoint. However, in planning synthetic routes from enamines (II), the commercially available 1,1-dimethoxy-3-butanone, which is obtaining from diacetylene, cannot be used as an equivalent.[74]

Ynamines (I) behave in a quite different way with bifunctional reagents. Thus, reaction with compounds having adjacent nucleophilic centres, such as hydrazine and hydroxylamine, affords acyclic adducts with participation of only the C_1 electrophilic centre of the ynamine (Scheme 7).[75] Amidrazones (LVI) based on 3-pentenoic acids are thereby produced in a manner not unlike the addition of hydrazine to ω-diethylaminophenylacetylene.[76]

Scheme 7

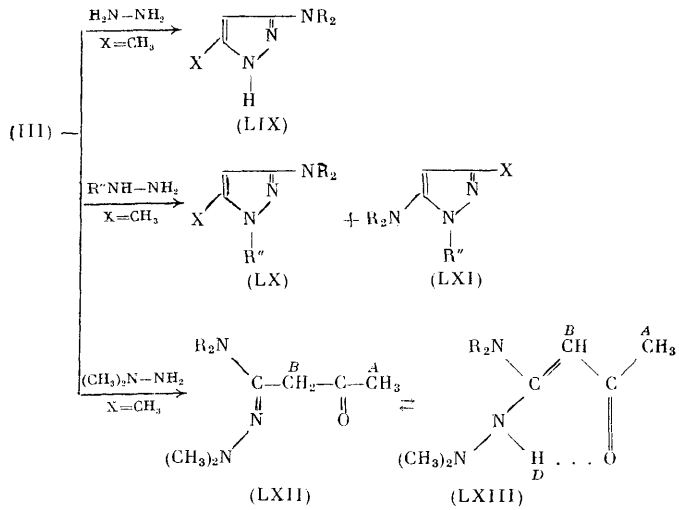


By adjusting the proportion of the reactants, e.g. by increasing the amount of hydrazine, it is possible to isolate adducts (LVII).[57] The reaction of ynamines (I) with non-symmetrical dialkylhydrazines leads in the same way to poly-N-substituted amidrazones (LVIII).[75]

The reaction of vinylacetylenic ynamines with hydrazine is markedly different from the reaction of vinylacetylenic enamines in that only the acetylene bond participates with the formation of monoadducts; the latter readily react with a second ynamine molecule. This observation is in keeping with the unusual mechanistic features of nucleophilic attack at an acetylenic bond in conjugation with a donor group.[77]

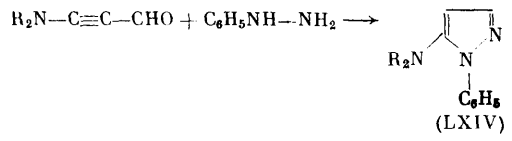
A study has also been made of the interaction of ynaminocarbonyl compounds (III) with supernucleophiles, such as hydrazine, alkyl- and phenyl-hydrazines, and unsymmetrical dimethylhydrazine. The reaction of 4-dialkylamino-3-butyn-2-ones with hydrazine proceeds with involvement of the C_1 and C_3 electrophilic centres to give 3(5)-dialkylamino-5(3)-methylpyrazoles in 56–63% yield (LIX) [78,79] (Scheme 8).

Scheme 8



The interaction of 4-dialkylamino-3-butyn-2-ones with monosubstituted hydrazines (methyl, propyl, and phenyl) leads in all cases to a mixture of isomeric products (LX) and (LXI),[79] as a result of the alternative approaches of the hydrazine group to the reactive centre of the ynaminoketone. According to ^{1}H NMR spectroscopic data and GLC analysis, the proportion of the two isomers in all cases is 3:4.

The obtained results would indicate that the reactivity of the two electrophilic centres in (III) is approximately equal. However, with ynaminoaldehydes, in which the activity of the carbonyl group is higher, the free amino group of the hydrazone predominantly attacks the carbonyl group. Thus, reaction of diethylaminopropynal with phenylhydrazine afforded predominantly isomer (LXIV) by attack of the free amino group on the carbonyl group.[80]



Ynaminoketones react on heating with the unsymmetrical dimethylhydrazine by exclusive attack at the reactive C_1 centre to give the corresponding N,N-dimethyl-3-oxobutanamidrazones (LXII, LXIII).[79]

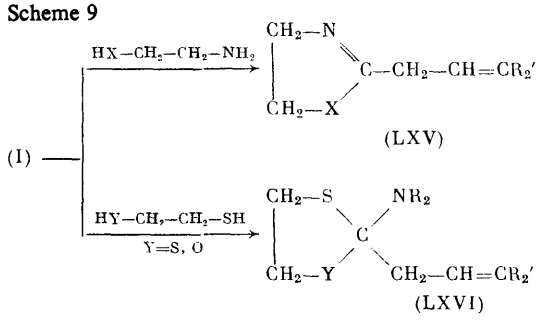
The ^{1}H NMR spectrum of (LXII) displayed signals in the region 2.10 p.p.m. corresponding to the methyl group of the acetyl fragment (H_A) and at 3.40 p.p.m. corresponding to the protons of the methylene group (H_B).

However, the enol tautometer (LXIII), stabilised by intramolecular hydrogen bonding, is present together with the keto form. The enol form is responsible for the signal at 1.84 p.p.m., corresponding to the methyl group (H_A), the signal at 5.00 p.p.m. corresponding to the vinyl proton (H_B), and the weak signal at 7.30 p.p.m. corresponding to the proton (H_D) of the hydroxyl group. The infrared spectra also reveal absorption at around 3400 cm^{-1} which can be ascribed to the associated hydroxyl group.

Thus, ynaminoketones react with hydrazine and its monosubstituted derivatives at both the C_1 and C_3 reactive centres affording a regioisomeric mixture of the corresponding pyrazoles. The unsymmetrical N,N-dimethylhydrazine adds exclusively across the triple bond of 1-dialkylamino-1-butyn-3-one with the formation of an acyclic product existing as a tautomeric mixture of keto and enol forms.

Treatment of alkenylynamines with aliphatic 1,2-dinucleophiles containing nitrogen, oxygen and sulphur functionality afford five-membered heterocyclics by attack of the two nucleophilic centres at the C_1 electrophilic centre (Scheme 9).

Scheme 9

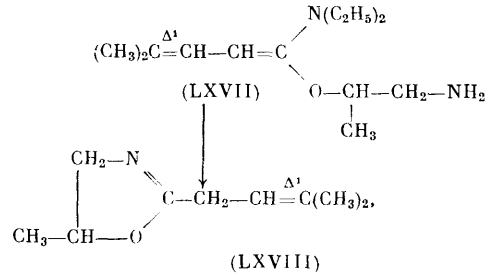


Thus, interaction of 1-dialkylamino-3-penten-1-ynes (I) with 1,2-diaminoethane and ethanolamine gave the corresponding 2-(2-buten-1-yl)imidazolines and 2-(2-buten-1-yl)oxazolines (LXVI), respectively.[81] In these reactions, 2-substituted imidazolines and oxazolines were formed by cleavage of the dialkylamino group. The non-conjugated ethylenic group at the 2-position of the side chain is thereby left intact, confirming the regioselectivity of reaction at the triple bond.

Regioselectivity is the same with sulphur-containing binucleophiles (2-mercaptoethanol, ethanedithiol), the corresponding products being 2-dialkylamino-(2-buten-1-yl-1,3-oxathiolanes and 2-dialkylamino-(2-buten-1-yl)1,3-dithiolanes (LXVI).[81]

The reactivity of nitrogen-, oxygen-, and sulphur-containing reagents towards alkenylynamines (I) increases with their acidity as a consequence of electrophilic catalysis of the addition process. Reagents which are more acidic than water (2-mercaptoethanol and 1,2-ethanedithiol) interact with alkenylynamines (I) in the absence of acid, while reactions with 1,2-diaminoethane and ethanolamine require the presence of a catalytic amount of acid, which is in accordance with the rule outlined above.[12,17]

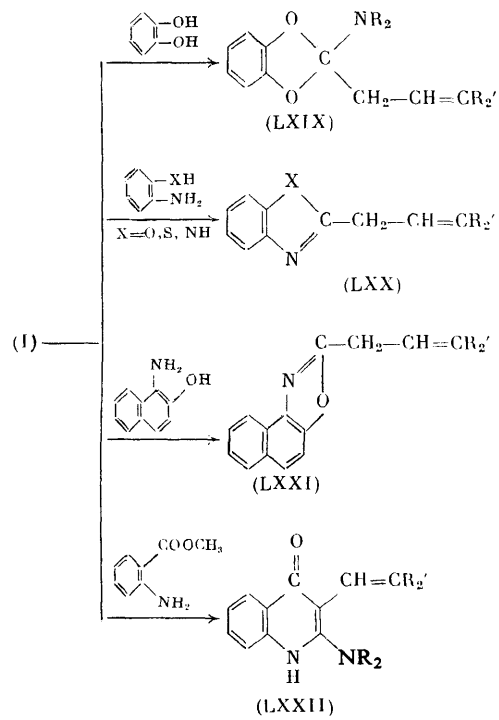
Reactions of alkenylynamines (I) with ethanolamine proceed similarly, but a two-stage process is involved with methylethanolamine. Thus, according to ^{1}H NMR spectral data, the product of reaction between methylethanolamine and 1-diethylamino-3-penten-1-yne affords, in addition to the expected cyclic product, a vinylketene O,N-acetal (LXVII), which is converted into the oxazoline (LXVIII) during the course of the reaction.[82] The isolation of the acyclic product (LXVII) is evidently a consequence of steric hindrance in the formation of the ring.



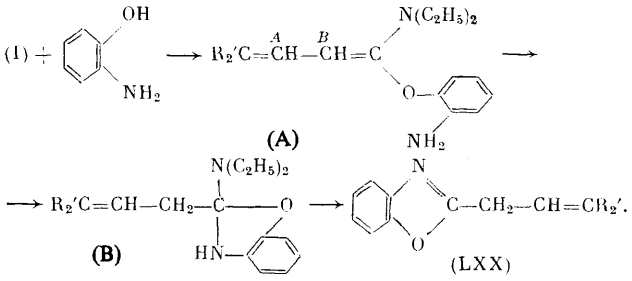
In order to determine the effect of the structure of the reagent and the stereochemistry of ring closure, a study has been made of reactions with aryl and naphthyl 1,2-dinucleophiles in which the nucleophilic residues are stereo-defined (Scheme 10). The interaction of alkenylynamines (I) with catechol (pK_a 9.44) proceeds on cooling to give the corresponding 2-dialkylamino-2-[3-methyl-2-buten-1-yl]-1,3-benzodioxoles (LXIX) in 70% yields.[83,84]

The reaction of alkenylynamines (I) with *o*-aminophenol, *o*-aminothiophenol, and *o*-phenylenediamine afforded the respective benzoxazole,[84,86] benzothiazole[85] and benzimidazole[84,87] derivatives of general structure (LXX), in which the side chain unsaturation at the 2-position is non-conjugated.

Scheme 10

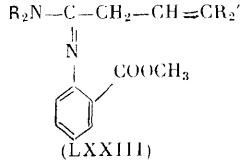


In the reaction of 1-diethylamino-(4-methyl)3-penten-1-yne with *o*-aminophenol it is possible to isolate all the intermediates.[84] Reaction proceeds smoothly and is exothermic; moreover, it is initiated by attack of the hydroxyl group since phenols react with ynamines at a much greater rate than amines. This is also confirmed by ^{1}H NMR spectral measurements during the reaction, which display proton signals at 4.78 p.p.m. (H_B, 1H) and 5.85 p.p.m. (H_A, 1H); according to the literature values for fragment $R_2'C=CH-CH=C(OPh)NR_2$ [12], these correspond with the signals for the vinylic protons of compounds of type (A). At the end of the reaction these signals have completely disappeared. When (A) could no longer be detected, the residue was shown to contain compound (B) which, on distillation, affords (LXX) by cleavage of the diethylamino group.



It was also shown that the condensation takes place with naphthalene derivatives. Thus, 1-amino-2-naphthol gave naphth[1,2-*d*]oxazoles (LXXI).[88]

If the difunctionalised reagent possesses groups which are different in nature, e.g. methyl anthranilate, then reaction with alkenylynamines takes place at C_1 and C_2 to give a six-membered ring without cleavage of the dialkylamino group, i.e. 2-dialkylamino-3-(2-methyl-1-propenyl)-4-quinolones (LXXII).[89] Reaction proceeds in two stages under acid catalysis. The intermediate (LXXIII), formed by initial addition of methyl anthranilate to the starting ynamine (I), was isolated.[69]



In the above-described reaction, the alkenylynamines (I) behave as rather unusual acylating agents, from which a number of 5-membered benzo-condensed 1,3-heterocyclics can be prepared with a non-conjugated unsaturated residue at the 2-position. Ynamines participate in the same type of heterocyclisation.[90]

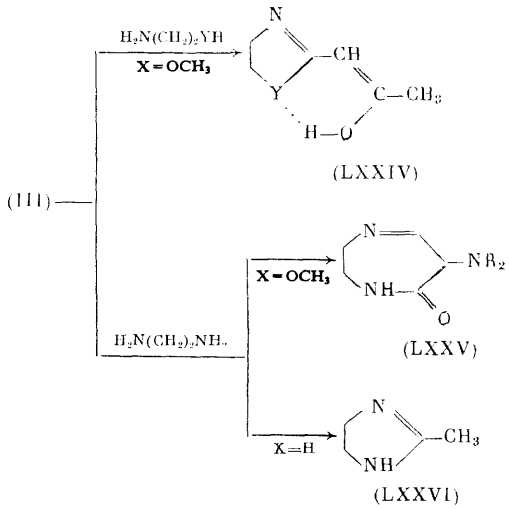
By comparing reactivity data for the reactions of alkynamines and alkenylynamines with *o*-phenylenediamine, *o*-aminothiophenol, and *o*-aminophenol, one arrives at the qualitative conclusion that, in the absence of acidic catalysis, addition becomes more facile with an increase in the acidity of the functional group in the order $NH_2 < OH < SH$. This is possibly associated with autocatalysis of the nucleophilic addition.

Thus it has been shown that the reaction of alkenylynamines (I) with bifunctional reagents containing nitrogen, oxygen and sulphur proceeds stepwise via initial atack at the electrophilic C_1 atom of the ynamine to give 5-membered heterocyclics with two heteroatoms and an unconjugated phenyl-type group at the 2-position. The interaction of aromatic *o*-substituted dinucleophiles proceeds by a concerted mechanism through a cyclic, 5-membered, resonance-stabilised transition state.

Acetylenic ynaminocarbonyl compounds (III) should display electrophilicity by virtue of the ynamine residue in conjugation with a polar carbonyl group. In fact, reactions with both mono- and dinucleophiles proceed without acid catalysis. Data on the reactivity of ynaminocarbonyl compounds show that they react in a different manner to ynamines[26], alkenylynamines and acetylenic ketones.[43]

Thus, in reactions with aliphatic 1,2-dinucleophiles, the nature of the heteroatom and the carbonyl group have a pronounced effect. For example, reactions of 4-dialkylamino-3-butyn-2-ones with 1,2-diaminoethane and 2-aminoethanol afford the corresponding 1-(2-imidazolinyl)-1-propen-2-ols[91,92] and 1-(2-oxazolinyl)-1-propen-2-ols (LXXIV) [91] (Scheme 11).

Scheme 11



The formation of imidazoline and oxazoline derivatives takes place as a result of a two-fold attack at the α-carbon atom of the acetylene group, i.e. the orientation of attack is the same as in reactions with ynamines[90] and conjugated ynamines.[81] According to one finding[93], 1-mercapto-2-aminoethane adds to acetylenic ketones at the β-carbon atom of the acetylene group under basic catalysis.

The geometry of the final product (LXXIV) is determined by stabilisation of the enol form through intramolecular hydrogen bonding. The literature does make reference to imidazolines having a completely enolised β-ketoalkyl residue.[94]

The course of the reaction is dependent on the nature of the carbonyl group. Thus, dialkylaminopropiolates react with 1,2-diaminoethane with the participation of both electrophilic centres to give 5-dialkylamino-2,3-dihydro-1,4-diazepin-7-ones (LXXV) in 68% yield.

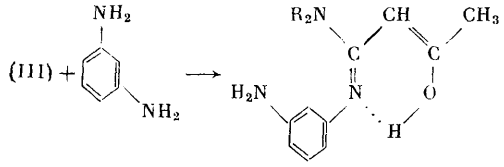
Evidently, the lower electrophilicity of the C_1 and C_3 centres in ynaminoesters, compared with ynaminoketones, is responsible for the concerted 1,3-attack of the bifunctional nitrogen-containng bases, the final outcome being the formation of diazepine derivatives. The facile intramolecular nuclophilic replacement of the methoxy group of the ester also dictates this mode of cyclisation.

With ynaminoaldehydes (III, X = H) the electrophilicity of the two centres is so high that two 1,2-diaminoethane molecules attack each of the reaction centres twice, affording a bis-adduct which

undergoes carbon-carbon bond cleavage with formation of 2-methyl-2-imidazoline (LXXVI).[97] This type of reaction is similar to that described earlier.[35]

The interpretation of ynaminocarbonyl compounds with aromatic 1,2-dinucleophiles leads to a different result. The reduced nucleophilicity of *o*-phenylenediamine relative to 1,2-diaminoethane, is responsible for the different mode of reaction with ynaminoketones. Thus, 4-dialkylamino-3-butyn-2-ones react with o-phenylenediamine to give seven-membered heterocyclic derivatives, namely 7(α)-R'-2-dialkylamino-4-methyl-3H-1,5-benzodiazepines (LXXVII) [95] (Scheme 12).

An NMR spectral study of the reaction between 4-dimethylamino-3-butyn-2-one and *m*-phenylenediamine was conducted in an NMR tube (i.e. non-preparatively) in order to elucidate the initial attack of the aromatic diamine. On heating in $CDCl_3$, *m*-phenylenediamine adds slowly to the ynaminoketone across the triple bond with the formation of an iminoenol tautometer (LXXXIII) as the final product.



X = CH_3.

(LXXXIII)

Of all the nucleophilic reagents studied, only *m*-phenylenediamine reacted to give a sufficiently stable iminoenol tautometer. The extent of conjugation, involving the two double bonds (C=C and C=N), the aromatic ring, and the hydroxyl group, is sufficient to provide such stabilisation. It is likely that, in the case of *o*-phenylenediamine, enolisation of the intermediate adduct favours ring closure to the benzodiazepine (LXXVIII).

The 1,3-mode of attack with *o*-phenylenediamine is again evident in the reaction with methyl 3-dialkylaminopropiolate, providing LXXVIII.[96]

The orientation of the reaction of acetylenic ketones with *o*-phenylenediamine is the same as that of ynaminoketones.[98]

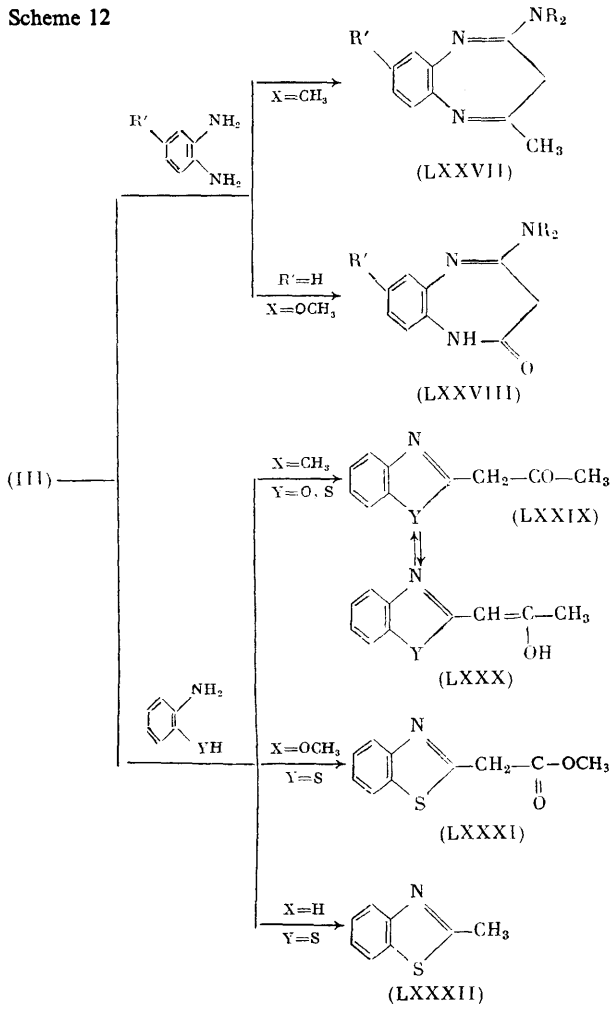
Treatment of 4-dialkylamino-4-butyn-2-ones with *o*-aminophenol and *o*-aminothiophenol afforded the corresponding fused 5-membered heterocyclics, namely 1-(2-benzoxazolyl)-2-propanone and 1-(2-benzothiazolyl)-2-propanone, which exist as a mixture of keto (LXXIX) and enol (LXXX) tautomers.[91]

Reaction of methyl 3-dialkylaminopropiolate with *o*-aminophenol and *o*-aminothiophenol affords 2-carbomethoxymethylbenzoxazole and 2-carbomethoxymethylbenzothiazole, respectively, (LXXXI).[96]

Just as in reaction with ethylenediamine, 3-(dialkylamino)propynal with *o*-aminothiophenol affords a product via double addition across both reaction centres; C–C bond cleavage then takes place to give 2-methylbenzothiazole (LXXXII).[97]

Thus, it has been shown that ynaminocarbonyl compounds react in the same way as simple ynamines, irrespective of the nature of the acceptor group. The course of the heterocyclisation of conjugated ynamines with acceptor groups depends both on the character of the carbonyl group and the nature of the nucleophile. Cyclisation with aliphatic nucleophiles depends on the acceptor ability of the carbonyl function. With weak nuclophiles (aromatic diamines) only 1,3-addition takes place, independent of the nature of the carbonyl group, and only the ynamine residue is involved in the reaction with nucleophiles containing hydroxyl and sulfhydryl groups. The preparation of five- and seven-membered heterocyclics containing two

Scheme 12

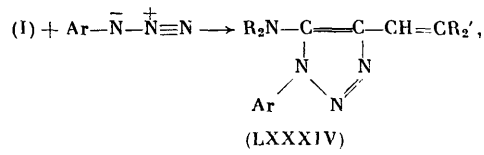


heteroatoms (nitrogen, oxygen, or sulphur) can thus be achieved by choosing a suitable carbonyl-containing ynamine and dinucleophile.

IV. 1,3-Dipolar cycloaddition

The 1,3-dipolar activity of both types of amine, (I) and (II), has been studied in order to assess the activating effect of the dialkylamino group on the reactivity of the α,β-unsaturation in conjugation with the π-system. It is known that acetylenic ynamines react with 1,3-dipoles to give 5-membered heterocyclics.[5,99] In the 1,3-dipolar cycloaddition of a variety of vinylacetylenic compounds, the double bond of the conjugated enyne system is significantly more reactive than the disubstituted triple bond.[99]

1-Aryl-4-vinyl-5-dialkylamino-1,2,3-triazoles (LXXXIV) were obtained by interaction of 1-dialkylamino-3-buten-1-ynes with aromatic azides.[100,101]

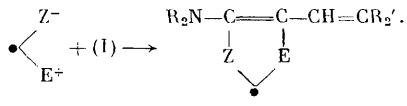


(LXXXIV)

Thus, the 1,3-dipole attacks the acetylenic bond rather than the terminal ethylenic bond with retention of the dialkylamino group.

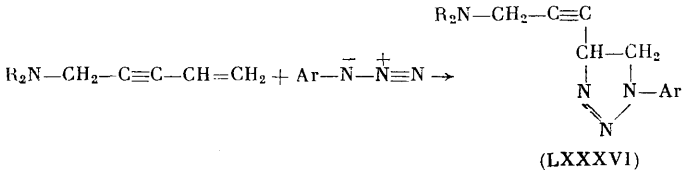
In all cases, addition of aryl azides to alkenylynamines (I) proceeds regiospecifically with the formation of only one isomer as has been confirmed by TLC and NMR spectroscopic studies of the product. The data accord well with literature values for the 1,3-dipolar cycloaddition of aryl azides with compounds having highly polar unsaturations, e.g. alkoxyacetylenes,[102] ynamines,[103,104] and acetylenic ketones and acids.[105,106]

The results obtained by studying the reactions of other octet-stabilised 1,3-dipoles (benzonitrile *N*-oxide, C-*p*-F-phenyl-*N*-nitrilimines) with alkenylynamines confirm the generality of the cycloaddition, which proceeds regioselectively at the acetylenic function independent of the structure of the ethylene fragment (LXXXV).



(LXXXV)

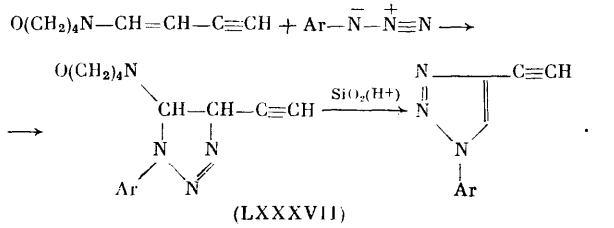
It is important to note that the incorporation of a methylene group between the nitrogen function and the vinylacetylene group significantly affects the order of addition of the 1,3-dipole, by comparison with alkenylynamines (I). The interaction of 1-diethylamino-4-penten-2-yne with aromatic azides leads to 1-aryl-4-(3-diethylamino-1-propynyl)-Δ^2-triazolines (LXXXVI).[101] In this reaction it is generally found that the terminal double bond of the vinylacetylene group is the more reactive unsaturation.[99]



(LXXXVI)

Thus, in vinylacetylenic compounds having an amino group on an unsaturation, the nitrogen atom activates the α,β-unsaturation for the addition of 1,3-dipoles. Where the amino group is not bonded to the unsaturation, the regioselectivity is determined by the position of the bond. This is supported by data obtained from the reaction between 1,3-dipoles and enamines (II).

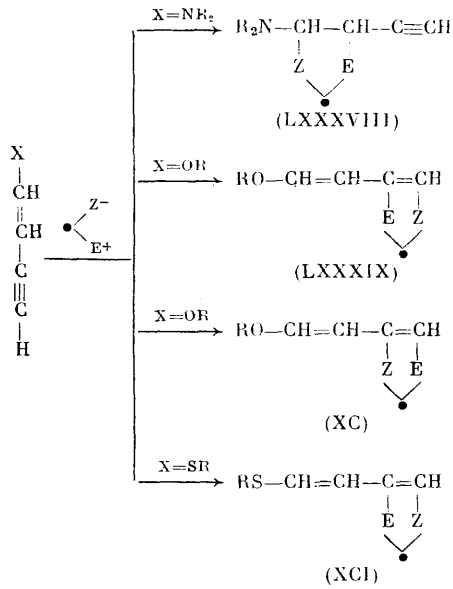
Thus, 1-morpholino-1-but-3-yne with aromatic azides affords 1-aryl-4-ethynyl-5-*N*-morpholino-Δ^2 triazolines (LXXXVII),[101] i.e. addition of the 1,3-dipole proceeds exclusively at the disubstituted ethylenic bond.



(LXXXVII)

In contrast, addition of 1,3-dipoles to 1,3-enynyl ethers and thioethers takes place at the terminal acetylene group with formation of 5-membered heterocyclics (LXXXIX), (XC) and (XCI) [101,107] (Scheme 13).

Scheme 13



(LXXXVIII)

(LXXXIX)

(XC)

(XCI)

Thus a study of 1,3-dipolar cycloaddition with both types of vinylacetylenic amine, (I) and (II), has shown that the conjugated *p*,π-system serves as dipolarophile, interacting with 1,3-dipolar systems in the usual manner. However, the amino group in such dipolarophiles has a specific directing influence on the cycloaddition.

The fact that conjugation with the amino group activates the α,β-unsaturation confirms the electrophilic nature of the reaction. However, the readiness of amines (I) and (II) to undergo electrophilic addition, as mentioned in earlier sections, and the requirement of an acid catalyst for nucleophilic addition, would suggest that the anomalous behaviour of the nitrogen-containing *p*,π-conjugated system is associated with the involvement of the nitrogen atom in the initial stage the cycloaddition, as is observed in the reactions of α,β-unsaturated tri-valent phosphorus compounds.[99,108]

The subsequent stabilisation of the system is effected by formation of the heterocyclic ring with participation of the α,β-unsaturation.

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Translated from *Uspekhi Khimii* 60 134–168 (1991) U.D.C. 547.567

Nucleophilic reactions of quinones

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ABSTRACT. Nucleophilic addition to, and substitution of, quinones have been systematically reviewed. Particular attention has been paid to establishing general trends in reactivity in the light of our present-day understanding of mechanistic chemistry.

The bibliography contains 188 references.

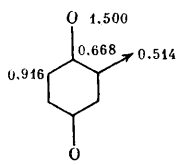
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I. Introduction

Quinones are widely distributed in nature and are produced industrially in all the developing countries. Historically the first, and still the major, application of quinones has been in the dye industry. At the present time, quinoidal compounds are used as dyes and luminophores in photography and electrophotography, in optical quantum generators (lasers), liquid crystalline and photochromic materials, and as scintillators.[1–5] However, the value of quinones is not restricted to dye chemistry. Our knowledge of the biological activity of quinones has developed enormously, not only with the discovery of the vitamin K group, but also with the preparation of drugs, herbicides, fungicides, and plant-growth regulators.[6–16] Quinones have also been used as analytical reagents, polymer modifiers, photoresistors, and catalysts.[17–21] Halogeno- and cyano-quinones are used in organic synthesis as indispensable dehydrogenating agents, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone being one of the most powerful organic oxidants.[22] No doubt applications of quinones will become even more widespread.

LCAO–MO calculations for 1,4-benzoquinone have shown that the distribution of π-electron density is very uneven,[23] as depicted below.

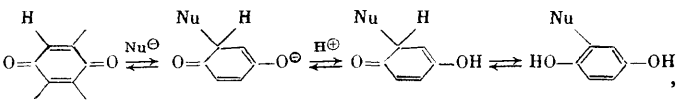


The wide variation in the electron density of quinones explains the broad spectrum of activity of this class of compound. In fact, quinones participate in an enormous number of homolytic and heterolytic reactions. This review is devoted to the most interesting of the heterolytic processes; nucleophilic reactions, which exemplify the rich synthetic potential of quinones. Electrophilic reactions are less varied, being limited to the interaction of quinones with hydrogen- and metal-containing reducing agents to give hydroquinones or semi-quinoidal complexes.[24–37]

In recent reviews devoted to various aspects of the chemistry and use of quinones, there is a notable absence of information on the nucleophilic and electrophilic reactions of quinones.[38–43] We have sought in this review to make good this deficiency. Data are presented here on the reactions of quinones with nucleophilic reagents in the light of our present-day understanding of mechanistic chemistry.

II. Nucleophilic addition to quinones

The general scheme of nucleophilic addition to 1,4-quinones is presented below (1,2-quinones interacting in a similar way).



$Nu^{\ominus}$ – nucleophile.

The final step in the scheme is shown as a reversible process. However, as a rule it is irreversible since it leads to the formation of a stable aromatic system. Here, a proton is depicted as the electrophile. With other electrophiles, the overall scheme is the same; only the detail changes.

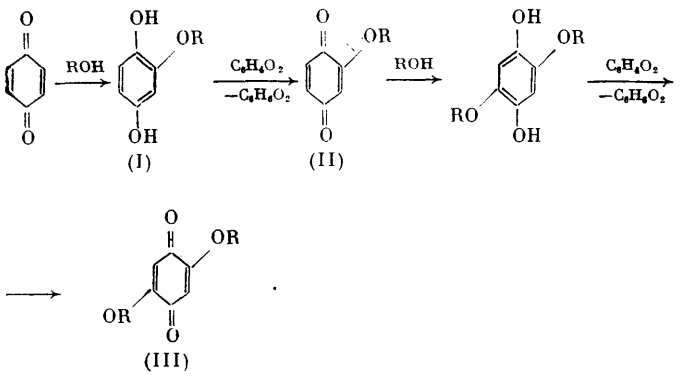
From molecular orbital calculations, the coefficients for the higher, occupied and lower, unfilled molecular orbitals have been determined for substituted 1,4-benzoquinones and 1,4-naphthoquinones. From this data, rules have been established for the orientating effects of substituents on nucleophilic addition. Thus, for 2-substituted 1,4-benzoquinones, the order of reactivity of ring positions is 5 > 2 > 6 for donor substituents, and 3 > 6 > 5 for acceptor or unsaturated substituents. The 2-position of 1,4-naphthoquinone is activated by donor substituents at C_2 and C_6 and by acceptor and unsaturated substituents of C_5. The 3-position activates donor substituents at C_5; an *anti*-5-OH group acts as a donor, while a *syn*-5-OH group acts as an acceptor.[44]

The calculations are generally in accord with resonance theory, as will be seen later, and are confirmed by experimental data except in the case of nucleophilic addition to carbon without a donor substituent.

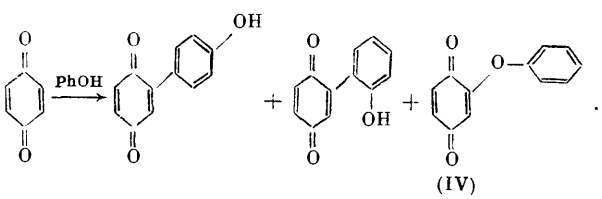
1. Reactions with *O*-nucleophiles

Normally, direct addition of water to quinones to give an adduct is not possible; one exception has been reported but it has no preparative value.[45] Primary alcohols react with quinones only in the presence of catalysts: zinc, cadmium, calcium and magnesium.

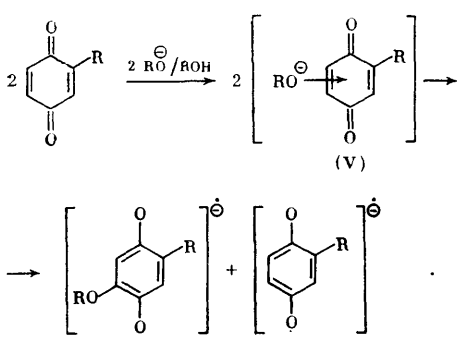
However, the highly active 2-acetyl-1,4-benzoquinone does react without a catalyst. Reaction involves initial nucleophilic addition of the alcohol to the quinone with formation of alkoxyhydroquinone (I); this is then oxidised by the starting quinone to alkoxyquinone (II). A second molecule of the alcohol adds to the latter to give the corresponding 2,5-dialkoxy-1,4-benzoquinone (III) as final product.



There are isolated examples of the reaction of secondary alcohols with quinones, but tertiary alcohols are unreactive. C-Arylated quinones are generally obtained by reaction of phenols with quinones. The yield of aryloxy derivatives (IV) is no more than 5%.[45]



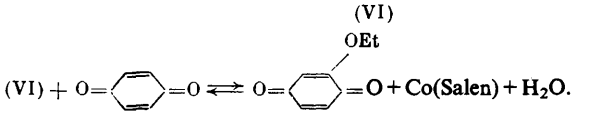
A kinetic study of the reaction of 1,4-quinones with alkoxide ion in alcoholic media has shown that the process involves initial formation of a charge-transfer complex (V) between the 1,4-quinone and alkoxide ion, followed by its conversion into quinol radical anions, the ratio of which depends on the nature of the alkoxide ion, the substituent on the 1,4-quinone ring, and the medium.[46]



There is virtually no reaction of 1,4-benzoquinone with ethanol in the absence of catalyst. Reaction is facile in the presence of bis(*N*,*N*-salicylideneethylenediaminato)cobalt, Co(Salen), and oxygen. It is thought that reaction involves three stages:

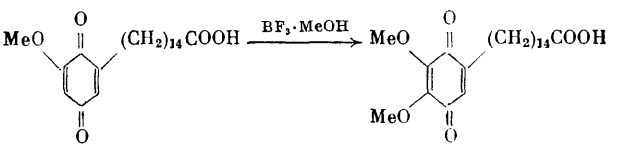
$$2\text{Co(Salen)} + O_2 \rightleftarrows 2\text{Co(Salen)}-O,$$

$$\text{Co(Salen)}-O + \text{EtOH} \rightleftarrows \underset{\text{(VI)}}{\text{EtO}-\text{Co(Salen)}-O},$$

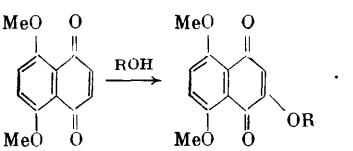


The last step is rate-determining. It has been suggested that Co(Salen) forms a 2:1 complex with O_2, existing as a dimer (with a Co–O–O–Co bond) in the solid state and in alcoholic media. The formation of complex (VI) requires cleavage of the O–O bond by attack of an alcohol molecule on cobalt. Increase in the size of the alcohol molecule hinders this cleavage for steric reasons, which explains the reduction is yield. ^{1}H NMR spectroscopic data indicated that complex formation between Co(Salen) and alcohols is a reversible process. Reaction is inhibited by the addition of chloroform [which forms a simple adduct with Co(Salen)] or benzene [which also associates with Co(Salen)], resulting in elimination of oxygen.[47]

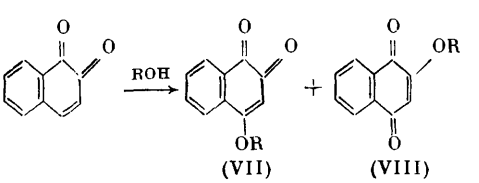
BF_3 may be used as catalyst for the reaction of quinones with alcohols. Methoxylation of substituted 1,4-benzoquinones takes place in the presence of BF_3.MeOH complex.[48]



1,4-Naphthoquinones with donor substituents in the 5 and 8 position react with alcohols to give 2-alkoxy derivatives in the presence of sulphuric acid and a little iron sulphate as catalyst.[49]



1,2-Quinones react with alcohols in the same way as 1,4-quinones in the presence of catalyst. A study has been made of the reaction of 1,2-napthoquinones with alcohols in the presence of sodium iodate and a metal salt ($CoCl_2$, $CoCl_2.6H_2O$, $NiCl_2.6H_2O$, $CuCl_2.2H_2O$, $LaCl_3.7H_2O$, $CeCl_3.7H_2O$).[50] The yield of the resulting 4-alkoxy-1,2-naphthoquinone (VII) increases according to the sequence of reagents shown, being 3% with $CoCl_2$ and 79% with $CeCl_2.7H_2O$. Quinone (VII) is not formed in the absence of catalyst. 2-Alkoxy-1,4-naphthoquinones (VIII) are formed in addition to (VII) on prolonging the reaction and increasing the temperature.

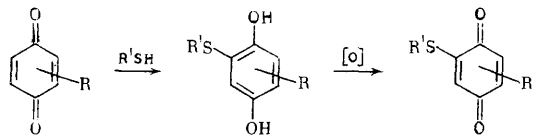


Alcoholysis of acenaphthoquinone and the related *o*-pleiadienoquinone leads to the formation of the corresponding quinone ketals.[51]

2. Reactions with *S*-nucleophiles

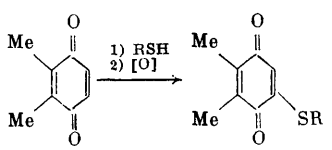
(a) With thiols

Thiols and thiophenols react with 1,4-quinones to give 1,4-adducts (IX), which, in the course of reaction, are oxidised by air or by the starting quinone to provide the corresponding alkylthio- or arylthioquinones (X).



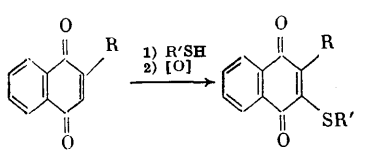
(IX) (X)

By using an excess of thiol, the organothio group may be introduced at various ring positions, depending on the nature of the substituents in the starting quinone. The following trend has been noted: quinones with donor substituents give mainly 2,5-isomers while quinones with acceptor substituents give 2,3-isomers. In such cases, and others, the corresponding 2,6-isomers are also formed. 1,4-Quinones with alkylthio and arylthio groups in the side-chain have attracted the attention of microbiologist and pharmaceutical chemists, as well as organic chemists, since such compounds display high biological activity. In particular, the products of the reaction between 2,3-dimethyl-1,4-benzoquinone and thiophenols are inhibitors of the enzymes succinoxidase and NAD-oxidase. In this respect, compound (XI) (where R = 2-naphthyl) is the most active.[52]



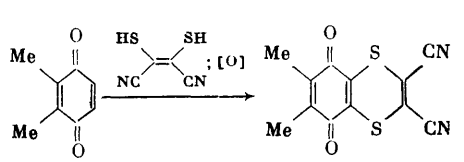
(XI)

Antimicrobial activity has been found with substituted naphthoquinones (XII), prepared as shown below.[53,54]

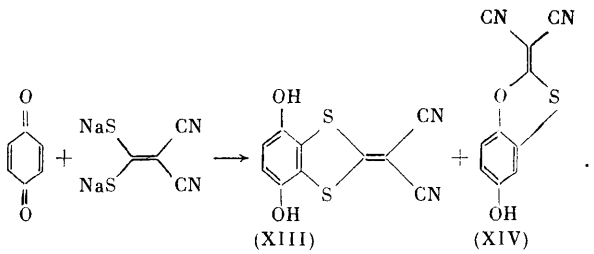


(XII)

While the reactions of thiols with quinones involve two stages (addition and oxidation), the interaction with dithiols involves four steps: (1) addition to the quinone of one mercapto group; (2) oxidation of the intermediate; (3) addition of the other mercapto group; (4) oxidation to give the final product. 2,3-Dimercaptomaleonitrile interacts with 2,3-dimethyl-1,4-benzoquinone according to this scheme with the formation of a rare class of compound, namely 1,4-dithiabenzo-5,8-quinones.[55]

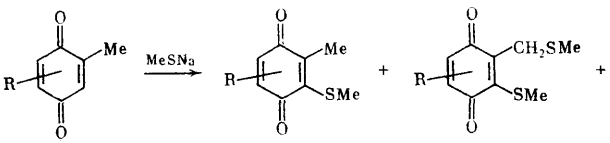


Metal dithiolates react with quinones in a more complex manner to give, in the example below, a mixture of the corresponding benzo-1,3-dithiole (XIII) and benzo-1,3-oxathiole (XIV) in 40% and 20% yield, respectively.[56]

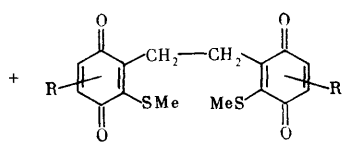


(XIII) (XIV)

Metal thiolates are extremely active nucleophiles, and their reactions with quinones are far more selective than reactions with thiols. The interaction of sodium methylmercaptide with methyl-substituted quinones produces mainly methylthio derivatives (XV)–(XVII) (by addition-oxidation), of which two, (XVI) and (XVII), are substituted in the side-chain.[57,58]

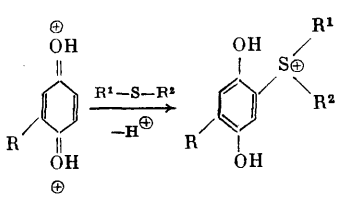


(XV) (XVI)



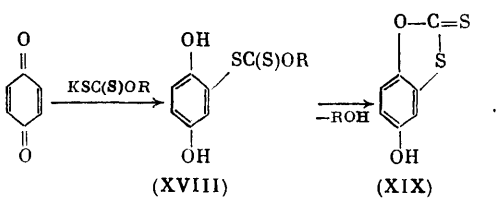
(XVII)

Thioethers on the other hand, are inert towards quinones. However, activation of the latter with 50% H_2SO_4 leads to the formation of sulfoniohydroquinones.[45,59]



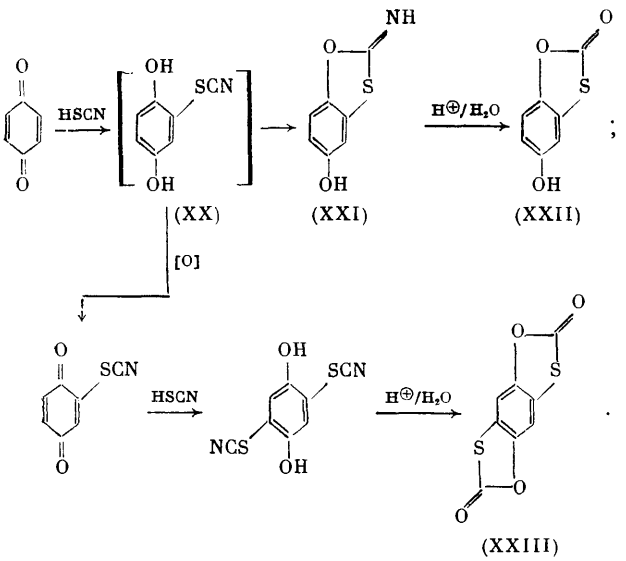
(b) With thiolic acids

In this section, we examine the reactions of quinones with SH-acids containing divalent sulphur. 1,4-Quinones interact with dithiocarboxylic acids and their salts. Reaction with potassium xanthate affords the condensation product (XIX) via the 1,4-adduct (XVIII).[45]



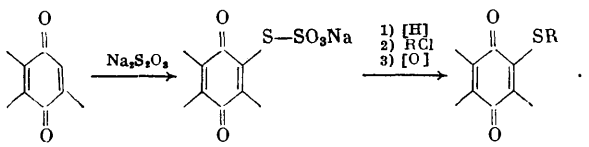
(XVIII) (XIX)

The interaction of thiocyanic acid with 1,4-benzoquinone gives the 1,3-benzoxathiolones (XXII) and (XXIII) rather than the thiocyanatohydroquinone (XX), as might have been expected. The reaction conditions determine which of the products (XXI–XXIII) are isolated.[60]



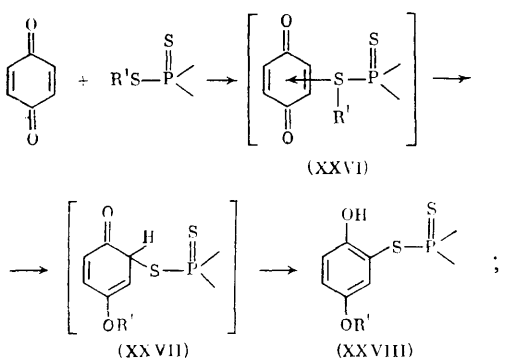
(XX) (XXI) (XXII) (XXIII)

Since the thiolic sulphur of the thiosulphate ion is the nucleophilic centre, the reaction of sodium thiosulphate with quinones leads to the formation of sulfothiohydroquinones (XXIV), which in certain cases have been used for the synthesis of alkylthio-1,4-benzoquinones (XXV).[45]



(XXIV) (XXV)

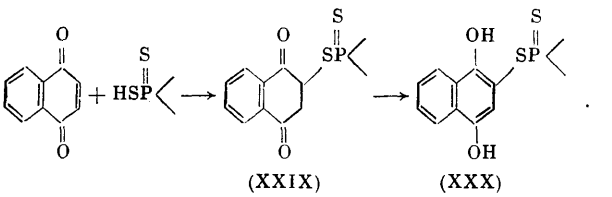
The interaction of dithiophosphoric acids and their trimethylsilyl esters with quinones is interesting. A detailed study of the reactions by kinetic and spectrophotometric methods has shown that a *p*,π-type complex (XXVI) is formed initially; this leads to intermediate (XXVII), and then to the final 1,4-adduct (XXVIII).



(XXVI) (XXVII) (XXVIII)

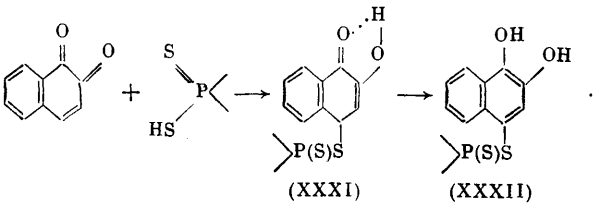
R' = H, SiMe .

The interaction with 1,4-naphthoquinone takes place by another route.



(XXIX) (XXX)

Initially, addition takes place across the C=C bond of the quinone to give (XXIX), which is converted into the thiophosphorylated dihydroxynaphthalene (XXX). The reaction of dithiophosphorus acids with 1,2-naphthoquinone is unusual. The intermediate (XXXI), which can be detected by IR-spectroscopy, isomerises as reaction progresses to give the 1,4-adduct (XXXII) as the final product.

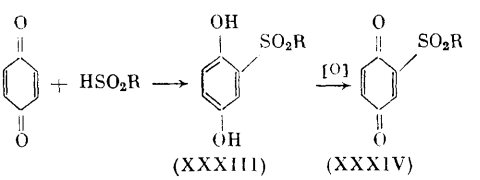


(XXXI) (XXXII)

The stability of the enol form of intermediate (XXXI) is energetically favourable by virtue of stabilisation by intramolecular hydrogen bonding.[61–63]

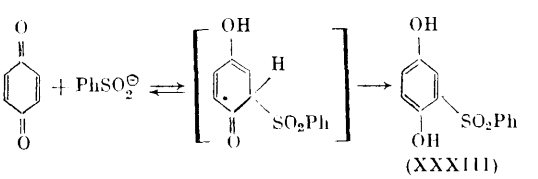
c) With sulphinic acids and sulphurous acid salts

Nucleophilic addition of sulphinic acids to 1,4-benzoquinone proceeds smoothly in the absence of catalyst to give the corresponding 2,5-hydroxy-1-alkyl(or aryl)sulphonylbenzenes (XXXIII), which can be converted to the corresponding sulphonylquinones (XXXIV).



(XXXIII) (XXXIV)

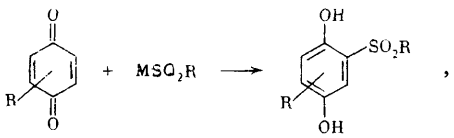
The mechanism of the reaction between 1,4-benzoquinone and phenylsulphinic acid in an aqueous medium has been established by kinetic studies with isotopes. Initially, there is a reversible addition of sulphinate anion to the ring system of the quinone to give an unstable adduct, which then isomerises to the sulphonylhydroquinone (XXXIII) as final product.



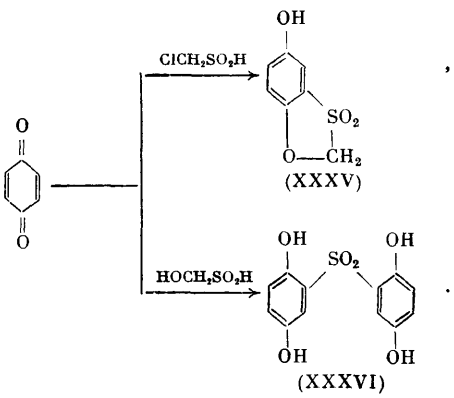
(XXXIII)

Kinetic data are in accord with a second order process, being first order in each reactant. The limiting step of the reaction is dependent on the pH of the medium. Thus, below 3.1, the rate-limiting step is the initial addition, while above pH 4.0 the isomerisation is the rate-determining stage.[64]

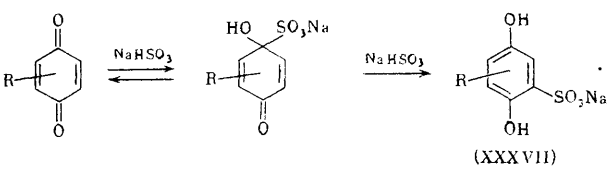
Sulphinic acid salts are stronger nucleophiles than the parent acids. They react with quinones to give sulphonylhydroquinones:[65]



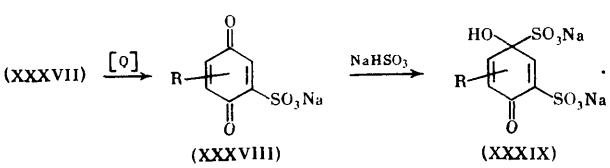
where M is an alkali or alkaline-earth metal or an organic cation. Chloromethanesulphinic and hydroxymethanesulphinic acid, as well as other sulphinyl compounds, interact with 1,4-benzoquinone to give unstable 1,4-adducts, which undergo intra- and inter-molecular condensation with the formation of the corresponding sulphones (XXXV) and (XXXVI).[45]



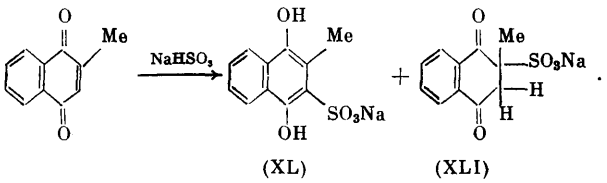
Reaction of sodium bisulphite with 1,4-benzoquinones involves a rapid, reversible, formation of a carbonyl-bisulphite adduct, followed by addition of bisulphite anion to give the hydroquinone-monosulphonates (XXXVII) as final product.[66,67]



A study of this reaction in buffered medium at pH 5–10 has shown that the highly reducing species (XXXIX) is formed. Its redox potential is more negative than that of hydroquinone. Thus, it is reasonable to conclude that compound (XXXIX) plays an important role in the mechanism of the action of hydroquinone-type indicators. It has been shown that compound (XXXIX) is formed by oxidation of the monosulphonate (XXXVII), followed by addition of sodium bisulphite to the carbonyl group of (XXXVIII).[68]

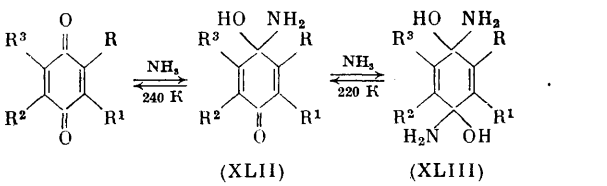


In the reaction of sodium bisulphite with 2-methyl-1,4-naphthoquinone a 1,2-adduct (XLI) is formed as well as the expected 1,4-adduct (XL). This 1,2-adduct arises by an unusual nucleophilic addition to the carbon-carbon double bond of the quinone.[68]

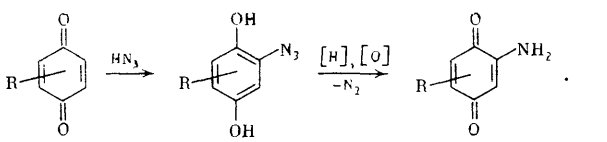


3. Reactions with *N*-nucleophiles

Gaseous ammonia interacts with unsubstituted quinones to give unstable amorphous products. Liquid ammonia reacts with substituted 1,4-benzoquinones at 240 K to give 1:1 adducts (XLII). At 220 K the diadduct (XLIII) is formed. The reaction is reversible: by addition of methylene chloride, followed by removal of ammonia, the starting 1,4-benzoquinones may be recovered.[69]

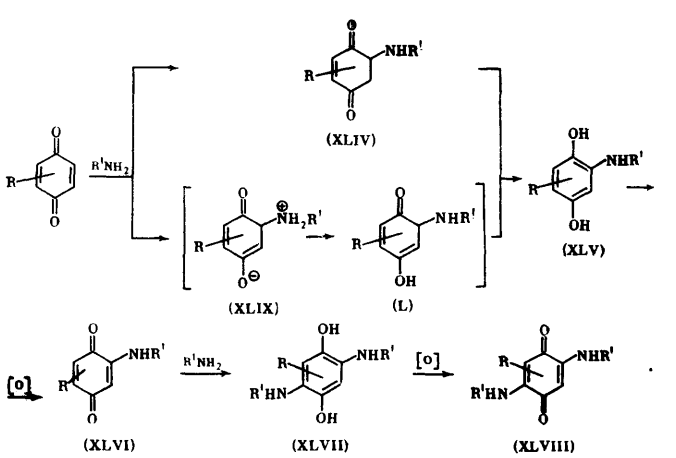


Nucleophilic addition of hydrazoic acid to 1,4-quinones provides a key method of preparing azidoquinones, from which aminoquinones can be obtained.[45,64]



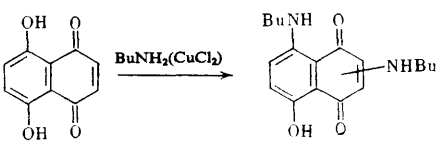
a) With primary amines

1,4-Benzoquinones react with primary aliphatic amines to give 2,5-diamino-1,4-benzoquinones (XLVIII), which are formed via oxidation of the intermediate 2,5-diaminohydroquinones (XLVII). It was not possible to isolate the initially-formed mono-aminated derivatives, (XLIV) and (XLVI).[70] This is possibly the reason why 2-amino-1,4-benzoquinones have not been reported.

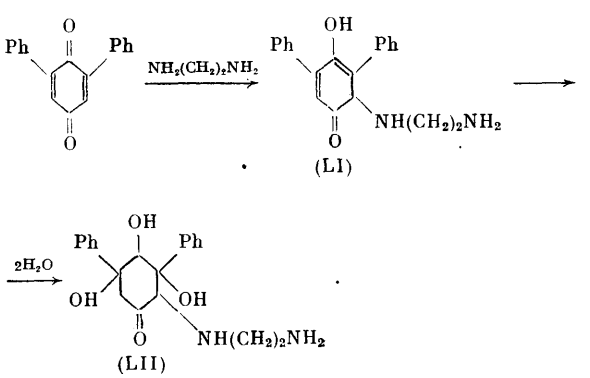


As shown above, the mechanism of the reaction involves an initial addition of the amine across a carbon-carbon double bond to give intermediate (XLIV), which isomerises into the aminohydroquinone (XLV) followed by oxidation to the monoaminoquinone (XLVI). Addition of a second amine molecule then gives the diaminoquinone (XLVIII).[45] In our opinion, reaction involves initial formation of a bipolar intermediate (XLIX), which isomerises into the cyclohexadienone (L) and thence to the aminohydroquinone (XLV). Such a scheme accords with the generally accepted mechanism of nucleophilic addition to unsaturated carbonyl compounds.[71]

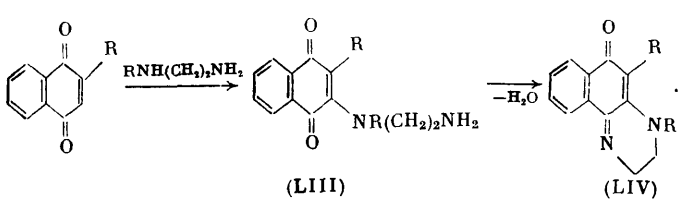
The interaction of 1,4-naphthoquinones with aliphatic amines leads to the formation of 2-amino-1,4-naphthoquinones. If there is a hydroxy substituent in the 1,4-naphthoquinone, then substitution takes place as well as addition-oxidation. 5,8-Dihydroxy-1,4-naphthoquinone reacts with butylamine in the presence of $CuCl_2$ to give 2,8- or 3,8-bis(butylamino)-5-hydroxy-1,4-naphthoquinone as the main product. The yield is less in the absence of catalyst.[72]



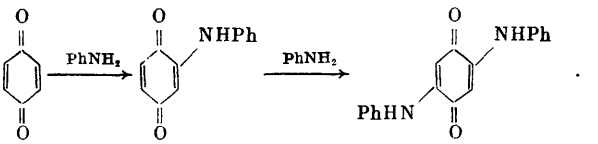
Reactions of 1,4-quinones with aliphatic diamines leads to the formation of a more complex product. The interaction of 2,6-diphenyl-1,4-benzoquinone with 1,2-diaminoethane, for example, affords an intermediate cyclohexadienone (LI), to which two water molecules add to give the cyclohexanone (LII) as final product. 1,6-Diaminohexane and piperazine react similarly.[73]



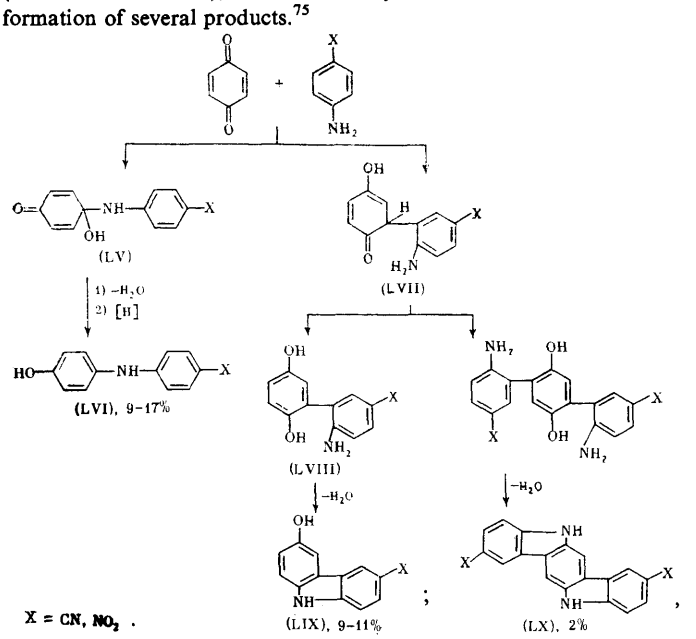
1,4-Naphthoquinone with diamines provides an initial 1,4-adduct (LIII), which subsequently loses a molecule of water to give a cyclic quinone imine (LIV).[74]



Aromatic amines are less active than aliphatic amines in their nucleophilic addition to quinones. As aniline is relatively inert, it has been possible to isolate both 2,5-dianilino-1,4-benzoquinone and 2-anilino-1,4-benzoquinone.[45]

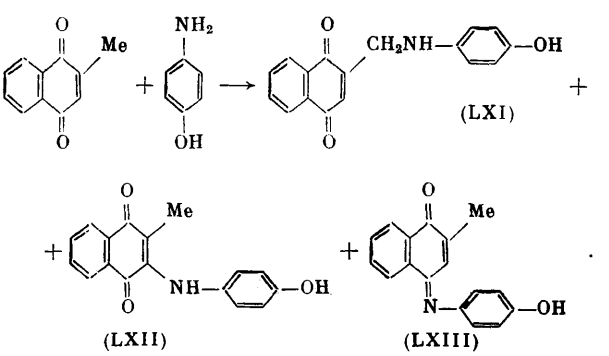


In a study of the interaction of substituted anilines with quinones (Nenitzescu reaction), low selectivity was recorded with the formation of several products.[75]

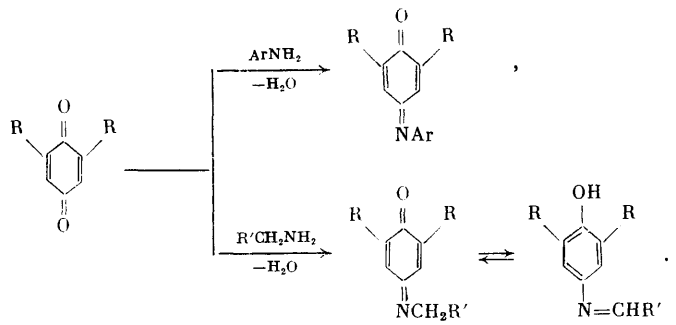


A reaction scheme was proposed according to which the final products (LVI, LIX, LX) were formed in parallel sequences: 1) 1,2-addition of aniline to a carbonyl group of the quinone to give the quinone aminoacetal (LV), followed by dehydration and reduction to produce the diphenylamine (LVI); 2) 1,4-addition of aniline to the conjugated system of the quinone to give the intermediate cyclohexadienone (LVII), which aromatises to the substituted hydroquinone (LVIII); the latter then dehydrates to give the carbazole (LIX). A second molecule of the starting aniline may also add to the cyclohexadienone, ultimately providing the dicarbazole (LX).

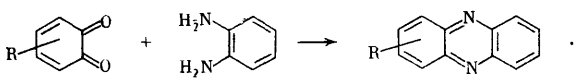
Several products are formed by interaction of 2-methyl-1,4-naphthoquinone with *p*-aminophenol. Thus, radical substitution affords quinone (LXI), while nucleophilic addition gives quinone (LXII) and quinone imine (LXIII).[76,77]



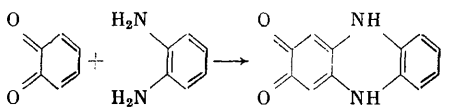
2,6-Disubstituted 1,4-benzoquinones, in which 1,4-addition is prevented by steric and electronic factors, react with primary aromatic amines by a condensation mechanism.[45,78]



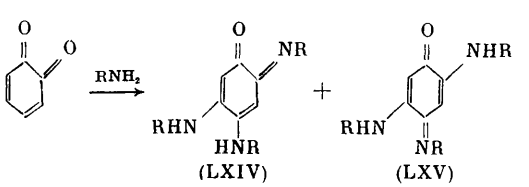
1,2-Quinones react vigorously with both aliphatic and aromatic amines in the same way as 1,4-quinones. However, it is possible to distinguish between 1,2- and 1,4-quinones by treatment with *o*-phenylenediamine: 1,2-quinones afford phenazine derivatives, whereas 1,4-quinones are unreactive



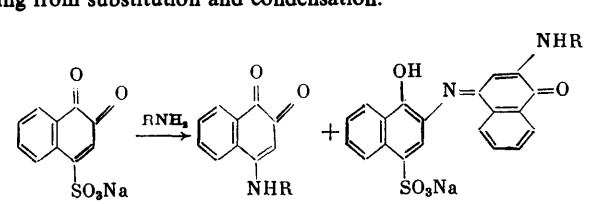
In the case of 1,2-benzoquinone itself, such a condensation does not take place; instead, an addition-oxidation leads to the formation of another type of cycloadduct.[45,64]



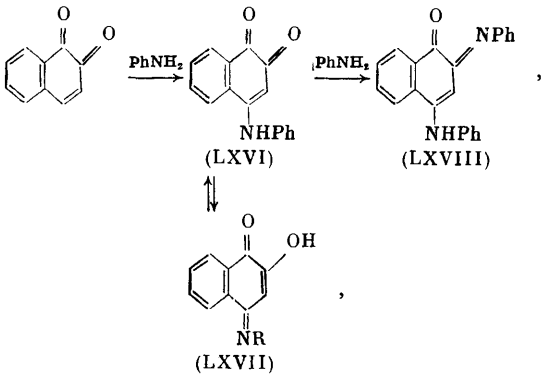
In general, unsubstituted 1,2-quinones react with amines by 1,4-addition. In the case of aromatic amines reaction is selective, but with aliphatic amines reaction is complicated by a concurrent condensation. For example, treatment of 1,2-benzoquinone with methyl-, ethyl-, propyl- and butyl-amine gives two types of product: 1,2-quinone imines (LXIV) and 1,4-quinone imines (LXV), formed as a result of consecutive double addition-oxidation and condensation.[79]



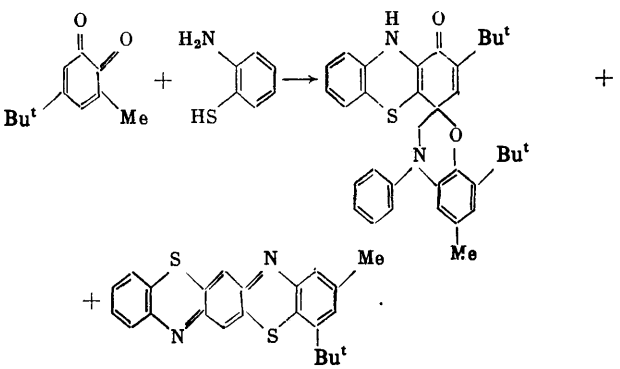
1,2-Naphthoquinone and substituted derivatives react with primary aliphatic amines to give several products, the most important resulting from substitution and condensation.[80]



Aniline participates in 1,4-addition with 1,2-naphthquinone, affording, after air oxidation, 4-anilino-1,2-naphthoquinone (LXVI) as the only isolable product.



If the reaction is carried out in the liquid phase, a second aniline molecule is added to give the quinone imine (LXVIII) as the final product.[45] It has been established that the substituted 1,2-quinone (LXVI) exists in the quinoidal form in the solid state or in alcoholic media, whereas it exists in the 1,4-quinone imine form (LXVII) in trifluoroacetic acid.[81] The reaction of 1,2-quinones with amines can be applied successfully for the preparation of complex structures which may be difficult or impossible to prepare by other means. The condensation of equimolar amounts of *o*-aminothiophenol and substituted 1,2-benzoquinones in the presence of $FeCl_3$ leads to the formation of unusual phenothiazines.[82]

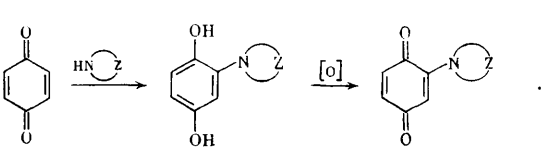


Quinone oximes with a variety of substituents are obtained by reaction of 4-substituted 1,2-naphthoquinones with ethylenediamine.[83]

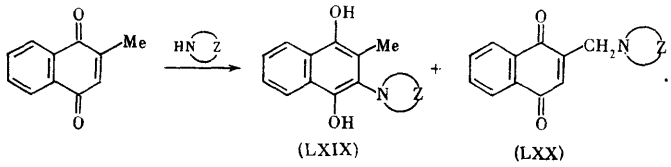
4,4'-Bis(1,2-naphthoquinone) interacts with aromatic amines in the same way as other 4-substituted 1,2-naphthoquinones to give condensation products involving the carbonyl group at the 2-position.[84,85]

b) With secondary amines

Secondary C_1-C_4 amines yield monoamino-substituted 1,4-benzoquinones exclusively.[64] Treatment of 1,4-benzoquinones with heterocyclic amines affords 2-substituted hydroquinones which are oxidised in air to give the corresponding quinones.[86]

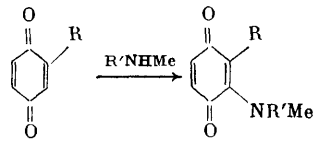


2-Methyl-1,4-naphthoquinones with pyrrolidine, piperidine, and heptamethyleneimine give stable 1,4-adducts (LXIX) as well as products derived by substitution of hydrogen at the methyl group (LXX).[87]



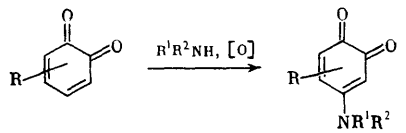
(LXIX) (LXX)

The study of the reaction of quinones with secondary amines has led to the development of the chemistry of biologically active quinones. Thus, aminoquinones (LXXI) have been prepared by interaction of 1,4-benzoquinone, 2-methyl-1,4-benzoquinone, 2-methyl-1,4-naphthoquinone and other 1,4-quinones with the following psychopharmacologically active amines: desipramine, nortryptyline, protryptyline, maprotyline and benzooctamine.[88–91]



(LXXI)

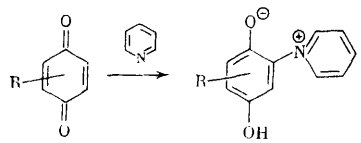
Treatment of 1,2-quinones with secondary amines affords 1,4-adducts which are converted to 4-amino,1,2-benzo(naphtho)-quinones in air.[45]



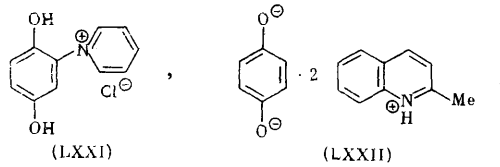
c) With tertiary amines and pyridine

In contrast with primary and secondary amines, tertiary amines do not react with quinones by nucleophilic addition. However, they do react with quinones by forming 1:1 or 1:2 charge-transfer complexes. In certain cases, complexes have been isolated and characterised as distinct entities,[92] but mostly they have only been detected by spectroscopic methods. The absorption of the complexes accords with a $p-\pi^*$-type transfer from the HOMO of the donor (amine) to the LUMO of the acceptor (quinone). The stability of the complexes depends markedly on the donor-acceptor properties of quinone-amine pair.[93]

The reaction of quinones with pyridine which, like tertiary amines lacks a labile hydrogen, is interesting in that there is no distinct complex-forming stage. Reaction proceeds directly to a bipolar compound.



2-Pyridiniohydroquinone chloride (LXXI) is obtained in the presence of HCl. A similar adduct is formed by reaction of quinones with quinoline. The salt (LXXII) is isolated from the interaction with quinaldine.[45]



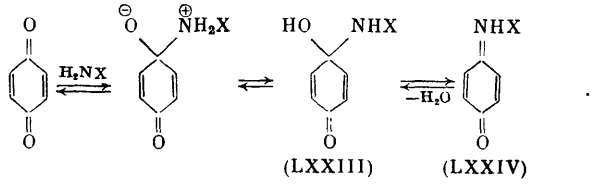
(LXXI) (LXXII)

Charge-transfer complexes are not only formed with tertiary amines. Others participate in the same way, e.g. aniline, toluidine, ethylamine, diethylamine, piperidine, and polyvinylpyridine.[94–96]

Thus, in the overall scheme for nucleophilic addition of amines to quinones, as illustrated above, there could be an additional stage involving the formation of a charge-transfer complex. However, it is clear that certain reactions of amines with quinones do not involve complex formation.

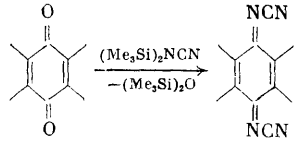
d) With cyanamide, hydroxylamine, hydrazines and hydrazides

This section is devoted to the reaction of quinones with *N*-nuclophiles, H_2NX, where X = CN, OH, NRR', NHC(O)R and $NHP(O)R_2$. Here, reaction takes place at a carbonyl function rather than by addition to the conjugated double bond (C=C–C=O). The mechanism of the reaction involves several reversible steps, of which the most important are nucleophilic addition of the nitrogen atom to the carbonyl group with formation of quinol (LXXIII), and dehydration of the latter with formation of quinone imine (LXXIV).

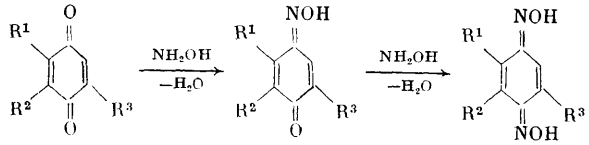


(LXXIII) (LXXIV)

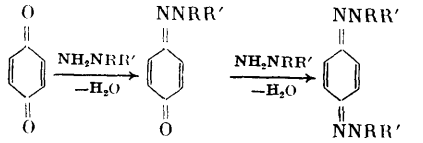
Quinones do not react with cyanamide. However, they react with silylcyanamides.[97]



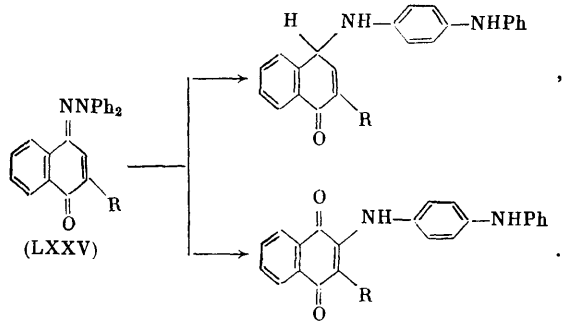
Hydroxylamine converts quinones into quinone mono- and di-oximes, which are particularly interesting as precursors for the synthesis of certain aromatic dinitroso compounds. More details on the oximation of quinones can be found in a monograph.[98]



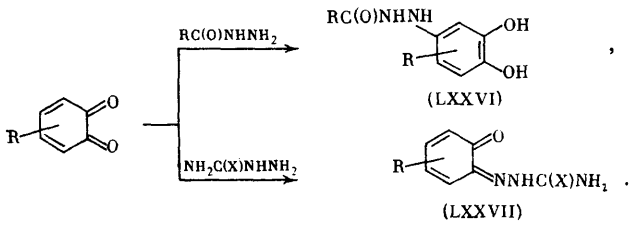
Hydrazine derivatives react with 1,4-quinones to give the corresponding quinone mono- and di-hydrazones.[99]



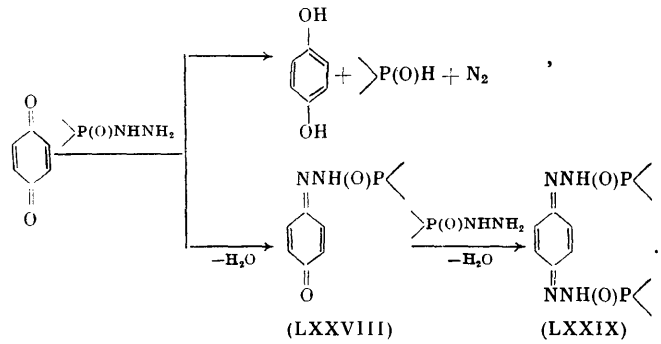
A redox reaction has been noted in certain cases, notably in the reaction with phenylhydrazine.[100–103] In this respect, we have focussed on the reaction of 1,4-naphthoquinones with diphenylhydrazine. Depending on the nature of the ring substituent, the initial condensation product (LXXV) is either converted to a semidine derivative or undergoes prototropic rearrangement.[104,105]



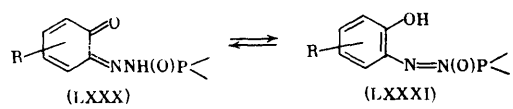
However, the nature of the hydrazine derivative, itself, largely determines the outcome of the reaction of 1,2-quinones. Thus, treatment of 1,2-quinones with hydrazine affords pyrocatechols by reduction. Acylhydrazines convert 1,2-quinones into 1,2-dihydroxy-3-acylhydrazinobenzenes (LXXVI), while semicarbazides and thiosemicarbazides condense to give the corresponding quinone semicarbazones (LXXVII).[45]



Phosphorohydrazidates react with quinones in a rather peculiar manner. Under mild conditions condensation takes place with the formation of phosphorylated quinone hydrazones (LXXVIII) and (LXXIX); however, above 20 °C in polar solvents, a redox reaction is set up, leading to hydroquinone, the corresponding phosphorus(III) acid, and nitrogen.[106–108]



Monohydrazones (LXXX) are formed with 1,2-quinones. There was no dihydrazone formation, probably because of steric hindrance.

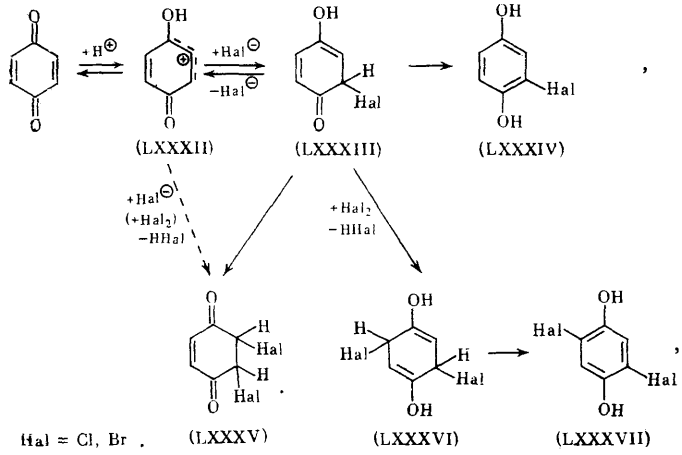


It has been established that the position of the quinone hydrazone ⇌ azophenol (LXXXI) equilibrium is largely determined by the nucleophilicity of the medium and the nature of the substituent on the quinoidal ring.[109]

Quinone hydrazones have been scrutinised for their biological activity. Notably, 1,4-naphthoquinone 4-aryl(aroyl)hydrazones have been prepared and shown to possess antimicrobial activity; they are potential tuberculostatic agents.[110]

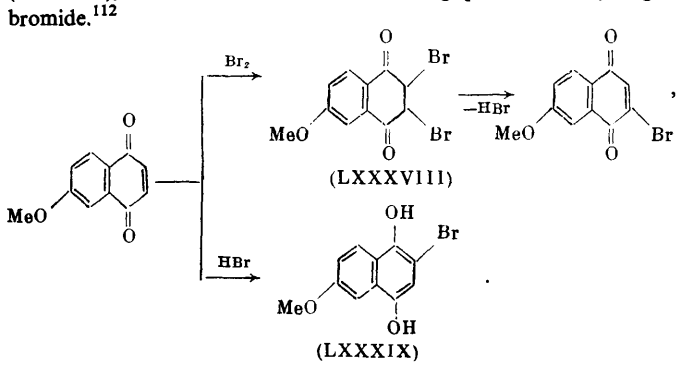
4. Reactions with halogen nucleophiles

Hydrogen iodide does not add to quinones, but reduces them to hydroquinones. Other hydrogen halides participate in 1,4-addition to give halogenohydroquinones (LXXXIV).[45,64,111]

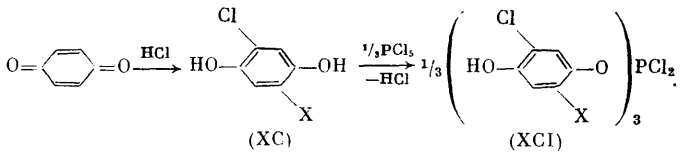


Reaction is initiated by protonation of the quinone with formation of cation (LXXXII); this undergoes attack by halide ion to give the corresponding 1,4-adduct (LXXXIII), which subsequently isomerises to the corresponding halogenohydroquinone (LXXXIV) as the final product. If free halogen is present in the medium, then adduct (LXXXIII), which by virtue of its unusual structural features is a very active nucleophile, adds a further halogen atom to give the dihalogenoquinone (LXXXV) or the cyclohexadiene (LXXXVI), stabilised in the dihalogenohydroquinone form (LXXXVII). It has been noted that the route (LXXXII → LXXXIII → LXXXIV) is more favourable than the route (LXXXII → LXXXIII → LXXXVI → LXXXVII) for steric reasons.[111]

In this section, it has also been considered appropriate to examine reactions of quinones with electrophilic reagents where the key step in the process involves nucleophilic addition. For example, the interaction of 6-methoxy-1,4-naphthoquinone with bromine affords, in addition to adduct (LXXXVIII), the nucleophilic addition product (LXXXIX), which is formed from the starting quinone and hydrogen bromide.[112]



The reaction of PCl_5 with 1,4-benzoquinones proceeds in a similar way.



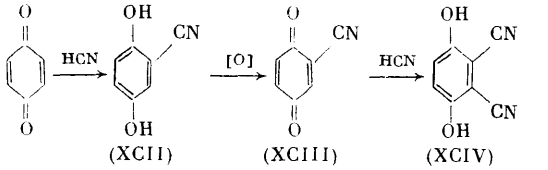
(XC) (XCI)

The interaction involves an autocatalytic chain process, the initial stage being the addition of hydrogen chloride to the quinone. The resulting chlorohydroquinone (XC) condenses with PCl_5 to give the dichlorophosphorane (XCI) as the final product with elimination of hydrogen chloride. The latter then adds to the starting quinone, thereby perpetuating the chain reaction.[113,114]

5. Reactions with *C*-nucleophiles

(a) With CH-acidic compounds

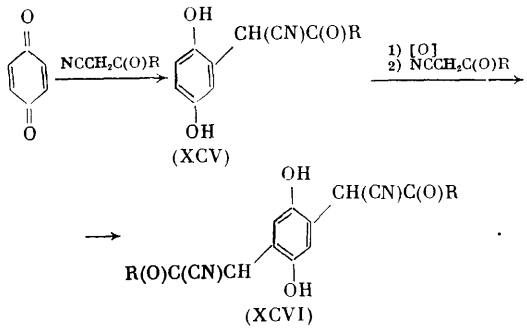
Hydrogen cyanide adds to 1,4-benzoquinone to give adduct (XCII), which is oxidised to the cyanoquinone (XCIII).



(XCII) (XCIII) (XCIV)

The interaction of a second HCN molecule with the cyanoquinone (XCIII) proceeds in an anomalous manner. Usually, all reactions of mono-substituted 1,4-quinones involve addition of nucleophiles at the 5-position (i.e. the *para*-position relative to the substituent). However, in the above case, the cyano group enters at the 3-position of the quinone to give (XCIV). There is no convincing explanation of this anomaly in the literature. Nevertheless, this reaction is preparatively very important for the synthesis of a number of cyanoquinones, amongst which the oxidant, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.[115]

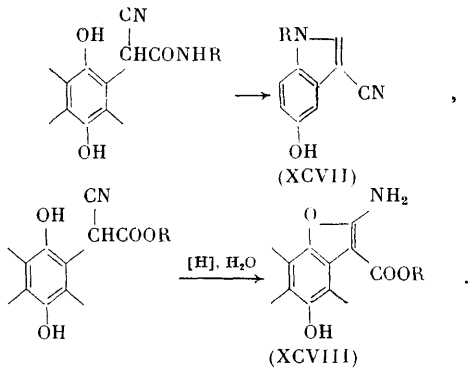
Of CH-acidic compounds, those with active methylene groups have been most studied in connection with quinone substitution. Carbonyl and nitrile substituents normally serve as activators.



(XCV) (XCVI)

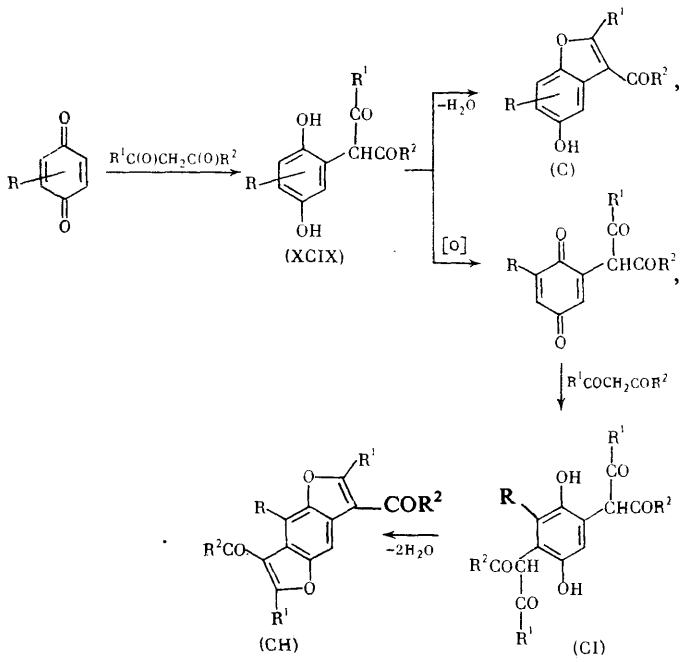
Thus, interaction of 1,4-quinones with 3-oxocarbonitriles involves initial 1,4-addition, followed by isomerisation of the resulting adduct to give the alkylhydroquinone (XCV). Oxidation of the latter, followed by addition of a second molecule of the nucleophile, may lead to the corresponding 2,5-dialkylhydroquinone (XCVI).[45,116,117]

Certain products undergo intramolecular cyclisation to give indoles (XCVII) and furans (XCVIII).[117,118]



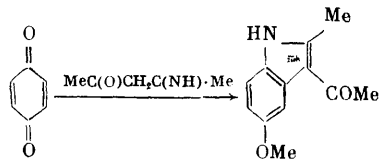
(XCVII) (XCVIII)

1,3-Dicarbonyl compounds and their derivatives react with quinones in a similar manner. The initially-formed 1,4-adduct (XCIX) is subsequently converted to benzofuran (C) via cyclodehydration, or undergoes oxidation-addition [to adduct (CI)] followed by cyclodehydration to the difuran (CII).[119,120]

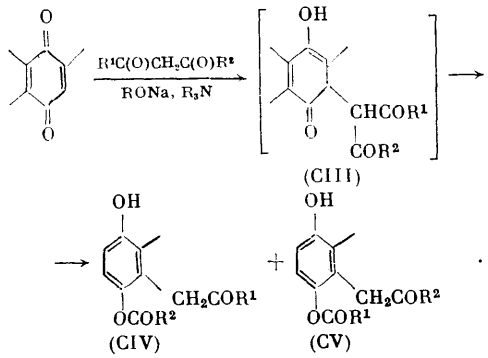


(XCIX) (C) (CH) (CI)

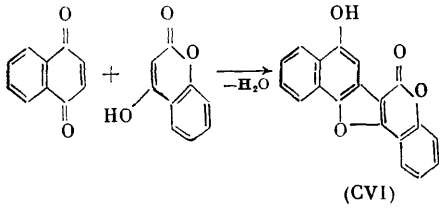
In certain cases, other processes are involved. Thus, the interaction of 1,4-benzoquinone with acetylacetone imine affords, unexpectedly, an indole derivative with a methoxy substituent in the benzene ring.[121]



In the presence of strong base, the reaction of substituted 1,4-benzoquinones with 1,3-diketones proceeds with the formation of substituted phenols (CIV) and (CV), rather than an adduct of type (XCIX). This is associated with an acylotropic conversion of intermediate (CIII).[122–125]

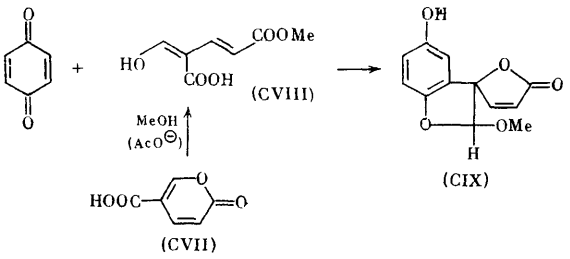


The reaction with 4-hydroxycoumarin is worthy of consideration here since, although it is not formally a CH-acidic compound, it can be viewed as the tautomeric form of a 1,3-dicarbonyl compound. Treatment with 1,4-naphthoquinone affords an adduct which subsequently cyclodehydrates to give furan (CVI).[126]



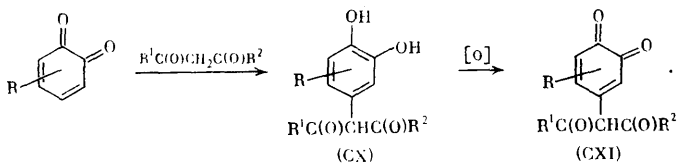
(CVI)

The spirobutenolide (CIX) is obtained by reaction of 1,4-benzoquinone with coumalic acid (CVII) in the presence of methanol, sodium acetate and acetic acid.



It is thought that acetate ion initiates pyrone ring opening with formation of enol (CVIII), which serves as a reactive form of coumalic acid.[127]

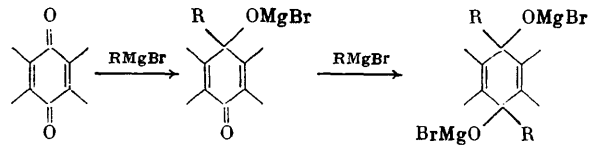
1,2-Quinones react with CH-acidic compounds in the same manner as 1,4-quinones to yield adducts (CX).[128–130]



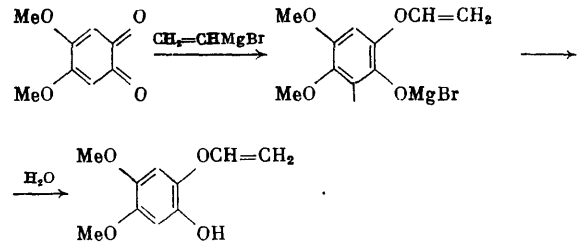
However, contrasting with the 1,4-quinone adducts (XCIX), which undergo a variety of reactions, the adducts (CX) are only oxidised with the formation of the corresponding 1,2-quinones (CXI).

b) With organometallic compounds

Substituted quinones react with the strongly nucleophilic Grigard reagents by nucleophilic addition. Addition to *p*-quinones involves one or both carbonyl groups.[45]

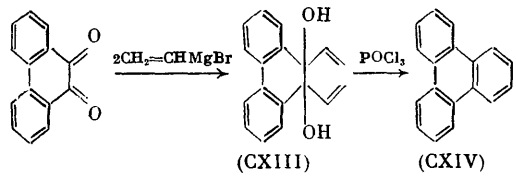


The reaction of vinylmagnesium bromide with 4,5-dimethoxy-1,2-benzoquinone leads to an adduct which is hydrolysed to a pyrocatechol vinyl ether (CXII).[131]

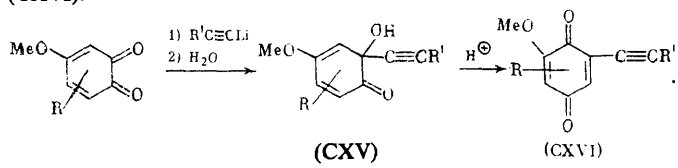


CXII

The interaction of vinylmagnesium bromide with phenanthraquinone yields the divinyldiol (CXIII) which is converted to triphenylene (CXIV) on treatment with $POCl_3$. Polycyclic hydrocarbons can thus be prepared by this route.[132]



Lithium acetylide adds to a carbonyl group of 1,2-benzoquinones with the formation of cyclohexadienones (CXV). In acidic media, the latter is hydrolysed to the relatively inaccessible alkynylquinones (CXVI).[133,134]



In this way, highly active nucleophiles, such as organometallic compounds, may add to one of the carbonyl groups of a quinone if the other is sterically hindered.

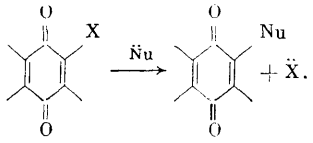
6. Reactions with *P*-nucleophiles

A vast amount of data is available on the interaction of organometallic compounds with quinones. In the majority of cases, the central atom of the organoelemental compound is not the reactive centre. Other reports deal with nucleophilic processes where

a heteroatom (in most cases phosphorus or arsenic) serves as the nucleophilic centre. In organophosphorus chemistry, it has been shown that almost all derivatives of di-, tri- and tetra-coordinated phosphorus acids, where the phosphorus atom is the reactive centre, interact with quinones via nucleophilic addition. A variety of products are obtainable depending on a number of factors, the most important being the nature of the substituents in the organophosphorus compound. More detailed information on the reactions of organophosphorus compounds with quinones are given in an earlier review.[135]

III. Nucleophilic substitution of quinones

The reactivity of quinones towards nucleophiles is dependent to a large degree on the π-acceptor character of the quinones. The π-acceptor properties are dependent primarily on the energy and symmetry of the lower unfilled molecular orbital (LUMO). In its turn, the energy of the latter is a function of electron affinity. Complex formation is one way to enhance electron affinity.[136–149] For example, in the complexes between 1,4-benzoquinone and $GaCl_3$ or $AlCl_3$, the structure of the LUMO is not changed, but its energy decreases from 0.15 to −1.7 eV.[145] This leads to an increased reactivity of the complexed quinone towards nucleophiles. Although quinone complexes with proton,[45] Lewis acids[137,141,142] and metal ions[139,140,147] have been used preparatively, the full potential of such quinone activation towards nucleophiles has not yet been explored. Electron affinity can also be increased by appropriate substitution of the quinone. Thus, the electron affinity of unsubstituted 1,4-benzoquinone is relatively low (1.91 eV),[146] but replacement of hydrogen by other atoms leads to a shift in electron affinity. Alkyl substitution, for example, lowers the value (1.59 eV for duroquinone), while halogens and, in particular, the cyano group, effect a marked increase (2.78 eV for chloranil, 2.50 eV for bromanil, and 3.40 eV for tetracyano-1,4-benzoquinone).[64,146] Thus, halogeno- and pseudohalogeno-quinones are the most reactive of substituted quinones towards nucleophiles.

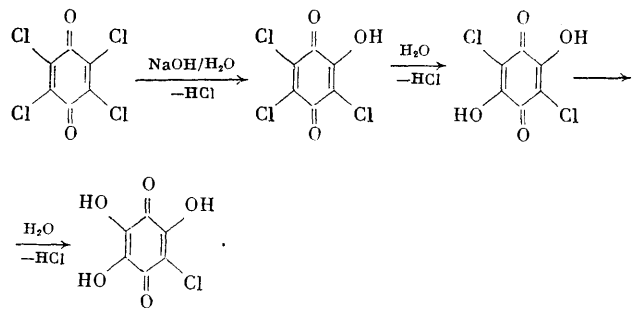


Both anions and neutral compounds with a free lone pair may be used as nucleophiles. The quinone may be substituted by halogen or a pseudohalogen or, in fact, any other electron-accepting group where polarisation of the C−X bond is possible.

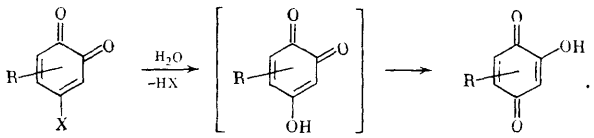
1. Reactions with *O*- and *S*-nucleophiles

The hydrolysis of halogenoquinones to hydroxyquinones is a classical example of a nucleophilic substitution of a quinone. Replacement of the halogen by a hydroxyl group proceeds most simply in the presence of a base—alkaline or pyridine. Acid-catalysed hydrolysis is rare. The completion of the reaction depends to a large extent on the effect of the ring substituent. Nevertheless, catalytic hydrolysis of substituted quinones normally proceeds readily and selectively in high yield.

With chloranil, exchange of chlorine atom by a hydroxyl group takes place in the presence of aqueous NaOH. Mono- and di-substituted hydroxyquinones can be prepared as required.

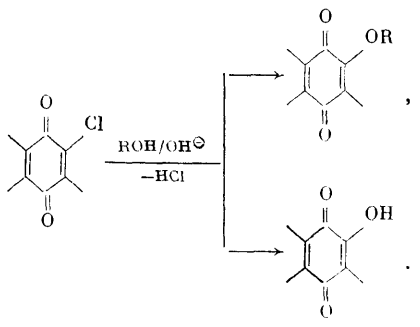


Hydrolysis of bromanil and fluoranil proceeds in the same way. With iodanil replacement of only one halogen atom is possible.[150] Quinones with alkoxy-, aryloxy-, alkylthio-, or arylthio-groups participate in a catalytic reaction with water. In each case, replacement of the substituents by a hydroxyl group takes place. However, substituted 1,2-quinones hydrolyse by a different route. The initially formed hydroxy-1,2-quinones (CXVII) are spontaneously converted into the energetically more favourable hydroxy-1,4-quinones (CXVIII).[45]

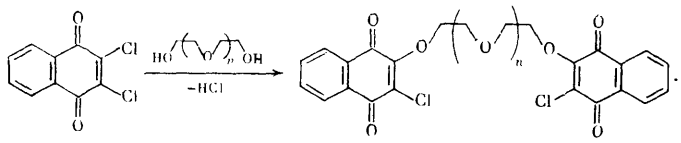


(CXVII) (CXVIII)

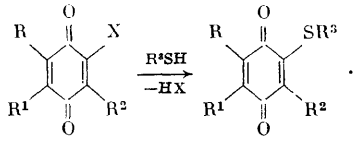
The interaction of halogenoquinones with alcohols and phenols normally proceeds in the presence of a base as catalyst, principally alkali metal alkoxides and aroxides or NaOH. As a rule, alkyoxylation or aryloxylation of the quinones takes place, although hydrolysis to hydroxyquinones has sometimes been observed.[151–153]



The alcoholysis of 2,3-dichloro-1,4-naphthoquinone was studied as long ago as the last century, and nowadays has found practical applications, notably in the synthesis of crown ethers with naphthoquinone fragments.[152,153]



The interaction of substituted quinones with aliphatic mercaptans and thiophenols is important since it permits the preparation of quinones with a sulphur functionality at a defined position.

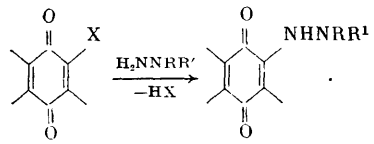


A base is required for the reaction of quinones with aliphatic mercaptans, and references have been made to the use of catalysts for the reaction with thiophenols.[45,64,154]

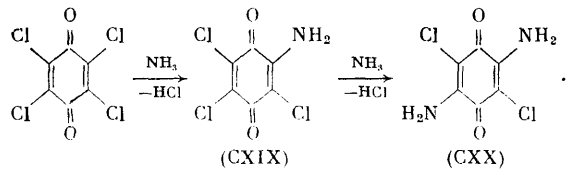
2. Reactions with *N*-nucleophiles

Nucleophilic substitution of quinones has been studied mostly with amines and other *N*-nucleophiles. The reactivity of *N*-nucleophiles decreases in the order: hydrazines ≥ ammonia > primary amines > secondary amines. The reactivity of aromatic amines is lowered by bulky substituents. Electron-accepting substituents in the benzene ring of aromatic amines also inhibits the reaction.

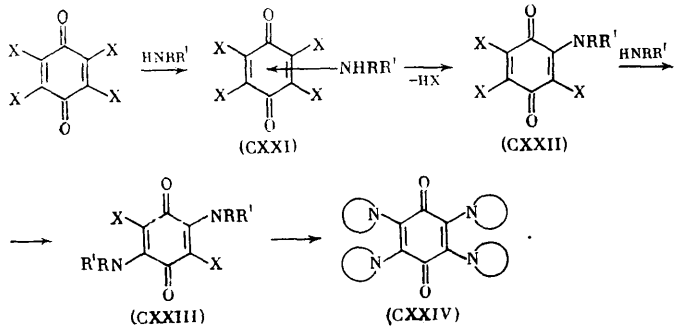
Hydrazines react with 1,4-quinones to give hydrazinoquinones.[155–157]



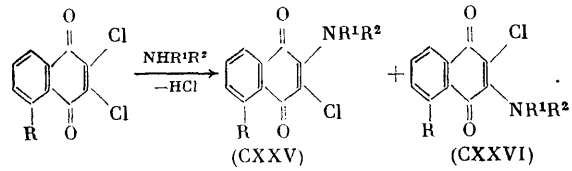
Treatment of chloranil with ammonia initially affords a monoaminoquinone (CXIX), which is further aminated to the diaminoquinone (CXX). The structure of the latter has been established by X-ray spectroscopy.[158]



The mechanism of the reaction of halogenanils with amines with a single N–H bond involves an initial complex formation to give (CXXI), which is subsequently converted into mono-, di- and tetraaminoquinones (CXXII–CXXIV).[159–164]



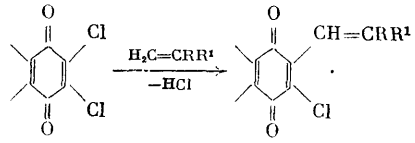
Such replacement of all halogen atoms is only possible with active cyclic amines (pyrazoles, imidazoles, 1,2,3- and 1,2,4-triazoles).[165,166] Treatment of halogen-substituted naphthoquinones with amines affords mono-amino derivatives, (CXXV) and (CXXVI). Both halogen atoms can be replaced by using nitrogen-containing heterocyclics.[167–185]



Studying this reaction has furnished much information: the ratio of 2-chloro- and 3-chloro-isomers (CXXV and CXXVI) is dependent on the structure of the amine;[169–172] this ring substituent influences the reactivity of the amine and the spectral characteristics of the products;[169] optimum conditions have been established for the synthesis of intensely coloured light-sensitive materials;[173] a convenient method of aminating halogenonaphthoquinones by phase transfer catalysis has been found;[174] and water-soluble naphthoquinones have been synthesised.[175,176]

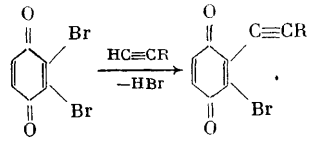
3. Reactions with *C*-nucleophiles

Halogenoquinones condense with *C*-nucleophiles to give quinoidal products with a new carbon–carbon bond. Olefins with an activated double bond interact with chloranil and 2,3-dichloro-1,4-naphthoquinone, providing alkenyl-substituted quinones.[177–180]

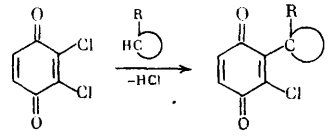


R = R¹ = OAlk, NAlk₂

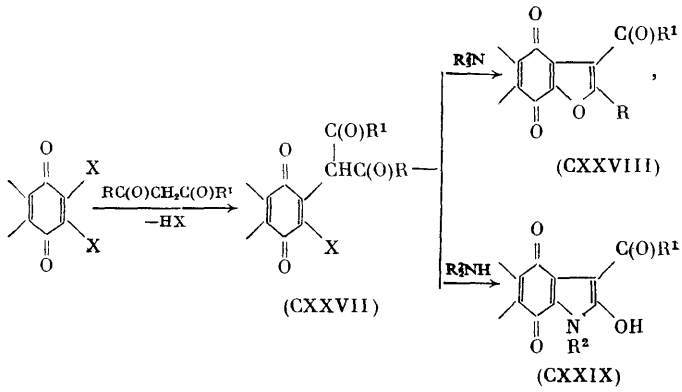
Acetylenes react similarly with halogenoquinones, yielding alkynylquinones in one step.[181]



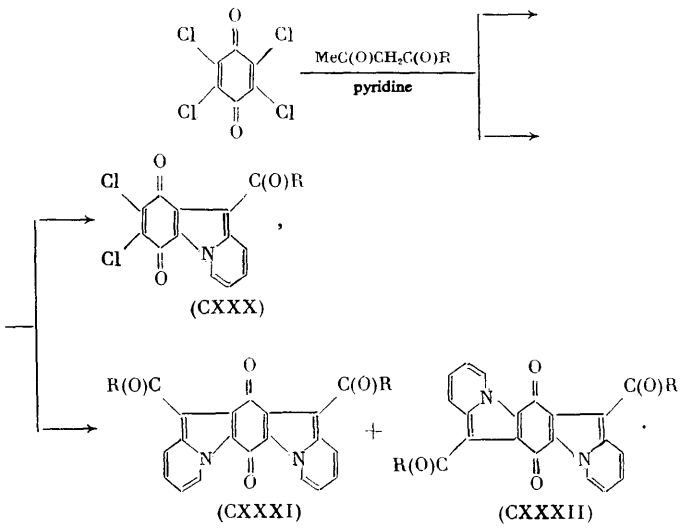
Cyclic hydrocarbons having a labile hydrogen also interact with halogenoquinones by nucleophilic substitution.[182,183]



The reaction of 1,3-dicarbonyl compounds with halogenoquinones is complex. It is initiated by replacement of a halogen to give quinones (CXXVII), which are converted to furan derivatives (CXXVIII) on treatment with tertiary amines; primary amines, however, yield indole derivatives (CXXIX).[180,184–186]



Many of the resulting furans (CXXVIII) and indoles (CXXIX) are biologically active. A rare three-component condensation is achieved by interaction of halogenoquinones with 1,3-dicarbonyl compounds and pyridine. Pyridoindoloquinones (CXXX) or benzodiindolizine-quinones (CXXXI and CXXXII) are formed depending on the proportion of the reactants.[180,187]

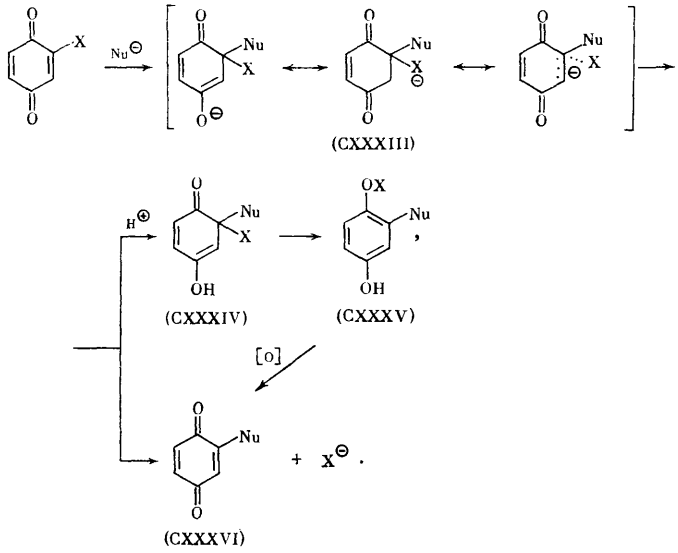


The overall scheme for this three-component conversion is exemplified by the reaction of 2,3-dichloro-1,4-naphthoquinone with indan-1,3-dione and pyridine.[188]

4. Reactions with *P*-nucleophiles

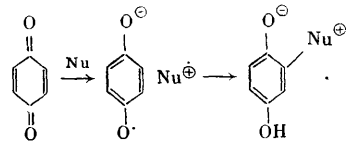
Detailed information on the interaction of quinones with organophosphorus compounds, where the phosphorus atom is the nucleophilic centre, is available in an earlier review.[135] It suffices only to point out that nucleophilic substitution is generally achieved by interaction of a phosphorus(III) compound (phosphines, phosphites, amidophosphites) with polyhalogenoquinones (e. g. chloranil, 2,3-dichloro-1,4-naphthoquinone). The substitution product is either a bipolar ion or a phosphonate with a quinone residue.[135]

Sometimes quinones are viewed as α,β-unsaturated carbonyl compounds. However, such is unrealistic, even in a formal sense, as the quinone system cannot be considered strictly as a carbonyl-conjugated structure, nor its chemical properties studied systematically on this basis. As an overview of the multitude of quinone reactions, the following should be borne in mind: 1) the main distinguishing feature of quinones and their derivatives is their readiness to form energetically favourable aromatic or semiquinoidal systems; 2) an important chemical property of quinones is their ability to exchange ring substituents without destroying the quinoidal system; 3) mechanistically, the majority of quinone reactions proceed by a heterolytic pathway with the formation of addition or substitution products. Nucleophilic reactions can be represented by a general scheme, the first step of which is unique for both Ad_N and S_N mechanisms. This comprises addition of the nucleophile, Nu^-, to a carbon atom of the ring with formation of a resonance structure (CXXXIII). Its stabilisation is achieved either by addition or substitution.



If the substituent (X) is a poor leaving group, e. g. hydride anion, then a proton (H^+) adds to the intermediate, followed by isomerisation of the adduct (CXXXIV) with formation of hydroquinone (CXXXV). With highly nucleofugal substituents (X = Hal^-, RO^-, R_2N^-), the intermediate (CXXXIII) is stabilised by cleavage of anion, X^-, and formation of quinone (CXXXVI). The arrow linking compounds (CXXXV) and CXXXVI) signifies that hydroquinones (CXXXV) with donor substituents are readily oxidised to the corresponding quinones (CXXXVI).

In certain cases, single electron transfer from the nucleophile to the quinone can be achieved with formation of a radical pair, the recombination of which leads to the formation of a betaine.[135]



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Translated from *Uspekhi Khimii* **60** 169–204 (1991) U.D.C. 541.127:542.941

Cyclisation reactions involving carbene complexes in the inner coordination sphere of transition metals

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ABSTRACT. The literature data on inner-sphere cyclisation reactions involving carbene complexes in the coordination sphere of transition metals are summarised.

The bibliography includes 136 references.

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I. Introduction

Cyclisation reactions that involve carbene complexes have been known for quite a long time, but they have mainly been studied in relation to the use of organometallic reagents in organic synthesis (see several reviews),[1–6] primarily for the synthesis of derivatives of naphthalene, indene, etc. In the present review we shall summarise those reactions of carbene complexes during which the carbene ligand combines with a molecule of substrate to form a cyclic (or metallacyclic) ligand, with all of the reactions occurring in the inner coordination sphere of the metal. It should be emphasised that there are no strict criteria which could be used to classify a given reaction as intramolecular. Very frequently it is only the structure of the final products that suggest the inner-sphere nature of the processes, since in the majority of cases the corresponding reactions are not typical for the uncoordinated ligands. Thus the term "inner-sphere cyclisation" is fairly arbitrary.

In the present review we shall mainly examine the processes which result in the reaction between a ligand that is already present and a molecule of reagent to form a new cyclic ligand which remains in the coordination sphere. Reactions of the formation of a cyclic ligand on a transition metal atom (template reactions) will be included subsequently, and it is also proposed to include data on catalytic cycloaddition reactions in the presence of transition metal complexes.

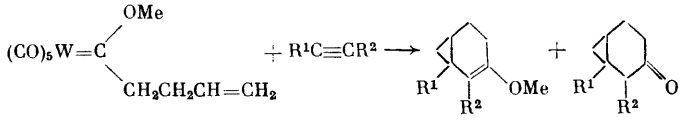
In general cycloaddition reactions have been covered in sufficient detail in the literature, so in this review there is no need to dwell on a detailed examination of them. With regard to cycloaddition reactions in the inner coordination sphere of transition metals, the number of theoretical studies in this area is clearly insufficient to raise the question now about finding a correspondence between theory and practice. In those cases where it was possible to do this, specific examples are given.

This review covers the original literature up to the end of 1989.

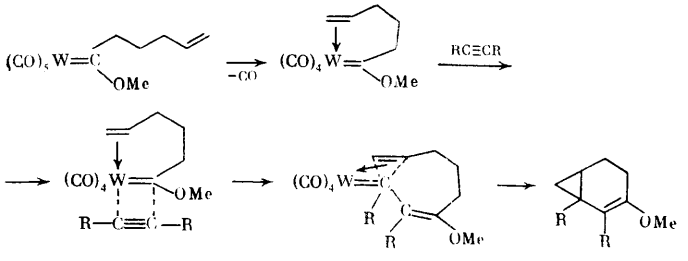
II. Reactions that lead to the formation of three-membered rings

Carbenes are known[6] to react with olefins to give cyclopropanes. The use of carbene complexes of transition metals as transfer agents of a carbene to an olefin in the synthesis of cyclopropanes was first described by Fischer.[7] In the present review there are examples of the formation of cyclopropanes from carbene complexes and acetylenes that occur without the formal cleavage of the metal–carbene bond at the intermediate stages of the reaction.

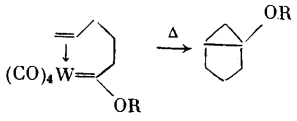
Carbene complexes of tungsten containing a multiple bond on the "periphery" of the carbene ligand react with disubstituted acetylenes to form condensed cyclopropanes:[8,9]



The reactions occur in the following way: at the first stage the alkyne is inserted into the metal–carbene bond to form a dienyl-substituted carbene intermediate in which intramolecular cyclopropanation of the double bond by the carbene ligand then occurs, as described by Fischer.[7] Initially the carbene complex may undergo isomerisation with elimination of CO and formation of a π-olefin carbene complex which can be isolated:[10,11]

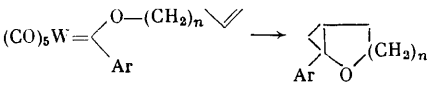


The intermediate π-olefin carbene complex may also form a cyclopropane derivative through intramolecular cyclopropanation:[10,11]



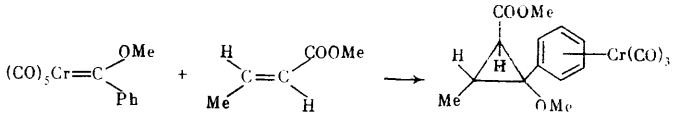
R = Me, Et.

Similar reactions have been reported for carbene complexes with an unsaturated alkoxyl residue:[12]



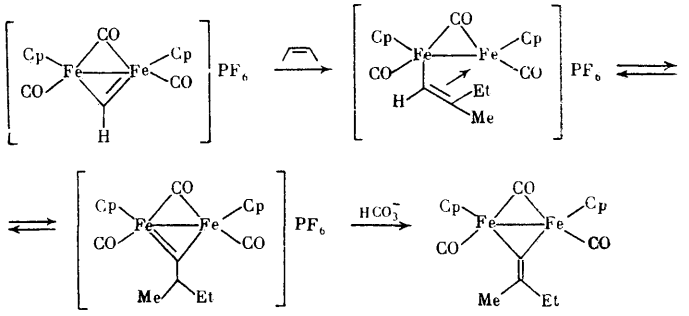
Ar = 4-MeC$_6$H$_4$; n = 2, 3.

When n = 1 only an allyl aryl ketone was isolated. A tungsten π-arene complex was obtained as a by-product. The formation of such π-arene complexes was detected in the cyclopropanation of olefins with chromium π-alkoxybenzylidene complexes:[13]

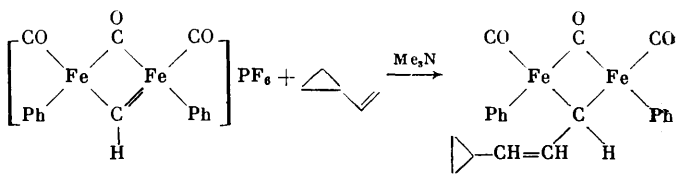


The reaction is stereoselective—a *trans*-cyclopropane is formed from a *trans*-olefin. The enantioselective synthesis of cyclopropanes using chiral iron carbene complexes has been reported.[14]

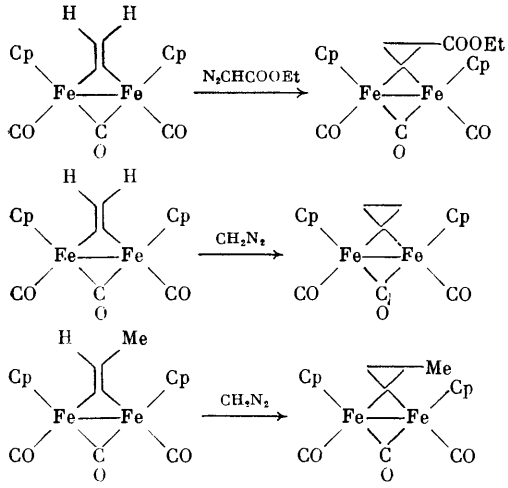
Cationic iron complexes with bridging carbene ligands react with olefins to form diferracyclopropanes:[15]



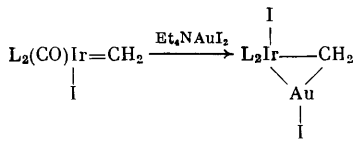
The reaction occurs via σ,π-olefin complexes which are formed as a result of the insertion of the olefin into the "double" C=Fe bond followed by a 1,3-hydrogen shift. Vinylcyclopropane reacts somewhat differently:[16]



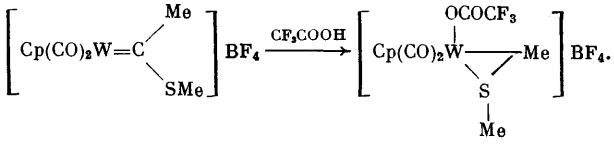
Iron alkylidene complexes obtained by reaction of olefins with bridging carbene derivatives react with diazoalkanes to form diferraspiropentanes:[17–19]



The formation of a three-membered dimetallacycle has been observed[20] in the reaction of an iridium carbene complex with tetraethylammonium diiodoaurate:



This reaction may be regarded as the addition of :AuI to the iridium–carbon double bond. The addition of trifluoroacetic acid to a tungsten–carbon double bond gives a thiatungstacyclopropane:[21]



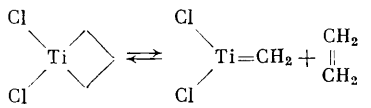
It may be concluded from the material examined that [1 + 2] cycloaddition reactions with the formation of π-cyclopropene or η^3-cyclopropenyl complexes are not typical for carbene compounds of transition metals.

III. Reactions that lead to the formation of four-membered rings

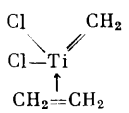
The formation of four-membered rings involving carbene complexes is possible as a result of either [1 + 3] cycloaddition or a [2 + 2] process. In the first case the formation of cyclobutenyl or cyclobutadienyl complexes are to be expected for an inner-sphere reaction, in the second case metallacycles are to be expected. This is true for all concerted reactions; but in the chemistry of organometallic compounds, as a result of a metal atom participating in the reaction, unconcerted multistage reactions are possible. It is

therefore probable that the formation of cyclisation products in the inner coordination sphere cannot always be strictly interpreted in terms of a given limiting mechanism.

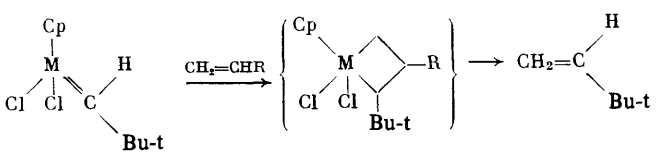
A theoretical analysis of $2\pi + 2\pi$ reactions that occur within the coordination sphere of a transition metal has been carried out for the system titanium alkylidene complex – olefin.[22]



It was found that the intermediate olefin(methylidene) complex

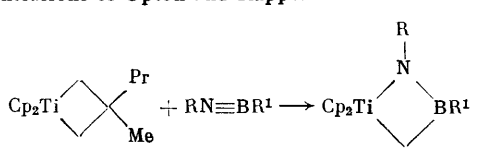


has an energy which exactly corresponds to that of the transition state of the reaction. The initial titanacyclobutane is 11.5 kcal mol^{-1} more stable than the intermediate complex and the conversion to the final products requires a further 10.4 kcal mol^{-1}. Thus, the reaction of olefins with metal carbene complexes with the formation of four-membered metallacycles is thermodynamically favourable. It is likely that the metathesis of olefins with niobium and tantalum (π-cyclopentadienyl)(neopentylidene) dichlorides occurs in this manner:[23]



M = Ta, Nb; R = H, Me, Ph.

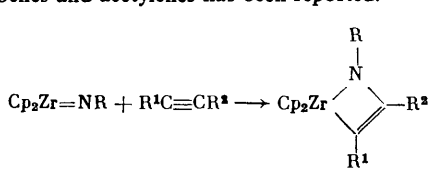
The suggestion of Paetrold et al.[24] that the reaction of a titanacyclobutane complex with RNBR^1 occurs via the formation of the intermediate carbene complex $Cp_2Ti{=}CH_2$ is not consistent with the conclusions of Upton and Rappe.[22]



R = iso-Pr, t-Bu; R^1 = iso-Pr, Bu, t-Bu, C_6F_5.

It is clear that the formation of azaboratitanacyclobutenes occurs in some other way, or the presence of the two geminal substituents in the four-membered ring of the initial complex considerably assists the elimination of an olefin with the separation of a methylene complex.

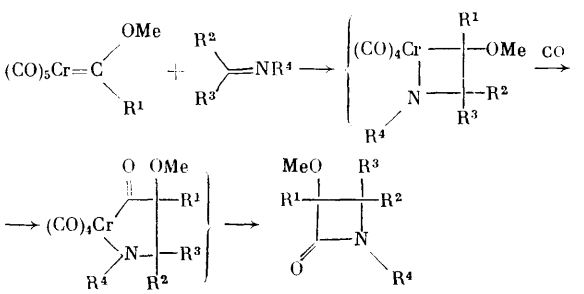
The formation of azazirconacyclobutenes from the aza analogues of carbenes and acetylenes has been reported.[25]



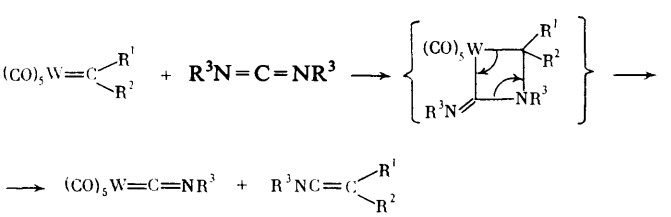
R	R^1	R^2
t-BuC$_6$H$_4$	Me	Ph
t-Bu	Ph	Ph
2,6-Me$_2$C$_6$H$_3$	Me	Me

The initial imidozirconocenes are generated by thermolysis of the respective products $Cp_2Zr(R^3)NHR$ (R^3 = Me, Ph) or by thermolysis of the bisamides $Cp_2Zr(NHR)_2$. In the case of a bulky substituent (R = t-Bu) the corresponding imide was isolated as an adduct with THF and its structure was established by X-ray diffraction analysis.[25] It is interesting that in the reaction of an imide with the asymmetric MeC≡CPh only one isomer is formed with the methyl group at the α-position relative to the nitrogen of the heterocycle, i.e., cycloaddition takes place contrary to Markownikoff's rule. The isoelectronic titanamethylidene complex $Cp_2Ti{=}CH_2$ undergoes similar reactions with alkynes.[26–28]

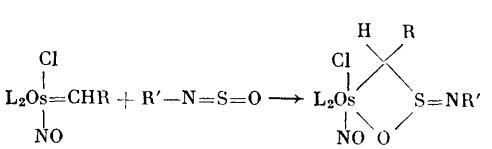
According to McGuize et al.[29,30] β-lactams are obtained in reactions between chromium carbene complexes and imines via azachromacyclobutanes, which are [2 + 2] cycloaddition products:



The metathesis of carbodiimides on treatment with tungsten carbene complexes to form intermediate four-membered metallacycles occurs in a similar manner:[31]

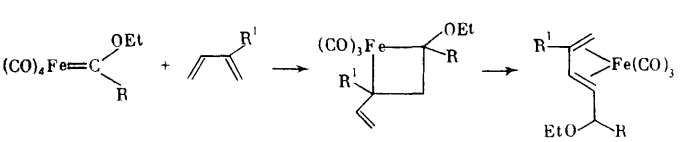


The reaction of sulphinylamines with osmium alkylidene complexes occurs as a [2 + 2] cycloaddition only on the S=O bond pseudocumulene [sic]:[32]



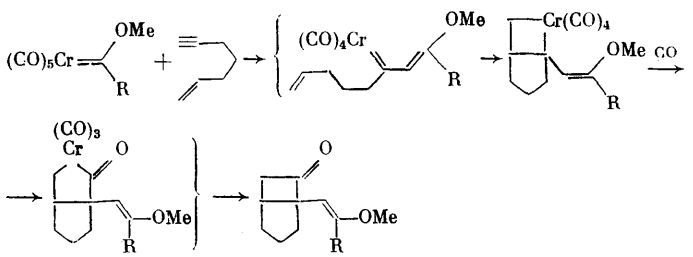
L = PPh_3, R = H, COOEt, R′ = Ts.

The reaction of 1,3-dienes with iron carbene derivatives also only takes place on one of the two double bonds:[33,35]

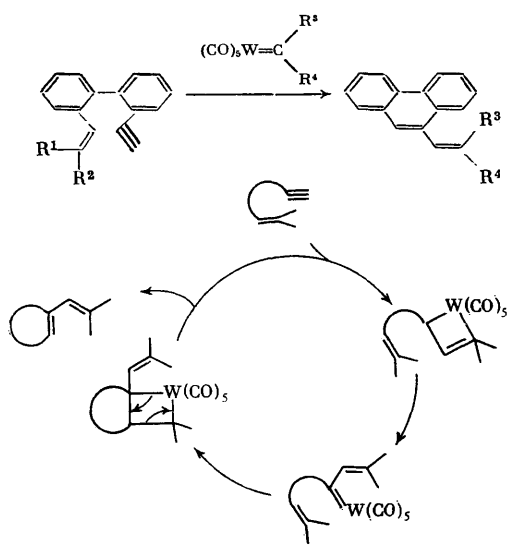


It should be noted that the idea of intermediate four-membered metallacycles being formed has been used to quite a significant extent to account for both catalytic and stoichiometric reactions of transition metal carbene complexes with olefins or acetylenes.

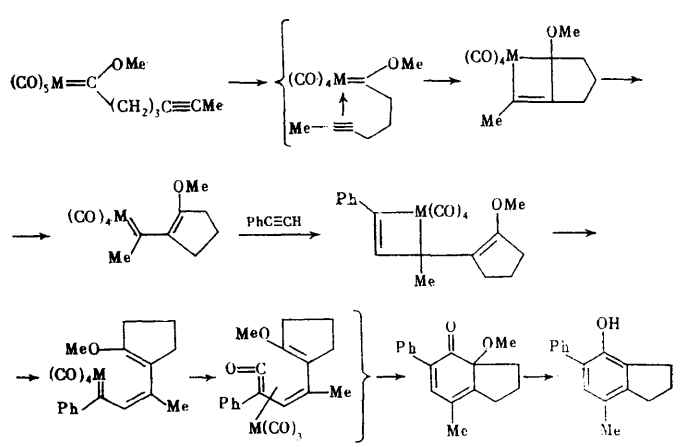
For example, the following scheme has been put forward for the stoichiometric reaction of hept-1-en-6-yne with chromium methoxycarbene complexes, which gives 1-vinyl-substituted bicyclo-[3.2.0]heptanones:[35]

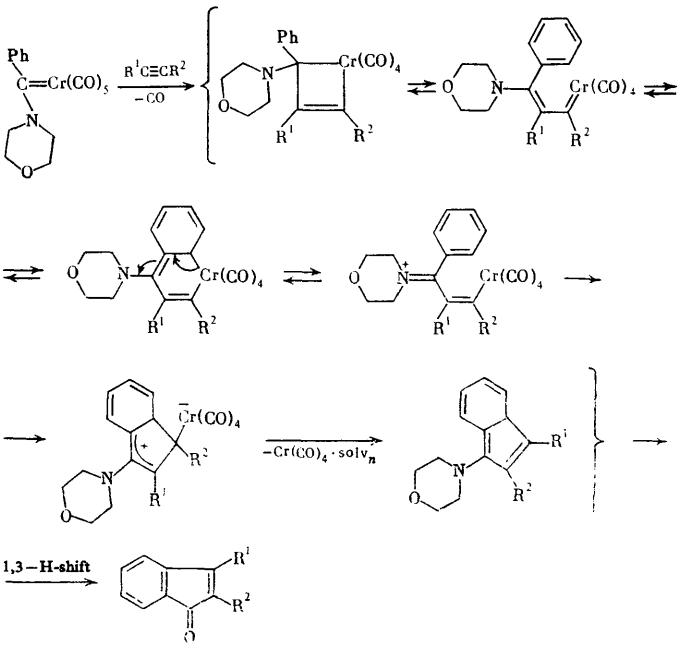


At the first stage acetylene is inserted into the metal–carbene bond, then intramolecular cyclisation, insertion of CO, and elimination take place. The formation of a metallacyclobutane can also occur at the first stage, as has been proposed for the catalytic reaction to obtain 9-vinylphenanthrenes from 1,1′-alkynyl(vinyl)biphenyls:[36]

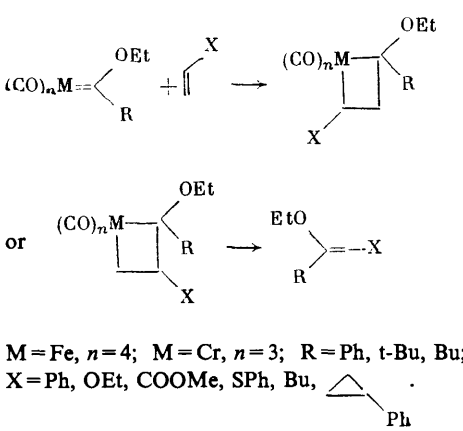


The reactions between alkynes and (1-methoxyhept-5-ynylidene)-pentacarbonylchromium[37] and between acetylenes and [(phenyl)-(morpholino)carbene]pentacarbonylchromium also occur in a similar manner:[38]



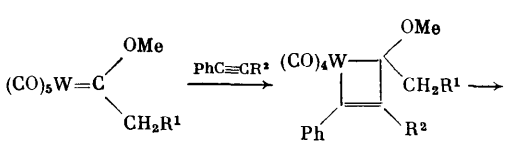


The metathesis of olefins on iron and chromium carbene complexes also occurs via intermediate metallacyclobutanes:[39]



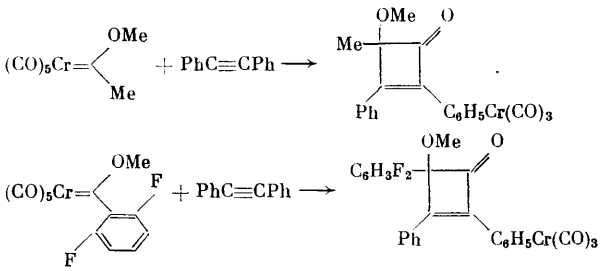
M = Fe, $n = 4$; M = Cr, $n = 3$; R = Ph, t-Bu, Bu;
X = Ph, OEt, COOMe, SPh, Bu, .

as does the addition of coordinated carbene ligands to acetylenes:[40]

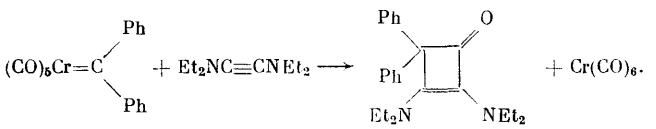


R^1	R^2	(A), %	(B), %
H	Ph	64	—
Me	Me	61	—
Me	Ph	12	50
Me	Me	19	42

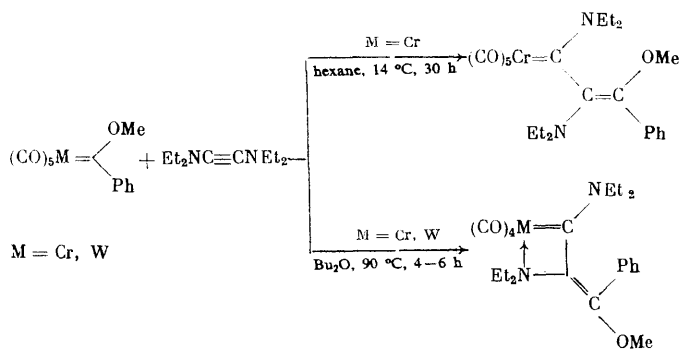
In the case of the addition of diphenylacetylene to a chromium methoxycarbene complex the $Cr(CO)_3$ residue remains coordinated in the reaction products:[41,42]



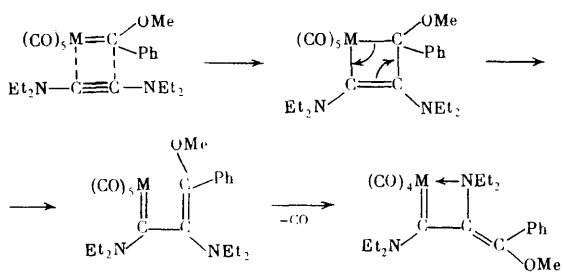
Confirmation of the coordination of $Cr(CO)_3$ with an aryl group of diphenylacetylene is provided by the reaction of bis(diethylamino)-acetylene with a chromium diphenylcarbene complex:[41]



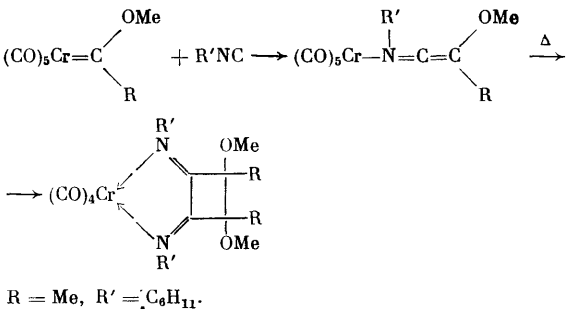
Interestingly, the reaction of bis(diethylamino)acetylene with chromium and tungsten (methoxybenzylidene)pentacarbonyls takes place in a different manner;[43]



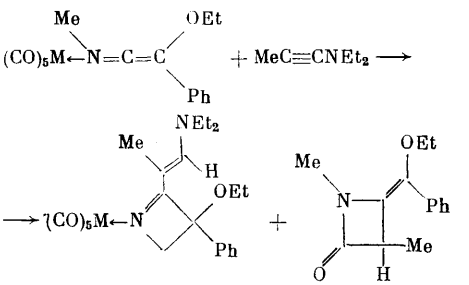
However, even in this case the formation of both complexes can be accounted for in terms of a four-membered metallacyclic intermediate:



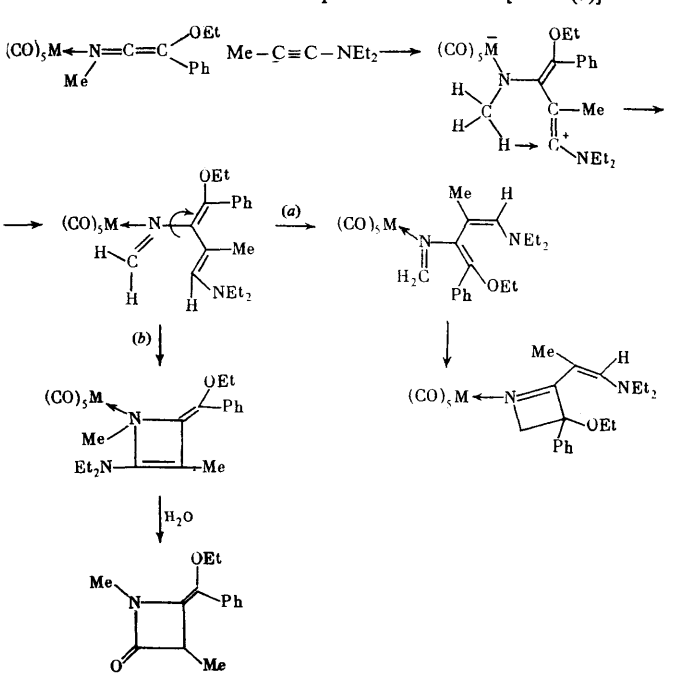
There have been instances reported where reactions of carbene complexes with isonitriles result in the formation of four-membered rings which remain within the coordination sphere of the metal atom by means of Cr–NC bonds with imine groups. These reactions occur as a [2 + 2] cyclisation of intermediate ketenimine complexes:[44,45]



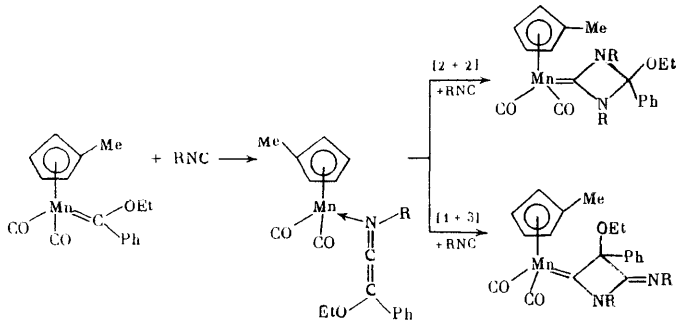
Interestingly, uncoordinated ketenimines dimerise differently, giving azetidines.[44] A similar type of cyclisation occurs[46] occurs in the reaction between chromium and tungsten ketinimine complexes and 1-diethylaminopropyne:



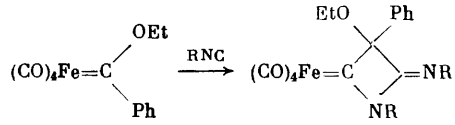
The formation of an azetine complex has been attributed[46] to the initial addition of alkyne to the N=C double bond of the coordinated imine, resulting in a zwitterionic dienamide derivative in which intramolecular addition of hydrogen from the methyl group to the carbocation site occurs with regeneration of an imine complex. The latter may undergo rotation about the C–N bond and a [2 + 2] cyclisation to an azetine [route (*a*); "normal" [2 + 2] cyclisation without rotation results in a complex with a lactam [route (*b*)]:



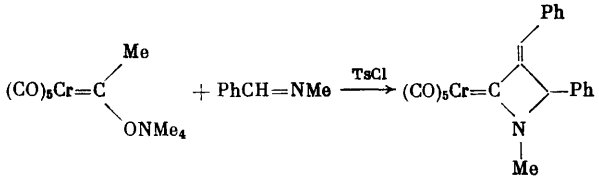
Intermediate ketenimine derivatives can react with excess isonitrile to form products of both [2 + 2] and [1 + 3] cycloaddition:[47]

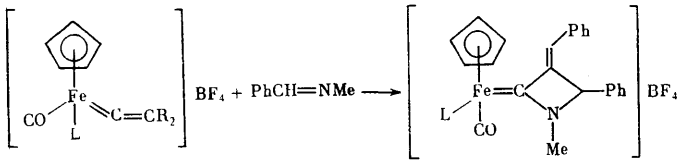


In the case of an iron complex only [1 + 3] cycloaddition occurs:[48]

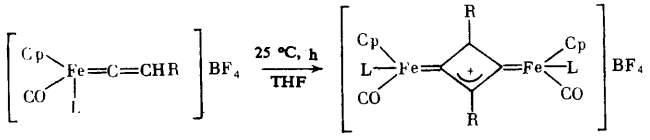


Schiff bases react with chromium[49] and iron[50] carbene complexes in a similar manner

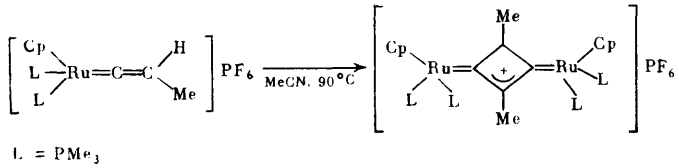




In the case of the chromium derivative the reaction route depends on the solvent—in CH_2Cl_2 or t-BuOH only cyclisation occurs while in MeOH the linear product $(CO)_5Cr=C(OMe)CH=CHPh$ is also formed.[49] Cationic iron[51–53] and ruthenium[54] vinylidene complexes can undergo a [2 + 2] homocyclisation to give very interesting products.

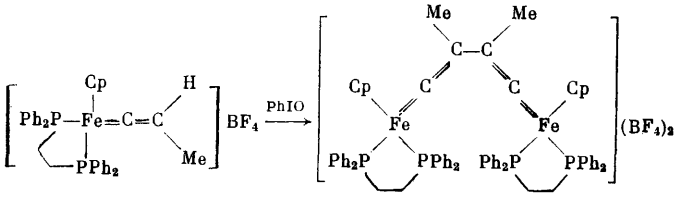


L = CO, PPh_3, $P(C_6H_{11})_3$;
R = H, Ph.

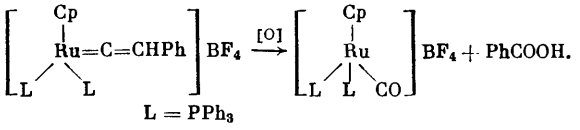


L = PMe_3

An iron vinylidene complex with a chelate diphosphine ligand also dimerises on treatment with iodosylbenzene, but forms a "linear" product:[55]

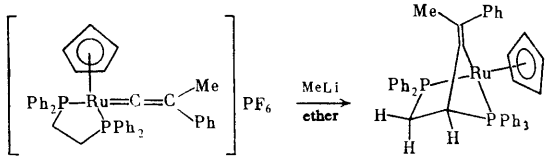


Under these conditions the ruthenium analogue doe not dimerise but its C=C bond is cleaved to form carbonyl derivatives and an acid:[56]



L = PPh_3

Ruthenium vinylidene complexes react with methyllithium quite differently:[57]



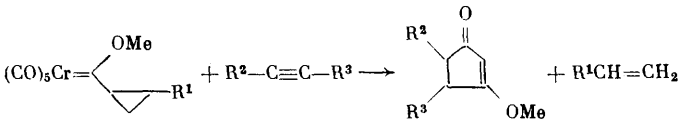
Protophilic attack on the α-CH_2 group of the diphosphine and intramolecular cyclisation with the formally carbocationic α-carbon atom of the vinylidene ligand occur.

In summarising the material presented in this section, it may be concluded that "pure" [1 + 3] cycloaddition reactions of the carbene ligand to form four-member π-ligands do not occur. There is a predominance of [2 + 2] cycloaddition processes to form metallacycles, cyclobutylidene complexes, and azacyclobutane derivatives bound to the metal atom by a coordination bond.

IV. Reactions that lead to the formation of five-membered rings

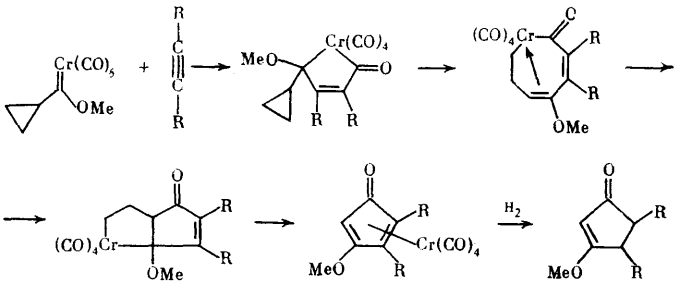
As the material of the previous section demonstrates, attempts to consider inner-sphere cyclisation reactions involving carbene complexes in terms of [*n* + *m*] cycloaddition processes are too formal, since in the majority of cases formation of the final products results from secondary reactions, a carbonyl ligand acting as the "supplier" of a further carbon atom to the ring may participate in ring formation. Strictly speaking, synchronism has not been demonstrated for a single reaction and the stereochemical result of the reactions is not always clear. In the present section an attempt will be made to classify the reactions according to the nature of the final products. Three types of reaction can be distinguished from the existing literature data: the formation of metallacycles, cyclopentylidene complexes, and five-membered rings that remain in the coordination sphere because of the *N*-donor groups present in them. Herndon et al.[58,59] have reported the formation of

cyclopentenes in the reaction between acetylenes and chromium (cyclopropyl)-(methoxy)carbene complexes:



R^1 = H, Ph; R^2 = H, Me, Pr, Ph; R^3 = Pr, Ph, C_5H_{11}.

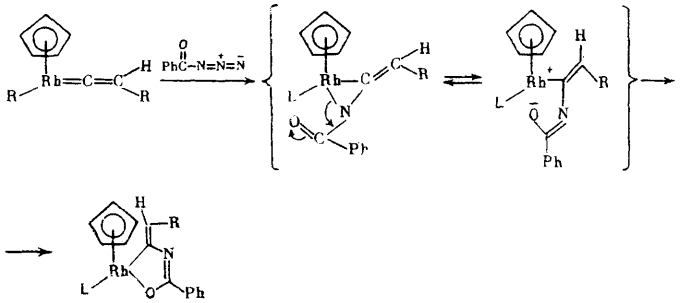
The following reaction scheme has been proposed:[58]



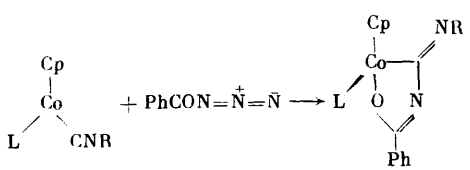
Because of this scheme, which includes intermediate five-membered metallacycles, the two studies of Herndon et al.[58,59] can formally be covered in the present section.

1. Formation of five-membered metallacycles

The reactions of rhodium and osmium vinylidene complexes with benzoyl azide gives metallaoxazoline derivatives,[60,61] these being accompanied by the elimination of nitrogen. It is possible that they take place as a [3 + 2] cycloaddition of the dipolar azide to the polar Ph=C group with initial formation of a five-membered metallacycle, which after elimination of nitrogen is converted to a three-membered metallacycle. The following reaction scheme has been proposed:[61]

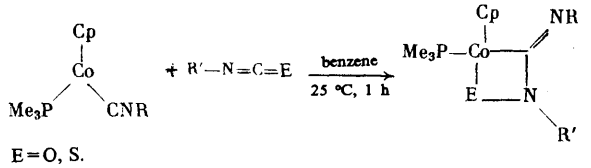


Similar cobaltaoxazoline derivatives are formed in the reaction between benzoyl azide and cobalt isonitrile complexes:[62]



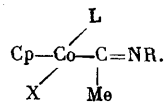
L = PMe_3; R = Ph, Me.

Interestingly, isocyanates and isothiocyanates react with cobalt isonitrile complexes to give four-membered metallacycles:[63]

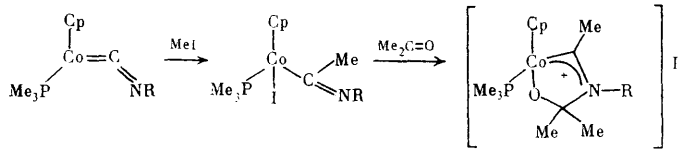


E = O, S.

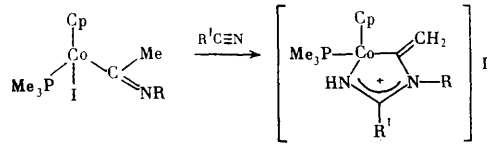
A series of studies[64–67] is devoted to the [3 + 2] cycloaddition reactions of different substrates (carbonyl compounds,[64] nitriles,[65] isothiocyanates,[66] and carbon disulphide[67]) to imidoylcobalt complexes of the type



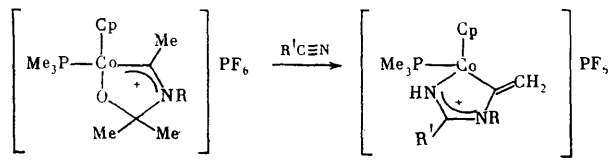
They are readily generated by addition of MeI to the corresponding isonitrile complexes;[64,65] in acetone solution[64] cyclisation to form cobaltaoxazoline occurs:[64]



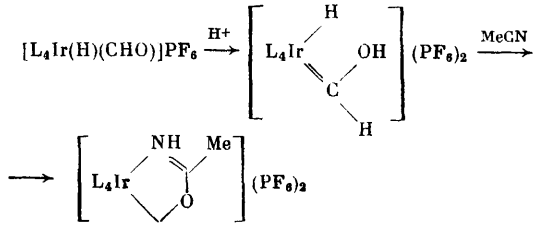
The reaction with aldehydes[64] and nitriles[65,68] occurs in a similar manner:



The same cobaltamidoazolines are formed when the cycloadducts with acetone are treated with nitrile:

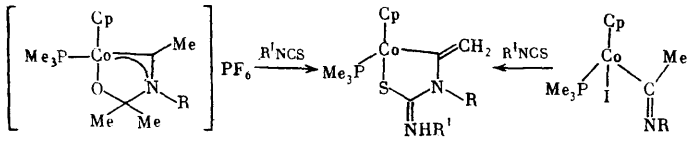


Interestingly, similar metallacycles have been obtained[69] by reaction of acetonitrile with an iridium hydroxycarbene complex:

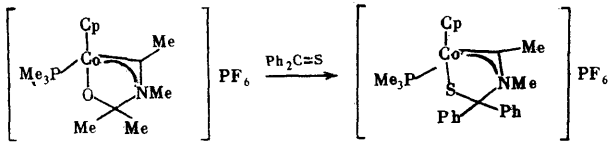


L = PMe_3

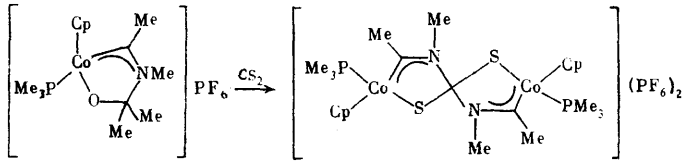
Isothiocyanates react[66] with imidoylcobalt complexes or with their acetone adducts to form cobaltathiazoline derivatives:



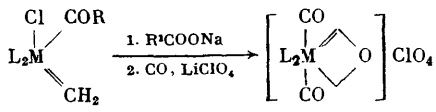
Diphenyl thioketone also displaces acetone from its adduct, giving a new heterocycle:[67]



Under these conditions carbon disulphide forms a spirocyclic complex:[67]

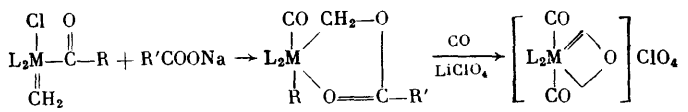


The complexes obtained by Werner et al.[64–67] contain a metallacycle with a multiple carbon–metal bond. Formally they are products of addition to the M=C bond in pseudocarbene complexes. Bohle et al.[70] have reported an example of intramolecular combination of a carbene ligand with an acyl residue:

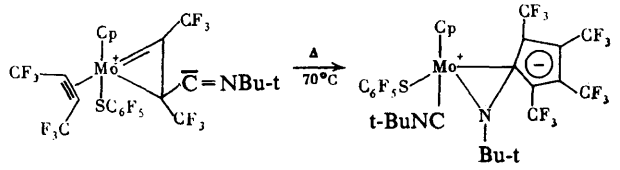


M = Ru, Os; L = PPh_3; R = Ph, $MeOC_6H_4$.

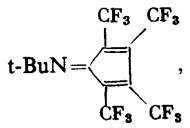
These authors assume that initially a five-membered metallacycle is formed through the addition of R'COONa to the $M=CH_2$ bond:



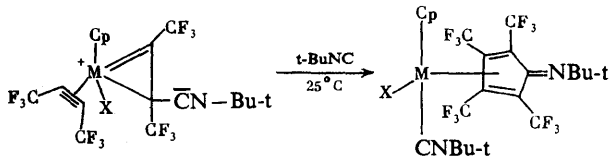
The preparation of a quite unusual cyclopentadienyl anion has been reported:[71]



On heating the cyclic carbene complex in a sealed ampoule, the sole product isolated is a complex containing the iminocyclopentadiene ligand

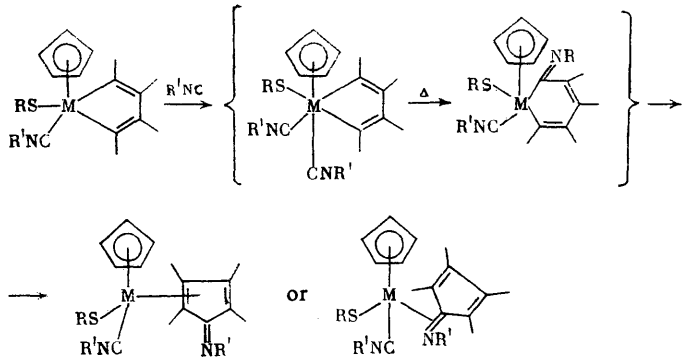


which does not have η^4-type coordination as occurs for the complexes reported by Carlton and Davidson[72]



M = Mo, W; X = CF_3, Cl.

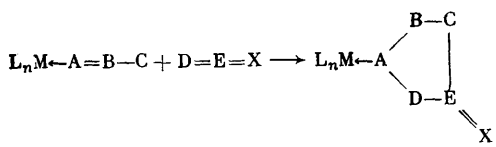
but has η^2-coordination via the imine bond. The preference for a given form of coordination in an iminocyclopentadiene is dictated by thermodynamic and kinetic factors. It is possible that the η^2-bonded isomer is generated from an initially formed η^4-complex.[71]



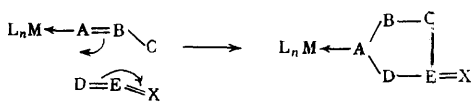
It is thought[71,73] that both isomers are derived from the same metallacyclopentadiene precursor.

2. Formation of cyclopentylidene complexes

In the present subsection we shall consider reactions of the following type:

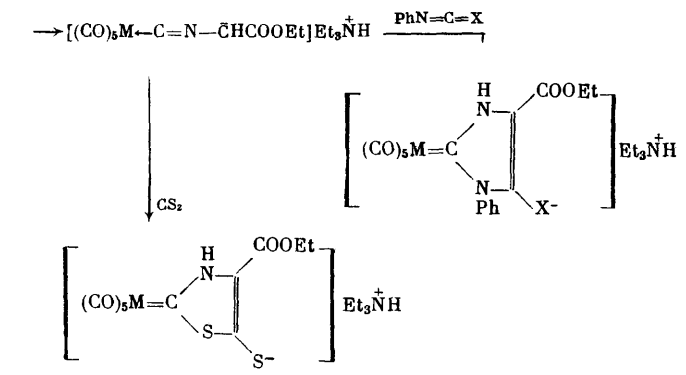


This is, in effect, a [3 + 2] cycloaddition:



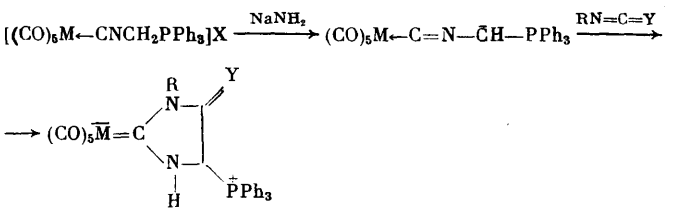
Whether these reactions are concerted or occur in stages is a question which most frequently remains outside the scope of investigation, but the authors of all the studies cited below adhere to the terminology of [*m* + *n*] processes. A necessary condition for

such reactions to occur is the presence in the initial complex of a multiple A=B bond. It is also desirable that the A=B–C residue should have a 1,3-dipole nature. This is achieved in various ways. For example, in the reaction of isocyanates, isothiocyanates,[74] and carbon disulphide[75] with chromium or tungsten ethoxycarbonylmethylisocyano derivatives, a base (Et_3N, t-BuOK) is used as a catalyst, removing a proton from the methylene group, as a result of which a 1,3-dipolar intermediate is formed. The latter undergoes cyclisation:



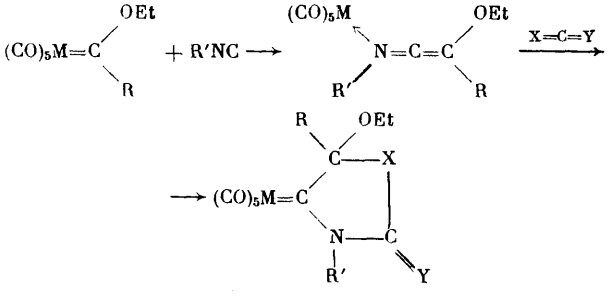
X = O, S.

In the case of complexes with triphenylphosphoranylmethylisonitrile deprotonation occurs on treatment with sodamide.[76,77] The resulting isocyanomethylenephosphoranes undergo a [3 + 2] cycloaddition reaction with isocyanates, isothiocyanates, carbon disulphide, nitriles, olefins, and acetylenes:



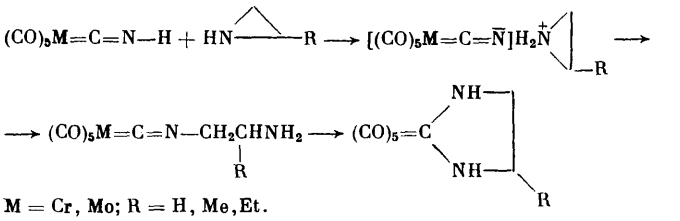
M = Cr, W; R = Ph, Me; X = Cl, PF_6; Y = O, S.

The reactions are similar[78,79] for metal ketenimine complexes (mention has been made of ketenimine complexes in Section III), which are formed by treatment of carbene derivatives with isonitriles:[78–80]



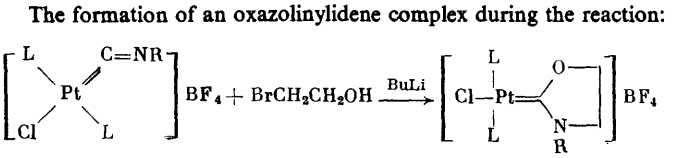
M = Cr, Mo; R = Ph, C_6H_{11}, $C_6H_3Me_2$-2,6;
R' = Ph, 2-thienyl;
X = O, NPh, NMe;
Y = O, NBu-t, NC_6H_{11}.

Isonitrilic acid complexes react with aziridines to form cyclic diaminocarbene derivatives.[81] In this case the aziridine acts both as a base and as part of the ring being formed:



M = Cr, Mo; R = H, Me, Et.

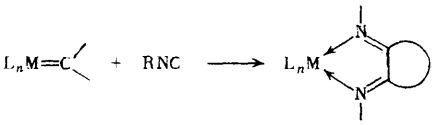
The formation of an oxazolinylidene complex during the reaction:



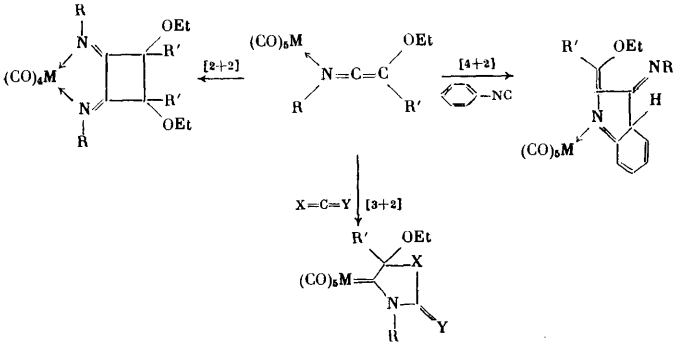
can be interpreted as attack by the dianion $^-CH_2CH_2O^-$ on the suitably polarised C=N bond of the isonitrile ligand.[82]

3. Formation of five-membered rings coordinated with *N*-donor groups

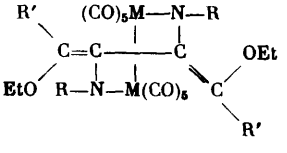
In this subsection we shall summarise reactions of the following type:



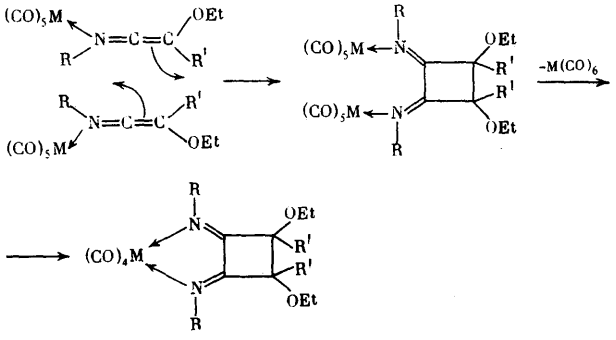
All of these reactions take place with the formation of intermediate ketenimine complexes $L_uM{\leftarrow}N(R){=}C{=}C\lessdot$ (see Section III), which have been isolated in a number of cases.[83–85] According to the data of Aumann et al.,[44,45,79] the ketenimine residues can undergo [2 + 2], [2 + 3], and [2 + 4] cycloaddition:



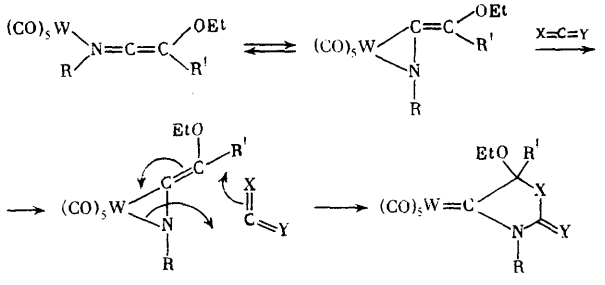
The [2 + 2] cycloaddition takes place via an intermediate of the type:



which is formed by treatment of the initial ketenimine complexes with isonitrile. The occurrence of a concerted process should also not be excluded:

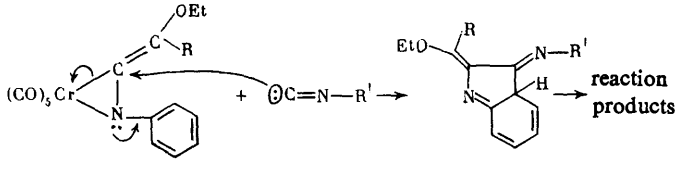


In order to account for the [3 + 2] reaction, the concept of an equilibrium between *N*- and π-coordinated ketenimine complexes (see Section III) has been adopted;[79] the π-imine derivative then undergoes a normal [3 + 2] cycloaddition:

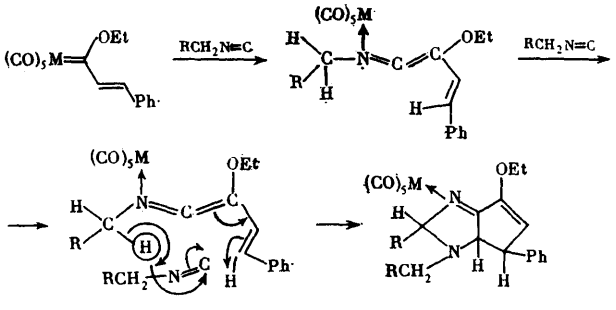


The choice between [2 + 2] and [3 + 2] processes is governed by steric factors—as steric hindrance increases the [3 + 2] cycloaddition predominates.

The interpretation of the [4 + 2] reactions is somewhat more complex.[79] The participation of a π-ketenimine intermediate and the C=C bond of the aromatic ring has been suggested:

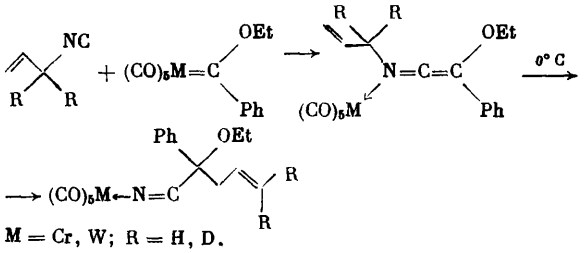


The formation of five-membered rings in two studies by Aumann et al.[83,85] is accounted for in terms of a [4 + 1] cycloaddition involving four double bonds and a single α-C–H bond of the isonitrile ligand:



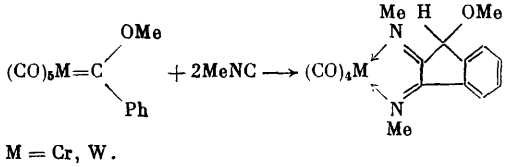
M = Cr, W ; R = H, Ph, CH_2=CH.

Allylisonitriles react with carbene complexes that do not contain a multiple bond in the carbene ligand without forming cyclic products. At low temperatures the intermediate ketenimine complexes rearrange to but-4-enylisonitrile complexes:[84]



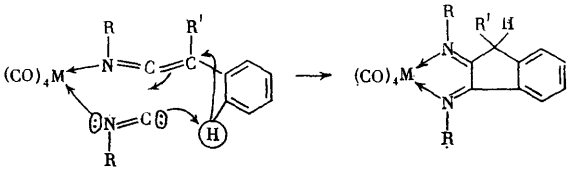
M = Cr, W; R = H, D.

In some cases the intermediate ketenimine adduct is not isolated:[86]

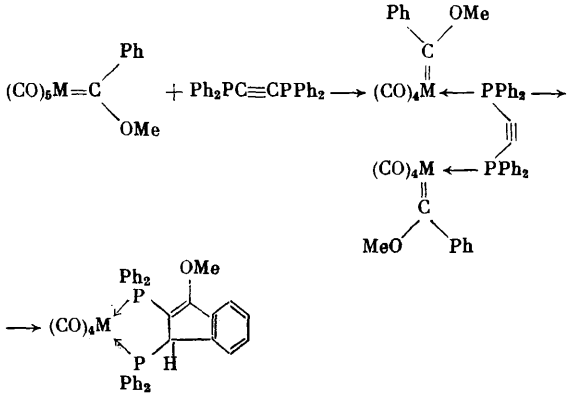


M = Cr, W.

In this case α- and *ipso*-carbon atoms of the aryl group of the carbene ligand participate in reaction. It is quite clear that this reaction is not synchronous. At the first stage a ketenimine intermediate is formed which adds a second isonitrile molecule, while the hydrogen on the α-carbon atom undergoes a 1,3-shift



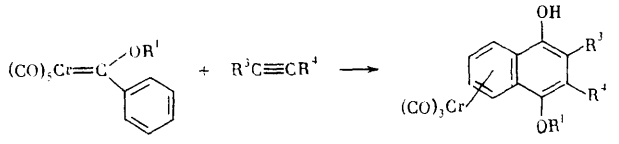
The formation of a chromium phosphine complex as described by Dötz et al.[97] is likely to occur in a similar manner:



Thus, despite the formalism of the concept of [*n* + *m*] cycloaddition (see beginning of Section IV) the attempt to classify the reactions according to the final products has essentially led to the same concept. It is clear from the material in this section that the formation of five-membered rings involving carbene complexes can result from [4 + 1], [3 + 2], and [2 + 2] reactions. In the latter case metallacycles are formed because of the participation of the metal atom.

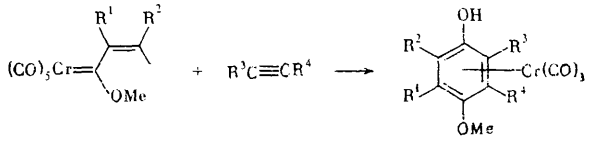
V. Reactions that lead to the formation of six-membered rings

There exists a considerable number of studies (see several reviews)[1-5,88] in which is described the formation of chromium arene complexes by reaction of alkynes with pentacarbonylchromium carbene derivatives containing an aryl substituent on the carbene carbon atom:



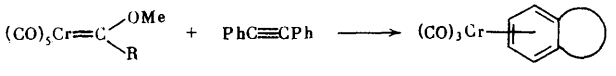
It is quite clear that the α-carbon atom of the phenyl group of the carbene ligand and one of the carbonyl groups bound to chromium participate in the reaction.

Another type of reaction that leads to arene complexes is characterised by the presence of a vinyl group on the carbene carbon atom:



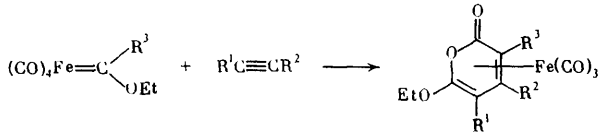
It is possible that this is a special case of the process shown above, since methoxyallylidene complexes can be formed by the reaction of alkynes with carbene complexes.

The synthesis of arene complexes from carbene derivatives with a five-membered ring on the carbene carbon atom has also been reported:



R = ferrocenyl, cycloalkenyl, pyrrolidinyl, furyl, thienyl, pyrrolyl.

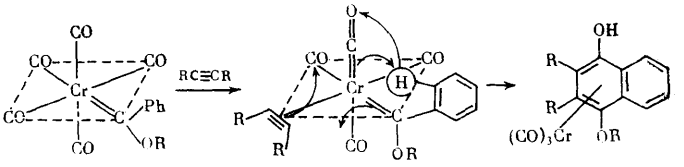
It is likely that in this case the formation of arene complexes is a secondary process. And finally, there is a small group of reactions leading to the formation of α-pyrone complexes:



These reactions take place in the presence of CO.

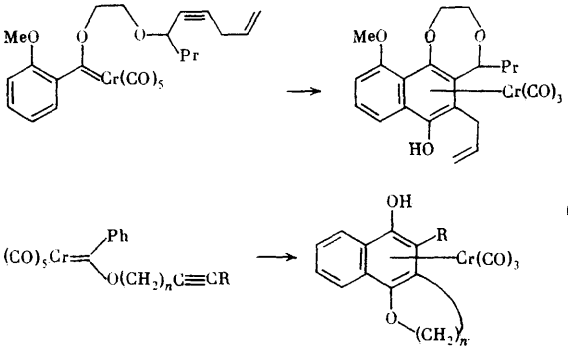
1. Formation of arene complexes from α-alkoxybenzylidene derivatives

In order for the formation of arene complexes from metal α-alkoxybenzylidene derivatives to occur successfully it is necessary for three components—alkyne, carbene, and carbonyl—to coordinate with the metal site at the same time. In order to coordinate the alkyne it is necessary to displace one carbonyl ligand from the coordination sphere. According to the data of two studies,[89,90] the CO ligand that is situated *cis* to the carbene ligand in chromium pentacarbonyl carbene complexes is the most readily replaced. As a result a *fac*-(alkyne)(carbene)carbonyl intermediate is formed, and the subsequent reaction may be regarded as a [3 + 2 + 1] cycloaddition:[2]



Under kinetically controlled conditions (low temperatures, short reaction time) a complex is obtained in which the metal is bound to the newly formed ring (1-8*a*-η^6-coordination). At higher temperatures and long reaction times the $Cr(CO)_3$ group migrates to the free ring, and the naphthalene ligand has 4*a*-8*a*-η^6-coordination in the complexes isolated. The literature data on the synthesis of chromium arene complexes starting from alkynes and α-alkoxybenzylidenepentacarbonylchromium are summarised in Table 1.

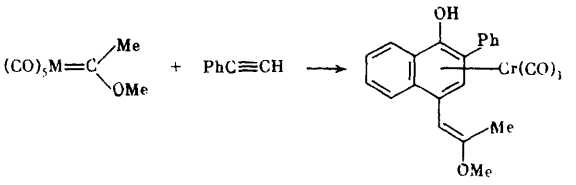
An intramolecular form of the reaction is possible when all three components—alkyne, carbene, and carbonyl—are present in the same molecule:[101,102]



n = 2 ÷ 4; R = H, Me

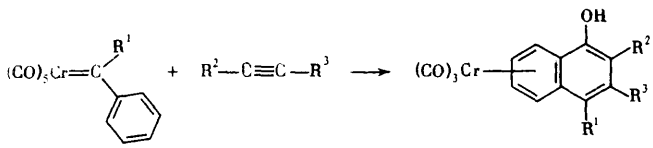
These reactions represent key stages in the synthesis of anthracyclinone antibiotics (desoxyfrenolicin, daunomycinone).[2] The regioselective reaction in the case of the *ortho* substituent in the benzene ring attacts attention. Two studies[103,104] have been devoted to this phenomenon.

In a number of cases[105,106] chromium tricarbonyl complexes of α-naphthols are formed in reactions with chromium carbene derivatives in which there is no aryl substituent on the carbene carbon atom:



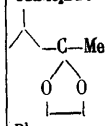
It is quite clear that a phenyl group of phenylacetylene participates in the formation of the naphthalene skeleton. It is thought[105] that in contrast to the [3 + 2 + 1] mechanism (see beginning of

Table 1. Chromium arene complexes obtained by the reaction



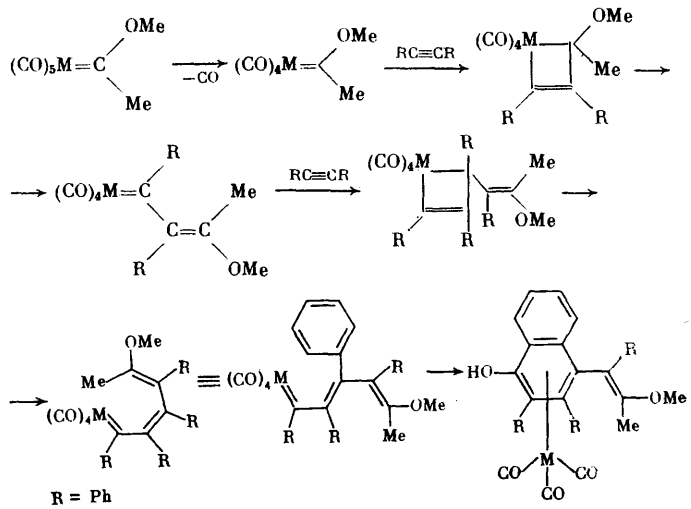
R^1	R^2	R^3	Yield, %	Refs.	Notes
OMe	Ph	Ph	62	[91]	
OMe	Ph	Ph	18	[92]	
OMe	Me	H	63	[93]	Isolated after oxidation as 2-methyl-1,4-naphthoquinone
OMe	Me	Phytyl *1	48	[93]	Isolated after oxidation as 3-methyl-2-(3,7,11,15-tetramethylhexadec-2-enyl)-1,4-naphthoquinone
OMe	Pr	H	45	[94]	Isolated as the 8a-4a-η^6-isomer
OMe	C_6H_{17}	H	59	[94]	8a-4a-η^6-isomer
OMe	t-Bu	H	79	[94]	ditto
OMe	Et	Pr	62	[94]	"
OMe	Et	t-Bu	66	[94]	"
OMe	Pr	Bu	62	[94]	"
OMe	Ph	Me	73	[94]	"
OMe	Et	Me	56	[94]	"
OMe	Pr	Me	80	[94]	"
OMe	t-Bu	Me	59	[94]	"
OMe	Phytyl *1	Me	58	[94]	"
OMe	Me	Phytyl *1	34	[94]	"
OMe	Ph	4-MeC_6H_4	52	[94]	"
OMe	Ph	4-$CF_3C_6H_4$	66	[94]	"
OMe	4-$CH_3C_6H_4$	4-$CF_3C_6H_4$	62	[94]	"
OMe	Me	Et	60	[95]	"
OMe	Et	H	35	[96]	"
OMe	Me	Me	68	[96]	"
OMe	Pr	H	45	[96]	"
OMe	Bu	H	45	[96]	"
OMe	Pr	Me	58	[96]	"
OMe	Et	Et	65	[96]	"
OMe	Me	Me	36	[96]	"
OMe	Pr	H	32	[96]	"
OMe	Bu	H	30	[96]	"
Ph	Me	Me	12	[96]	"
Ph	Pr	H	11	[96]	"
Ph	Ph	H	27	[96]	"
Ph	Ph	Ph	20	[96]	"
Ph	Ph	COOEt	7	[96]	"
Ph	H	H	9	[96]	"
OMe	Ph	Ph	61	[96]	Obtained from diphenylacetylene and a tris(4-fluorophenyl)-phosphine complex
OMe	Ph	Ph	11	[96]	Obtained from diphenylacetylene and a tributylphosphine complex
OMe	Me_3Si	H	76	[97]	Isolated as the 8a-4a-η^6-isomer
OMe	Me	Phytyl *1	58	[98]	ditto
OMe	Phytyl *1	Me	34	[98]	"
OMe	H	$CH_2CH{=}CMe_2$	60	[98]	"
OMe	Me	$CH_2CH{=}CMe_2$	85	[98]	Isolated as the 8a-4a-η^6-isomer
OMe	Me	$C_{10}H_{17}$ *2	91	[98]	ditto
OMe	Me	$C_{15}H_{25}$ *3	90	[98]	"
OMe	Ph	Ph	—	[99]	"
OMe	Ph	4-MeC_6H_4	52	[99]	Mixture of 8a-4a-η^6- and 4a-8a-η^6-isomers
OMe	Ph	4-$CF_3C_6H_4$	66	[99]	ditto
OMe	4-$CH_3C_6H_4$	4-$CF_3C_6H_4$	62	[99]	"
OMe	Ph	Me	73	[99]	Isolated as the 8a-4a-η^6-isomer

Table 1 (cont.).

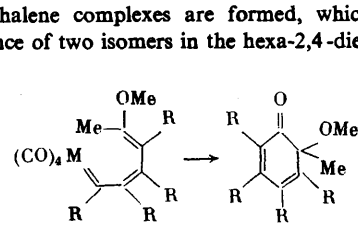
R^1	R^2	R^3	Yield, %	Refs.	Notes
OMe	Ac	H	42	[100]	Isolated after oxidation as the respective 2-substituted 4-methoxy-α-naphthol
OMe	EtOCO	H	41	[100]	ditto
OMe	t-$BuMe_2SiOCMe_2$–	EtO	54	[100]	"
OMe	$OSiMe_2Bu$-t	EtO	45	[100]	"
					
OMe	Ph	COOEt	22	[100]	Isolated after oxidation as the respective substituted 4-methoxy-α-naphthol
OMe	C_5H_{11}	COOEt	60	[100]	ditto
OMe	Et	COOEt	38	[100]	"

*1 Phytyl = 3,7,11,15-tetramethylhexadec-2-enyl.
*2 $R^3 = CH_2CH{=}C(Me)CH_2CH_2CH{=}CMe_2$.
*3 $R^3 = CH_2CH{=}C(Me)CH_2CH_2CH{=}C(Me)CH_2CH{=}CMe_2$.

Section V.1), in this case a [2 + 2 + 2] cycloaddition involving two alkyne molecules occurs:

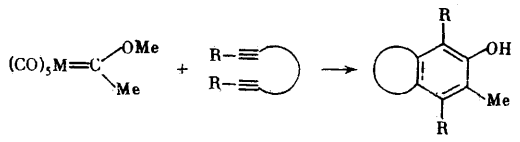


When R = alkyl, cyclohexadienone complexes rather than naphthalene complexes are formed, which is attributed[105] to the presence of two isomers in the hexa-2,4-dienylidene intermediate:

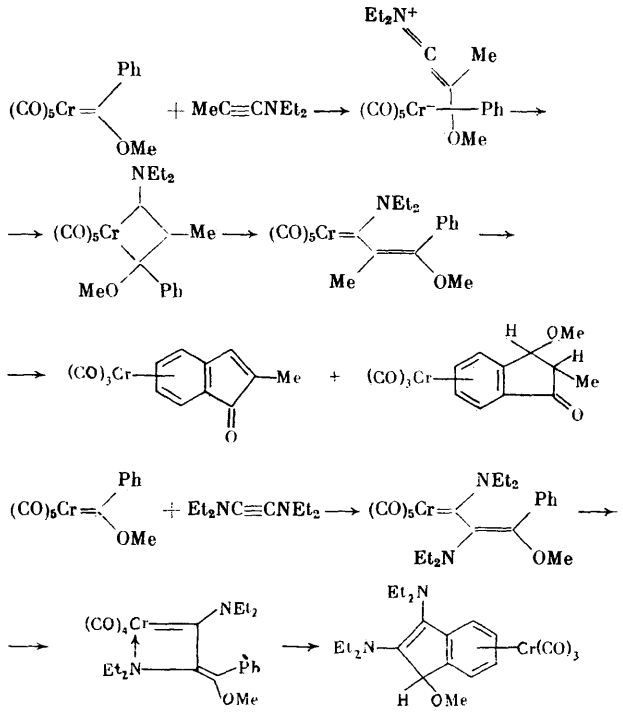


R = Me, Pr.

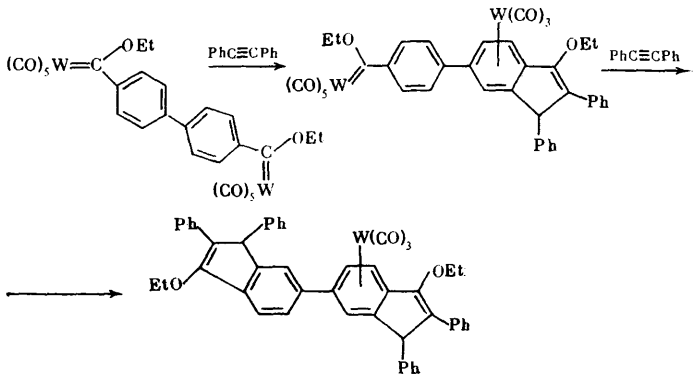
Annelation reactions involving two alkynyl residues can be carried out in an intramolecular form:[106]



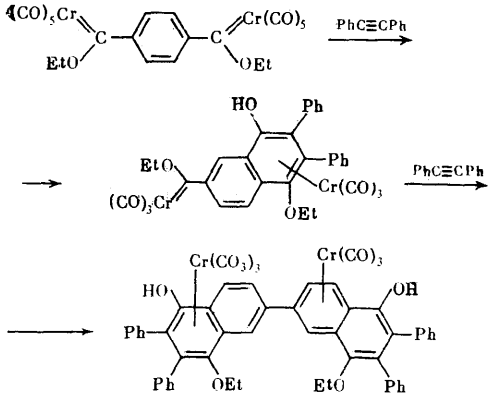
Derivatives of indene and naphthalene are obtained in this manner.[107] According to Dötz,[2] the formation of compounds with an indene skeleton occurs by insertion of alkyne into the metal–carbene bond, possibly via a four-membered metallacyclic intermediate. Nucleophilic alkynes as a rule participate in such reactions:[108–110]



However, the formation of indenes is also possible in reactions with normal alkynes such as diphenylacetylene.[92,111] An interesting reaction has been reported by Hoa and Lefloch.[112]



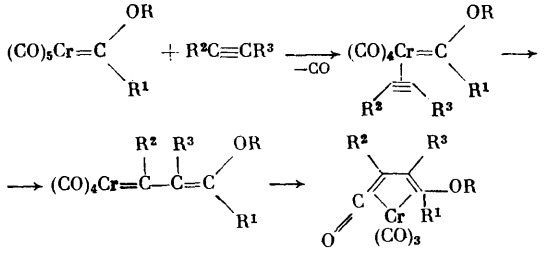
In the case of the chromium analogue a chromium naphthalene complex is formed:[122]



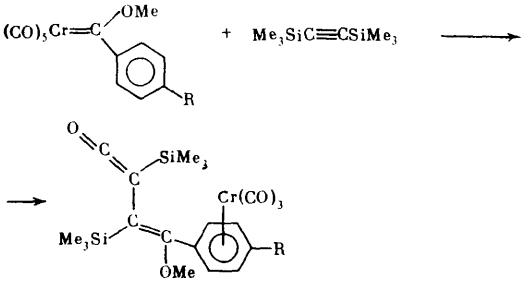
In contrast to tungsten the μ-η^6:η^6-derivative was isolated.

2. Formation of arene complexes from α-alkoxyallylidene derivatives

As was indicated above, α-alkoxyallylidene intermediates can be formed by reaction of alkynes with transition metal carbene complexes. In some instances[97,105] this is only postulated, but in a number of cases, especially for nucleophilic alkynes,[113–118] these intermediates have been isolated. They can participate in subsequent reactions. One of these is the insertion of a carbonyl ligand into the metal–carbene bond to form ketene derivatives:[97,117,119]

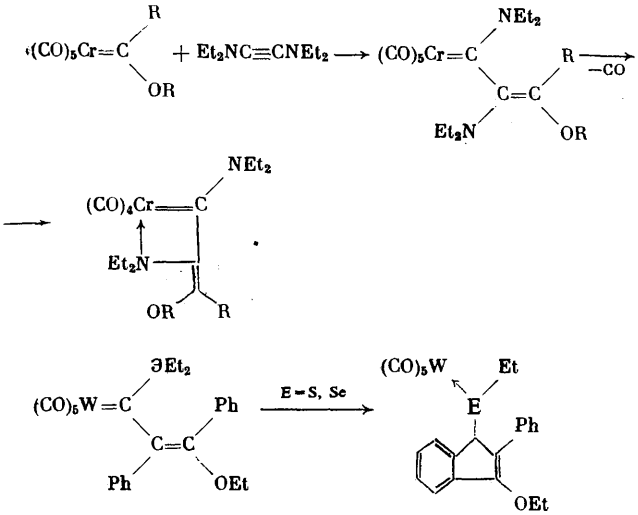


In fact, in a number of cases[97] such ketenes have been isolated, for example

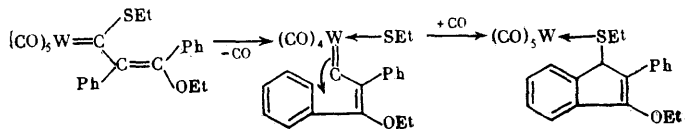


R = H, Me, OMe, CF_3.

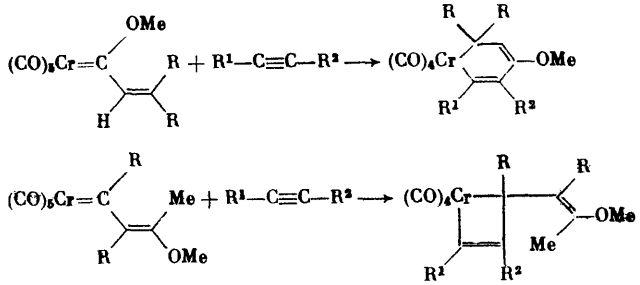
Another reaction is intramolecular cyclisation through coordination of the metal atom with *N*-donor groups present in the alkyne molecule:[110,120]



The latter reaction appears to be unusual. It can be given by a scheme, one of the stages of which is formation of a three-membered metallacyclic intermediate. This metallacycle subsequently decomposes through cleavage of the metal–carbon double bond of the carbene ligand, with a five-membered ring being formed:

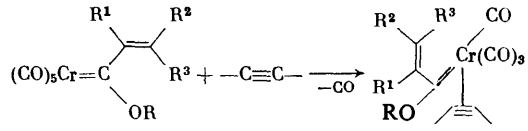


The formation of "true" metallacycles with metal–carbon σ-bonds is also possible:[105,121]

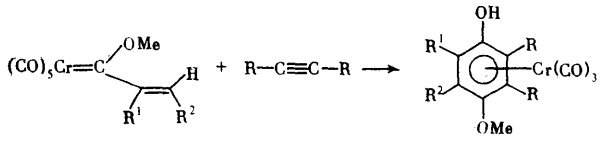


Interestingly, whatever the size of the ring in the resulting intermediate, in the latter two cases the same final product—2-methoxy-2-methyl-3,4,5,6-tetrasubstituted cyclohexa-3,5-dienone—was isolated, although Tang and Wulff[121] in the case of the six-membered metallacyclic intermediate expected to obtain a 3-methoxycyclopentadiene—a product derived from the β-elimination of $HCr(CO)_5$. However, Herndon et al.[122] on reacting pentacarbonyl[(methoxy)(cyclopropyl)carbene]chromium with diphenylacetylene isolated 4,5-diphenylcyclopent-3-enone—the expected reaction product.

Thus, all reactions of α-substituted allylidene complexes with alkynes can be represented[2] by the formation of an (alkyne)(carbene)carbonyl intermediate:



This is essentially the same intermediate as that depicted at the beginning of Section V.1, and its subsequent fate depends on the nature of substituents R^1, R^2, and R^3. When R^3 = H, arene complexes are formed:[123–126]

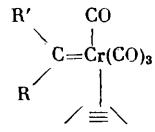


R^1 = Me, H; R^2 = H, Me, Ph; R^1, R^2 = $-(CH_2)_n-$, where n = 3, 4.

Terminal acetylenes react regioselectively, the substituent going into the *ortho* position relative to the OH group.[125]

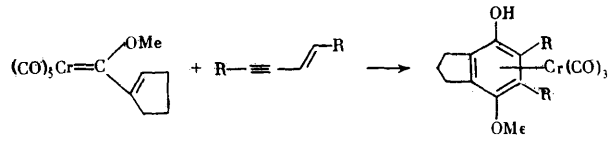
3. Formation of arene complexes from carbene complexes with a five-membered ring on the carbene carbon atom

The five-membered ring on the carbene carbon atom in carbene complexes can be a heterocycle,[117,127–132] alicycle,[125,127] or cyclopentadienyl ring of a ferrocenyl residue.[133] In all cases the results (alkyne)(carbene)carbonyl intermediate (see Section V.1) takes the following form:

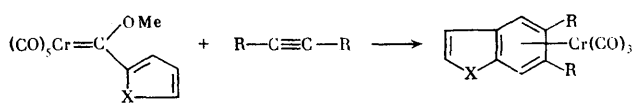


R′ = five-membered ring.

The fate of this intermediate is known[125,127] when R′ is an alicyclic group—η^6-indane derivatives are formed. It is interesting that in the reaction



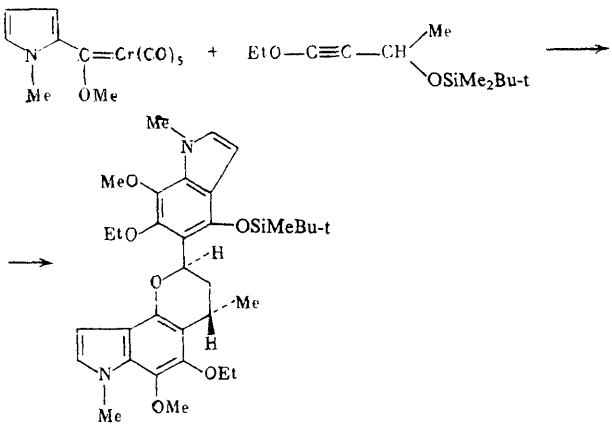
the C=C double bond of the ring rather than that of vinylacetylene is involved in the cycloaddition process.[125] When R′ - α-pyrrolyl,[129] α-furyl,[127,132] and α-thienyl[127] annelation also occurs in a normal manner—the corresponding benzo derivatives of the heterocycles are formed:



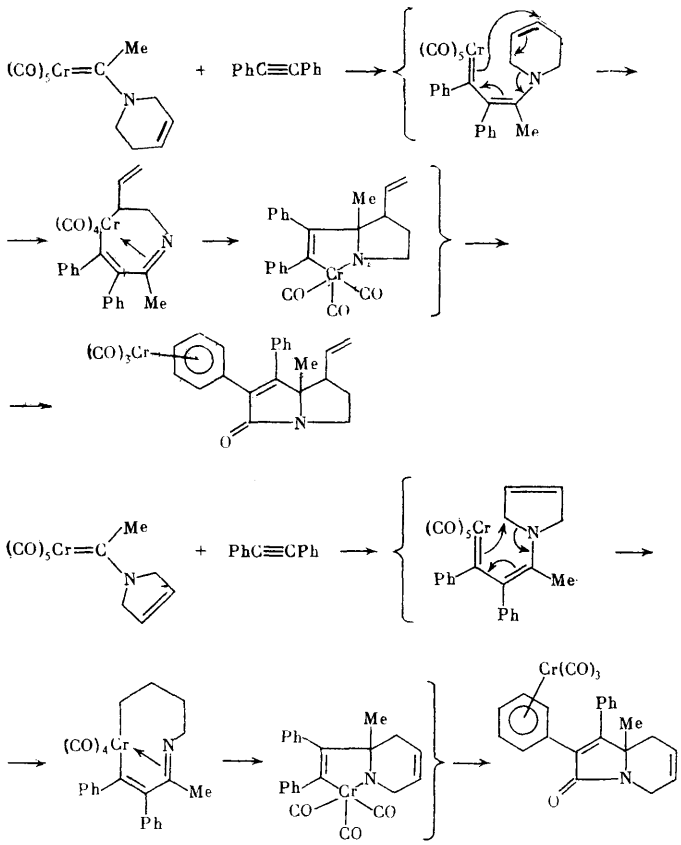
X=O, S, NMe; R = H, Me, Et, EtO, COOMe, Bu, Ph.

However, there are exceptions. For example, the reaction of a chromium α-pyrrolylcarbene derivative with 1-ethoxy-3-[dimethyl-

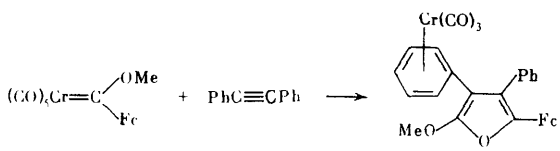
(t-butyl)siloxy]but-2-yne yields its dimer rather than the expected indole:[128]



Annelation can also occur through a more remote double bond:[130,131]

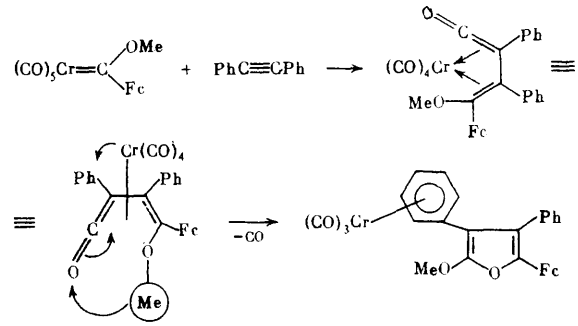


In the case of an α-ferrocenylcarbene complex a furan derivative is formed:[133]



Fc = C_5H_4FeCp.

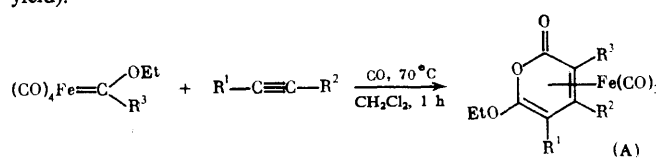
It is possible that the reaction occurs via a ketene intermediate:



The structure of the resulting ferrocene-benzenechromium tricarbonyl derivative has been established by X-ray diffraction analysis.[133]

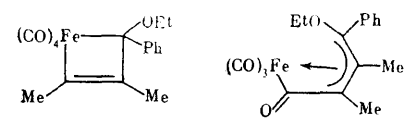
4. Formation of iron α-pyrone complexes

The reaction of iron alkylidene compounds with various alkynes under pressure in an atmosphere of carbon monoxide leads to the formation of complexes of iron with an α-pyrone ligand (in high yield):[134]

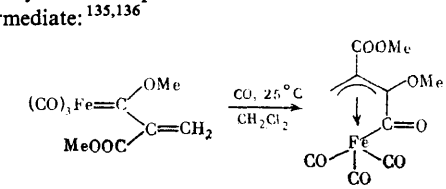


R^1	R^2	R^3	Yield (A), %
Me	Me	Ph	89
Ph	H	Ph	74
Et	H	Ph	33
Ph	Ph	Ph	93
COOMe	Me	Ph	15
Me	Me	t-Bu	60
Ph	H	t-Bu	39
Me	Me	Bu	33

The structure of the complexes obtained (A) has been established by X-ray diffraction analysis. The formation of the α-pyrone skeleton requires the participation of two carbonyl ligands. Moreover, migration of the ethoxyl group from the carbene carbon atom occurs during reaction. When the reaction was carried out in the absence of carbon monoxide, an unstable product was isolated, for which two alternative structures—metallacyclic and π-allylacyl—were proposed on the basis of the ^1H NMR and IR spectra:

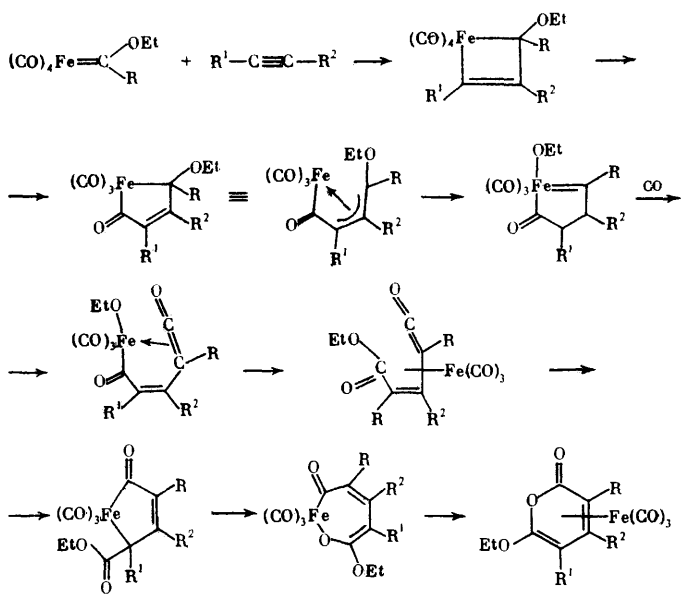


The fact that a π-allylacyl complex is formed when carbon monoxide reacts with a (1-methoxy-2-methoxycarbonylprop-2-enylidene)tricarbonyliron compound is evidence in favour of the second intermediate:[135,136]



However, Semmelhack et al.[134] favour a metallacyclic intermediate, since in the ^{13}C NMR spectrum of the isolated complex there is no signal due to an acyl carbon atom. They

proposed the following scheme for formation of α-pyrone complexes:[134]



This scheme includes the two alternative intermediates. The formation of intermediate ketene complexes is also known,[97] so this sequence of reactions reflects the process mechanism sufficiently objectively.

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Thus, the "carbene site" in transition metal complexes represents a unique matrix on which the most varied cyclic ligands can be built up as a result of an inner-sphere reaction. These processes are treated as [*n* + *m*] cycloaddition reactions, although they are not such types and occur in an unconcerted manner, including stages that are typical of the chemistry of π-complexes such as the initial coordination of substrate, insertion of ligands, elimination, etc. These ring-formation processes in the inner coordination sphere involving carbene complexes are of interest to organic chemists since they act as convenient models for an understanding of the reaction mechanisms of organic compounds in the presence of transition metal complexes.

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Translated from *Uspekhi Khimii* **60** 205–237 (1991) U.D.C. 541.14:541.64

Electron phototransfer in the initiation of polymerisation

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ABSTRACT. The results of studies on the participation of exciplexes and other products of electron phototransfer in the initiation of polymerisation are correlated in this review. The relationship between the nature of the primary radical species and the mechanism of formation of a polymerisation chain is discussed. Particular attention is given to the effect of the electronic structure of the photoinitiator, the chemical nature of the activator and monomer, and the polarity of the medium on the mechanism of photoinitiation and its efficiency.

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I. Introduction

Photopolymerisation processes have been widely applied in current practical methods.[1–4] They are carried out with the participation of active products that are generated in various photochemical reactions. These can be products of unimolecular photodissociation[5–9] or products of bimolecular reactions involving electron or hydrogen atom transfer.[10–19] Recently a large number of reports have been published on the participation in polymerisation photoinitiation processes of different intermediates of electron phototransfer, principally exciplexes,[20–26] which help to increase the efficiency of the process.

The role of photoinitiators in polymerisation processes is very important. They determine the region of spectroscopic sensitivity of the polymerising compositions,[2,25] and the kinetics and mechanism of not only the initiation process but also that of the overall polymerisation reaction.[20–29] To a certain extent they influence the physicochemical and mechanism properties of the polymer materials obtained.[2,28] Meanwhile the question of the mechanism of photoinitiation with the most effective binary systems that are susceptible to electron phototransfer has received virtually no study.

This review attempts to correlate the existing literature data on the participation of exciplexes and other electron phototransfer products in the initiation of polymerisation in order to establish the scientific principles for the choice of initiating systems that can achieve effective polymerisation over a wide spectroscopic range.

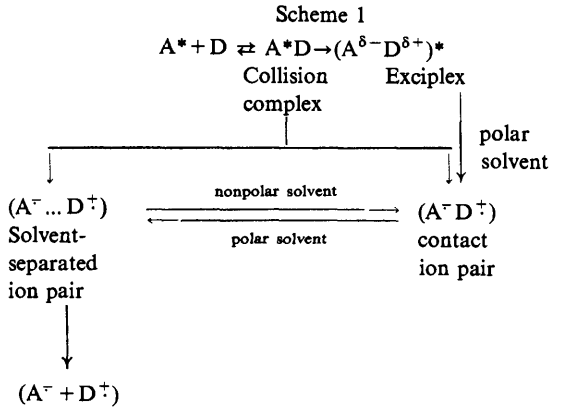
We shall consider the main questions relating to the phenomenon of electron phototransfer.

II. Main mechanisms of electron phototransfer

1. Classification of the intermediates of electron phototransfer

The formation of exciplexes and their photophysics have formed the subject of a number of reviews.[30–35] An exciplex is an excited molecular complex of a given stoichiometric composition which is stabilised in an excited state and unstable in its ground state.[31] It has a specific geometry that is characterised by a bond energy of the order of 5–200 kcal mol^{-1}, a significant dipole moment which is to a certain extent a measure of the charge transfer,[36] and a lifetime that is sufficient for emission of fluorescence or phosphorescence (depending on its multiplicity). An exciplex is one of the intermediates formed during electron phototransfer (EPT). According to the ideas put forward in one of the most recent reviews,[35] the scheme for electron transfer (ET) can be depicted as follows:

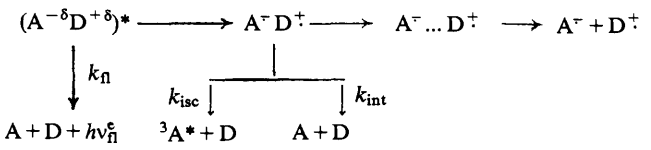
Scheme 1



In this case all the intermediate products are classified according to lifetime, distance between the partners, and number of solvent molecules inserted between them. The lifetime of the collision complex (of the order of 10^{-9}–10^{-10} s) is sufficient for "quenching" of the excited state of the photoactive component by an ET mechanism to occur.[35–37] In this case the collision complex is initially converted to a contact ion pair going via or avoiding the formation of an exciplex, depending on the conditions. It follows from Scheme 1 that the solvent, depending on its polarity, can stabilise contact or solvent-separated ion pairs, combined under the general title of geminate ion pairs. Solvent-separated radical ions that are situated at considerable distances from each other in solution are known as free solvated radical ions. They are completely independent of their partner and in a similar manner to free radicals can exist as independent species for a relatively long period.

If a strong interaction occurs between A* and D in the collision complex, it is converted to an exciplex. When stabilisation of the exciplex is determined to a considerable extent by a charge-transfer interaction, with an increase in polarity of the medium all the electron transfer processes described above can also occur via an exciplex in accordance with Schemes 1 and 2. Deactivation of an exciplex occurs through radiationless processes of internal conversion and intersystem crossing as well as through fluorescence (if a singlet exciplex is involved).[22]

Scheme 2



Fluorescence occurs when there is a transition from the equilibrium state of the exciplex to the dissociative ground state in accordance with the Franck–Condon principle. If the intramolecular transitions are accompanied by a considerable nuclear rearrangement of the components, emission is absent, namely, the exciplex does not fluoresce and its properties are similar to those of a contact ion pair.[35]

Triplet exciplexes exist in addition to singlet exciplexes, and these have been discussed in detail in reivews.[31,38,39] They are formed either through the interaction of a triplet-excited molecule with an electron donor or acceptor[40] or through the intersystem crossing of a singlet exciplex or weak charge-transfer complex occurring in the ground state.[39,41]

The wave function of the exciplex, whatever its multiplicity, can be represented as a combination of wave functions of states with the excitation localised on one of the components of the complex and a state with complete charge transfer:[42]

$$\psi_{ex} = c_1\psi(D^*A) + c_2\psi(DA^*) + c_3\psi(D^+A^-), \quad (1)$$

where c_1, c_2, and c_3 are coefficients denoting the contribution of each of the states of Ψ_{ex}.

If $c_3 \gg c_2$ and $c_3 \gg c_1$, the contribution of charge-transfer states to the stabilisation energy of the exciplex is very large.

The EP scheme involving a singlet exciplex considered above can be applied equally to a triplet exciplex with the distinction that in the latter case a triplet radical ion pair is formed instead of a singlet solvent-separated radical ion pair.

Singlet fluorescing exciplexes are readily identified from the appearance of a structureless emission band which is shifted to longer wavelength in the spectrum relative to the fluorescence band of the uncomplexed photoactive component. Similarly, formation of triplet exciplexes can be monitored (in extremely rare cases in the condensed state because of the very low quantum yields, it is true) from the formation of a structureless fluorescence band, which is shifted to the "red" region relative to phosphorescence from the initial molecule.[43]

Fast kinetic methods can now be used to study singlet and triplet exciplexes, making it possible to record short-lived intermediates with a lifetime of the order of 10^{-11} s or more and to follow the kinetics of their deactivation.[44–46]

2. Thermodynamic and kinetic aspects of electron phototransfer

Electron phototransfer takes place whenever the changes in free energy of the processes $\Delta G_{ET} \ll 0$. Whatever the pathway of electron transfer, the expression for ΔG_{ET} has the following form:[35]

$$\Delta G_{ET} = E_{D^+/D} - E_{A/A^-} - e^2/\varepsilon R - E_{00}, \quad (2)$$

where $E_{D^+/D}$ and E_{A/A^-} are the values of the half-wave potentials of polarographic oxidation of the donor and polarographic reduction of the acceptor, $e^2/\varepsilon R$ is the Coulombic interaction energy between components A and D, ε is the dielectric constant of the solvent, R is the distance between the centres of molecules A and D, E_{00} is the energy of the excited state of molecule A.

Expression (2) does not take into account the structural changes which occur in electron donor-acceptor (EDA) systems during electron phototransfer. However, in a number of cases it is these which determine the probability of electron transfer. In the theory of Marcus,[47–50] which describes a mechanism for outer-sphere electron transfer, the effect of configurational changes, including changes in bond angles and bond lengths of the reactants, their steric configuration and the reorientation of the solvent molecules around them, in the initial and final states is examined. According to this theory the expression for the rate constant of the electron transfer has the following form:[50]

$$k_{ET} = Zk\exp(-\Delta G^{\neq}/RT), \quad (3)$$

where Z is the number of collisions, equal to 10^{11} litre mol^{-1} s^{-1}, k is a constant that depends on the magnitude of the electronic reaction barrier, and $\Delta G^{\neq}$ is the free energy of activation, including the contribution of the nuclear reaction barrier.

The electronic reaction barrier depends on the degree of overlap of the filled orbital of donor with the vacant unoccupied orbital of acceptor, their symmetry and relative steric configuration.

The nuclear reaction barrier is taken to mean the energy needed to change the bond angles and bond lengths and to change the molecular orientation resulting from both intramolecular factors and solvation effects during electron transfer.

The expression for the free energy of activation of electron transfer for neutral organic molecules has the form

$$\Delta G^{\neq} = (\lambda/4)(1 + \Delta G_{ET}/\lambda)^2, \quad (4)$$

where λ is the internal reaction barrier. It is equal to

$$\lambda = \lambda_i + \lambda^0, \quad (5)$$

where λ_i is a component that takes into account the energy expended on the change in bond lengths and λ_0 is a component that takes into account the energy expended on the reorientation of solvent molecules.[47,48]

Eqn. (4) gives the parabolic dependence of $\Delta G^{\neq}$ on ΔG_{ET}. The region of highly exothermic values of ΔG, where the free energy of activation starts to increase and the rate constant of electron transfer correspondingly decreases is known in the literature as the "inverted" region.[49]

The efficiency of EPT is determined to a considerable extent by the lifetime of the excited state of the photoactive component. It must be sufficiently long for EPT to occur in preference to the other deactivation processes competing with it. The probability of the latter depends on the photophysical properties of the excited

molecules (electron configuration and multiplicity of the excited state of the photoactive molecules) and their photochemical activity.

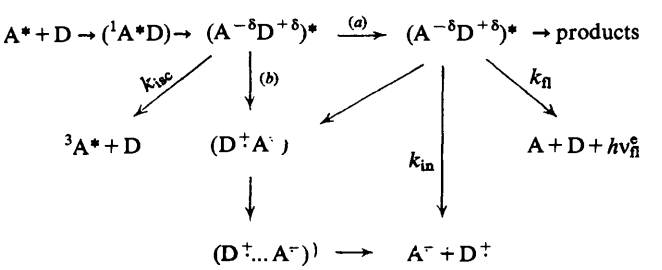
Electron transfer that involves an exciplex is the most rapid process, since in this case the maximum possible overlap of the orbitals of the electron donor and acceptor occurs.[35] Obvious examples of this are provided by exciplexes of the "sandwich" $\pi\pi$-type, formed between polynuclear aromatic amines, where favourable conditions for effective electronic interaction are created because of the similar symmetry of the overlapping orbitals.[51]

Together with this during electron transfer many systems involving an exciplex exhibit hindrances which increase the height of both the nuclear and electronic reaction barriers. In this case there are differences between the non-equilibrium Franck–Condon state $(A^{-\delta}D^{+\delta})^*$ and the equilibrium state of the exciplex $(A^{-\delta}D^{+\delta})^*$.[38,52,53] The first of these has a new electronic configuration as a result of charge transfer, distinct from the electronic configuration of the ground state and a nuclear configuration which corresponds to the electronic configuration of the initial state. In the non-equilibrium state the structure of the exciplex is flexible. During relaxation, which is accompanied by changes in bond lengths and bond angles in the molecules making up the complex and a reorientation of solvent molecules around them, the system changes to an equilibrium state from which the exciplex emits (if the probability of the radiative transition is sufficiently high). In such systems a significant Stokes shift of the fluorescence of the complex due to the molecular rearrangements which occur in them has been recorded.[54]

Non-equilibrium and equilibrium states of the exciplex were detected during emission of the system pyrene–tri(n-butyl)amine.[55] The nuclear electron transfer barrier in this system increased because of the unfavourable (tetrahedral) configuration of the amine molecule for formation of a complex relative to the pyrene molecule. The high values of the Franck–Condon energy of destabilisation of the exciplexes in the ground state (~90 kJ mol^{-1}) and the large Stokes shift of fluorescence of the exciplexes of aromatic azines with *N,N*-dimethylaniline (DMA) is also in all probability due to the two-stage nature of their formation.[56] In this case the geometric hindrance for formation of a complex is due to bending of the π-skeleton of molecules of the photoactive components during excitation. On the other hand, the exciplex of the "sandwich" $\pi\pi$-type structure between anthracene and DMA is formed in a single stage, as shown by the results of study over a picosecond timescale.[57]

The subsequent deactivation processes of exciplexes (internal conversion and intersystem crossing, dissociation in low-polarity or polar media, the formation of secondary products) can occur from both an equilibrium and a non-equilibrium state in accordance with Scheme 3.[58] As ε increases the probability of deactivation by route (*b*) increases.

Scheme 3



The probability of each of these will be determined by kinetic factors. Kuzmin et al.[53] have proposed a method for determining the probability of a Franck–Condon state participating in secondary reactions.

The kinetics of radiationless transition processes are governed by the energy gap principle but together with this principle the values of the rate constants of these processes show a significant dependence on characteristics of the electronic structure of the components of the exciplex. Thus a relatively slow relaxation of the Franck–Condon state of the exciplex to the equilibrium state caused by the unfavourable steric configuration of the components for electron transfer (perpendicular or inclined relative configuration of the planes of the partner molecules) is a prerequisite for the occurrence of a "rapid" intersystem crossing to a triplet state from the non-equilibrium state of the complex. The high rate constant for intersystem crossing ($k_{disc} \approx 10^9 - 10^{10}$ s^{-1}) is due, in the opinion of several authors,[58–61] to the considerable dependence of the matrix element of the spin-orbit interaction between the charge-transfer state of the singlet exciplex and the locally excited triplet state of the photoactive component on the geometry of the components in the exciplex. When the respective orbitals of the partner molecules of the complex are perpendicular to each other, the value of k_{isc} increases sharply.[59–61] In the case of a parallel orientation of the partner molecules, which is typical of exciplexes of polycondensed hydrocarbons with aromatic amines, intersystem crossing occurs relatively slowly ($k_{isc} \approx 10^8$ s^{-1}) from the equilibrium state of the exciplex.[62]

3. Relationship between the rate constant of fluorescence quenching and the efficiency of photodissociation with a change in free energy during electron transfer

One of the arguments in support of EPT is the existence of a correlation between the efficiency of quenching of the photoexcited state of the molecules being studied and the electron-donating (electron-acceptor) properties of the quencher. The efficiency of quenching in this case is determined by the expression[35]

$$\Phi_{ET} = \varphi_{S(T)} \frac{k_q[Q]}{k_q[Q] + k_d + k_q'[Q]}, \qquad (6)$$

where $\varphi_{S(T)}$ is the quantum yield of formation of the respective excited state, k_q and k_q' are the bimolecular rate constants of quenching due to electron transfer and other reactions respectively, k_d is the rate constant of monomolecular deactivation processes, [Q] is the concentration of quencher.

If the quenching process is due to electron transfer, the expression for k_q has the following form:[63]

$$k_q = \frac{2 \cdot 10^{10}}{1 + 0.25[\exp(\Delta G^{\neq}/RT) + \exp(\Delta G_{ET}/RT)]} \qquad (7)$$

According to this equation a linear dependence must occur between $\lg k_q$ and ΔG_{ET} with a plateau being reached at values of k_q close to the diffusion-controlled rate constant.[63,64] The slope of the linear section of this curve is equal to $1/RT$,[65] which can serve as evidence for the existence of electron transfer in a study of bimolecular quenching processes of excited states.

However, it should be remembered that the rate constant of quenching k_q is not always identical to the rate constant of electron transfer. When electron transfer is slow, $k_q = k_{ET}$. During rapid electron transfer ($k_{ET} \gg k_{diff}$) the rate constrant of quenching is

limited by the rate constant for diffusion. It was shown in two studies[66,67] that this is one of the reasons for the absence of an inverted region in the experimentally observed dependences of $\lg k_q$ on ΔG_{ET}.

In the diffusion-controlled region of the rate constants of quenching there is no systematic relationship between the quantum yield of photodissociation and the value of ΔG_{ET}.[52,68] Thus, the quantum yields of photodissociation for systems containing naphthalene derivatives as the electron donor are considerably higher than would be expected from their values of ΔG_{ET}. At the same time the efficiency of photodissociation for systems with electron donors containing a nitrogen, oxygen, and sulphur atom is considerably lower than the expected values.

However, there is a significant effect of the chemical nature of the reacting compounds and the multiplicity of their excited states on the quantum yield of photodissociation φ_D. In terms of the values of φ_D, the most frequently used quenchers of the excited state of photoactive compounds can be divided into 4 classes: amines, nitriles, esters, and anhydrides.[52] Within each class of quenchers it is already possible to establish some correlations between the values of φ_D and ΔG_{ET}. Thus, in a series of donors or acceptors of a single type φ_D decreases with an increase in oxidising potential of the electron donor or reducing capacity of the electron acceptor, in other words, with the shift of ΔG_{ET} to the exothermic region. The observed mechanism is quite obvious if account is taken of the fact that when $\Delta G_{ET} < 0$, in addition to the increase in probability of photodissociation processes, the probability of a competing process of radiationless transfer to the ground state also increases due to the decrease in the energy gap between it and the state with complete electron transfer.

4. Effect of solvent on the process of electron phototransfer

The solvent has a considerable effect on the mechanism of electron transfer. In this respect electrostatic (dipole-dipole and dipole-polarisation) interactions of the excited complex and its partners with the medium must be taken into consideration. These interactions are of a universal nature and are determined by such factors as the dielectric constant ε and refractive index n of the solvent. As a result of the solvating effect of the solvent a change in the electronic structure of the exciplex and its geometry is possible as is a change in the kinetics of electron transfer.[52] The polarity of the medium determines the dynamics and succession of stages in electron transfer (see Scheme 1). It is known that with an increase in the dielectric constant of the solvent, the probability of electron transfer in the collision complex increases, with the stage involving formation of an exciplex being absent.[52] With an increase in polarity of the medium ($\varepsilon > 7$) the final products of deactivation of the exciplex or contact ion pair are solvent-separated radical ions or geminal ion pairs possessing sufficient energy for subsequent conversions classified as secondary reactions of electron transfer.

It was noted earlier that the quantum yield of photodissociation (φ_D) depends strongly on the chemical properties of the partners that participate in electron transfer. Along with this there is a specific relationship between φ_D and the dielectric constant of the solvent[52]

$$\lg(1/\varphi_D) = A/\varepsilon + B, \qquad (8)$$

where A and B are constants that do not depend on ε. This equation is identical to the expression obtained from the Onsager model of ionic recombination.[69]

According to expression (8), an increase in φ_D is to be expected as ε increases, namely, with a shift of ΔG_{ET} towards the exothermic region. In fact, this type of dependence occurs in many cases.[69]

Donor-acceptor systems of a similar chemical nature having approximately the same values of ΔG_{ET} but which have φ_D values that differ considerably in polar solvents are known.[70] Recently it has been possible to account for these apparent contradictions by taking into account the nature of the solvating effect in vibrational relaxation processes during electron transfer.[70–73] The expression obtained by Mataga et al.[70–73] was used in an analysis of the magnitudes of the rate constants of charge separation v_S and recombination v_R at the following stages of electron transfer:

$$A^*...D \rightarrow A^{\cdot-}...D^{\cdot+} \rightarrow A...D.$$

As a result of this analysis the following conclusions were made. The rate constant of charge separation (dissociation constant) v_S is virtually independent of the magnitude of the energy gap between the initial ($A^*...D$) and final ($A^{\cdot-}...D^{\cdot+}$) states since the energy of activation of this process is extremely small. This conclusion is in complete agreement with the dependence of $\lg k_{eq}$ on ΔG_{ET} in the inverted region.[63] The rate constant of recombination v_R depends to a considerable extent on the energy gap between the initial ($A^{\cdot-}...D^{\cdot+}$) and final ($A...D$) states. Apart from this, the magnitude of v_R, in contrast to v_S, is determined to an appreciable extent by the individual properties of the participants in electron transfer (their donor-acceptor properties, steric configuration, relative orientation, etc.). It may be assumed that the ratio of the rate constants for charge separation and for recombination which depend on ΔG_{ET} will also determine the true value of the quantum yield of photodissociation.

One of the reasons for the existence of an inverted region may be related to secondary proton-transfer reactions.[67]

5. Secondary proton-transfer reactions

We shall only consider below those systems in which proton transfer follows electron transfer. Protonation can occur in one of the intermediates: in the collision complex,[74,75] exciplex,[76] contact radical ion,[77] or solvent-separated ion pair[78] in accordance with Scheme 4:

Scheme 4

$$^{1,3}A^* + DH \xrightarrow{k_q} {}^{1,3}(ADH)^* \xrightarrow{k_{PT}} (AH^{\cdot}...D^{\cdot}) \xrightarrow{k_{sep}} AH^{\cdot} + D^{\cdot}$$

$$k_{int}: \quad A + DH \qquad k_{fl}: \quad A + DH + h\nu_{fl} \qquad k_{diss}: \quad A^{\cdot-} + DH^{\cdot+}$$

where $^{1,3}(ADH)^*$ is any of the intermediates of EPT.

The formation of intermediates naturally reduces the potential barrier of proton transfer through the convergence of the partners and as a rule it produces a more favourable orientation for their interaction. Apart from this, the radical cations formed as a result of EPT are stronger acids and the radical anions are correspondingly stronger bases than their electron-neutral precursors.[78] Thus EPT assists an increase in not only kinetic but also thermodynamic acidity of proton donors, by increasing their reactivity. According to Marcus,[79] the expression for the rate constant of proton transfer is similar to expression (3) and has the form:

$$k_{PT} = Z \exp(-\Delta G^{\neq}_{PT}/RT), \qquad (9)$$

where $\Delta G^{\neq}_{PT}$ is the Gibbs free energy of activation

$$\Delta G^{\neq}_{PT} = W_R + (\lambda/4)(1 + \Delta G_{PT}/\lambda^2). \quad (10)$$

Here W_R is the change in free energy needed for convergence of the components and their rearrangement required for proton transfer. In turn

$$W_R = \omega^R - RT \ln S^r s^r, \quad (11)$$

where ω^R is the Coulombic interaction energy between the reaction partners expended on their convergence to a distance r, S^r and s^r are values representing steric and statistical factors.

During exothermic proton transfer (this occurs in all of the systems examined in this section), the rate-limiting stage of the overall process is proton transfer. Its rate constant depends on the relative orientation of donor and acceptor in the complex, the chemical nature of the reaction partners, and in particular on the type of hydrogen bond undergoing cleavage and the polarity of the medium.

If the resulting intermediate has a geometry which is favourable for proton transfer, the latter occurs freely with a rate constant exceeding the diffusion constant. Thus, in the system benzophenone–triethylamine in acetonitrile the formation of a ketyl radical occurs within 1.5×10^{-12} s after flash photolysis. Its precursor is an excited charge-transfer complex (CTC) ($\tau < 10^{-11}$ s), which comprises a superposition of radical ions[19]. Here the C–H bond of the α-carbon atom is positioned parallel to the half-filled orbital of the unshared electron pair of the nitrogen atom. In the system benzophenone–*N,N*-dimethyl(diethyl)aniline the corresponding process is slower. Formation of a ketyl radical occurs only 2×10^{-9} s after flash photolysis, and its generating contact pair is formed after $\tau = 3 \times 10^{-10}$ s.[77] The triplet exciplex of benzophenone with *N,N*-dimethylaniline is known to have two conformations of $n\pi$ and $\pi\pi$ type.[80] The second conformation corresponds to free proton transfer. In all probability the slight delay in the proton transfer time in this system is due to the need to transform the geometry of the contact ion pair. The rate constant of proton transfer in this case is equal to 2×10^{-9} s.

Proton transfer in the system anthracene–*N,N*-dimethylaniline, where a stable sandwich-type exciplex is formed, is considerably inhibited. On the basis of calculated data, the rate constant of proton transfer in this case is equal to $\sim 1-5 \times 10^6$ s^{-1}.[81]

The efficiency of proton transfer and the type of radical products formed depend to a considerable extent on the chemical nature of the proton donor. Thus, if tertiary amines are used as the donor, the proton of the α-C–H bond proves the most active. In this case an α-aminoalkyl radical is formed as a result of deprotonation. Radicals of this type have a low ionisation potential because of the formation of a three-electron bond (>N̈–Ċ<), and they are excellent reducing agents.[82] The rate constant of proton transfer by these amines depends on the size of the alkyl substituent (it increases in the series isopropyl < ethyl < methyl),[84] on the symmetry of their configuration relative to the nitrogen atom, and on the donor-acceptor properties of the substituents.

The most active proton in secondary amines is that of the N–H bond. In many cases it can participate in the formation of a hydrogen bond with the acceptor molecule, which gives additional stabilisation to the exciplex. Such a situation occurs in exciplexes of pyrene with primary and secondary amines.[84] The resulting hydrogen bond between the partners reduces the energy of cleavage of the N–H bond compared to the α-C–H bond and gives rise to a favourable geometry of the complex for proton transfer. As a result of deprotonation, radical cations of primary and secondary amines form mainly aminyl radicals.

Together with these, the formation of α-aminoalkyl radicals cannot be excluded. An increase in electron-accepting capacity of the partner[85] and an increase in polarity of the medium weakens the hydrogen bond and reduces the proton-donating activity of primary and secondary amines. It was established that as the polarity of the medium increases, the yield of aminyl radicals decreases relative to α-aminoalkyl radicals.[86]

The probability of proton transfer can vary according to the solvating properties of the solvent. With an increase in the dielectric constant of the solvent the exciplex becomes more polar and with complete electron transfer it is converted to a radical ion pair. As already mentioned, this results in a significant increase in the acidity of the proton donor and the basicity of the acceptor. It may be assumed that the type of EPT intermediate in which proton transfer occurs is determined by the thermodynamic condition $\Delta G_{PT} \leqslant 0$ for this process. The change in free energy of proton transfer ΔG_{PT} has the following form:[87]

$$\Delta G_{PT} = 2.3RT[pK_a(DH^{+\cdot}) - \pi K_a(AH^{\cdot})]. \quad (12)$$

If the acidity of the proton donor and the basicity of the acceptor are sufficient high, proton transfer is thermodynamically possible even in a collision complex which achieves a convergence of partners.[74,75] If the acidity of the donor is low, an initial complete electron transfer is necessary for proton transfer to occur. In this case the process only occurs in the radical ion pair.[77] For high values of ε, when the efficiency of the dissociation process competing with proton transfer (see Scheme 5) increases markedly, the rate of the latter decreases sharply. This is very clear in the case of the benzophenone–*N,N*-dimethylaniline system, in which the quantum yield of photodissociation of the complex increases from zero to unity with an increase in polarity of the medium while the quantum yield for formation of ketyl radicals correspondingly falls.[8] At high values of ε the molecules of the polar solvent stabilise the solvent-separated radical ions. This conteracts the convergence of the partners that is necessary for subsequent proton transfer. It follows from this that the role of a polar medium involves control of the kinetic and thermodynamic conditions for proton transfer.

III. Photoinitiation of polymerisation with organic redox systems

1. General ideas about the initiation of photopolymerisation with electron donor-acceptor systems

Thus, electron phototransfer between the components of a redox system can result in the formation of two types of active product that are energy-rich. These are radical ions or radical ion pairs which are formed as a result of complete electron transfer and free radicals that are the secondary products of proton transfer. Depending on the nature of the substrate that converts a monomer molecule to a lower-valence species, polymerisation is classified as being initiated by free radicals, ions, or radical ions (electron transfer).[147] In addition to this there is another classification, which does not take into account the nature of the initiated species. In this case the nature of the end of the growing chain (free radical or ionic) is the distinctive feature. Subsequently, in establishing the

mechanisms of polymerisation initiation and chain propagation we shall use the latter classification, which is based on the combination of features listed in Table 1, in each specific case. But at the same time we shall adhere to currently accepted principles. As a rule free radicals initiate radical polymerisation and ions initiate ionic polymerisation. Systems in which initiation is achieved using radical ions are conventionally grouped under ionic polymerisation in the majority of cases, since it is impossible to determine *a priori* which function—ionic or radical—generates the chain.[39,147]

Table 1. Distinctive features of free-radical and ionic polymerisation.

No.	Distinctive feature	Type of polymerisation		
		free-radical	ionic	
			cationic	anionic
1	Effect of polarity of the medium on polymerisation rate	Has almost no effect (with an increase it even decreases slightly)	Rate increases sharply with an increase in polarity of the medium	
2	Dependence of V on [M]	$V \approx k[M]^1$	$V \approx k[M]^n$ ($n \gtrsim 1-2$)	
3	Induction period in the presence of O_2	Occurs	None	
4	"Post-effect"	Occurs	None	
5	Value of k_p/k_t	$k_p^2/k_t \approx 10^{-2}-10^{-1}$	$k_p/k_t \geqslant 10^2$	
6	Effect of acceptors of primary active products	On introducing radical acceptors (eg., nitrobenzene, diphenylphosphate, 1,1-diphenyl-2-picrylhydrazyl, etc.) termination of polymerisation chain occurs	Polymerisation terminates in the presence of added amines or water	Polymerisation terminates in the presence of added oxygen
7	Temperature system	$T > 20$ °C	$T \ll 20$ °C	

Data on the most familiar redox systems that initiate polymerisation by light excitation at $\lambda > 300$ nm are given in Table 2. For the majority of them (systems 1–18) the primary photochemical stage is interaction of an excited molecule of photoinitiator (PI) with a molecule of monomer, resulting in the formation of primary active products of the monomer (free radicals or radical ions) which produce a polymerisation chain. In the absence of a PI, polymerisation does not occur on exposure to low-energy light quanta.

There are a number of systems (19–41) that consist of an initiator whose range of photosensitivity can vary from 300 to 700 nm and a so-called activator,[13,112] co-activator,[113] or promoter[90] between which electron transfer occurs. The activator is an electron donor or acceptor that is insensitive to light with $\lambda > 300$ nm and inert (as a polymerisation initiator) under these conditions. In contrast to this, the photoactive component of the redox system (PI) can independently initiate polymerisation which, however, takes place at a low rate. When it is used in combination with an activator it is possible to accelerate the process by a factor of 10^1-10^2 or more.

The fundamental processes for generation of radicals $R^\cdot$ that generate the polymerisation chain can be given in the form of Scheme 5;

Scheme 5

$$P \xrightarrow{h\nu} {}^{1,3}P^*, \quad {}^{1,3}P^* + A \xrightarrow{k_1} {}^{1,3}(PA)^*,$$

$${}^{1,3}(PA)^* \xrightarrow{k_2} R^\cdot, \quad {}^{1,3}(PA)^* \xrightarrow{k_3} P + A,$$

$$R^\cdot + M \xrightarrow{k_4} M^\cdot, \quad M^\cdot + M_{m-1} \xrightarrow{k_p} M_m^\cdot,$$

$$M_m^\cdot + M_n^\cdot \xrightarrow{k_o} M_{m+n},$$

where P and A are molecules of photoactive component and its partner in complexation (monomer or co-initiator) respectively.

It can readily be demonstrated that the solution of differential equations derived from a formal kinetic scheme such as Scheme 5 using the steady-state concentration method gives the following expression for the initial rate of polymerisation V:[133]

$$V = BI^{n_1}[P]^{n_2}[A]^{n_3}[M]^{n_4}, \tag{13}$$

where B is a proportionality constant that is dependent on the ratio k_p/k_o of the polymerising monomer and on the rate constants of the mono- and bi-molecular deactivation processes of the excited state of the PI; I is the intensity of incident light; [P], [A], and [M] are the concentrations of the PI, co-initiator, and monomer, n_1, n_2, n_3, and n_4 are exponents that are dependent on the polymerisation mechanism and the initiation mechanism. When the monomer is involved in the initiation process, $n_4 \geqslant 1$ and $n_3 = 0$.[93,119] Comparison of expression (13) for V obtained from treatment of the formal kinetic scheme with the experimentally observed value proves to be productive for study of the mechanism of polymerisation.

2. Photoinitiation of polymerisation with secondary products of proton transfer

In the photoinitiation systems (19–30 in Table 2) studied in this section, the thermodynamic condition for electron transfer is fulfilled. It is therefore to be expected that the probability of proton transfer between the components of these systems is high. In fact, in systems 20 and 22 the formation of an exciplex is detected while in systems 23–27 and 29 the quenching of fluorescence is established or bimolecular deactivation of the triplet state of the PI occurs, on which the mechanism of electron transfer is based. Since photopolymerisation initiated with these systems (see Table 2) corresponds to a free radical mechanism in accordance with the criteria indicated in Table 1, it may be assumed that the only possible active products are protonated and deprotonated free radicals that have left the solvent "cage". In accordance with the ideas put forward in Section II, it may be assumed that the initial formation of some form of intermediate involving electron transfer should be conducive to proton transfer.

It follows from Table 2 that amines, in particular tertiary amines †, are used as activators in the vast majority of cases in these redox systems. It was mentioned earlier (see Section II.5) that they

† We will not stop to analyse dye–activator photoinitiation systems in this review. These systems have been described in detail.[13] We shall merely point out that in addition to amines other classes of compounds, including sulphonates, carboxylates, organometallic compounds, etc., are used as activators in these systems.

Table 2. Systems that photoinitiate polymerisation.

No.	Initiating system	Monomer	Acceleration effect	Solvent	Evidence for ET or exciplex	Expression for initial rate of polymerisation	Polymerisation mechanism	Evidence for initiation mechanism	Refs.
1	2	3	4	5	6	7	8	9	10
1	^{3}Anthracene* + ^{3}Pyrene* + ^{3}Chyrsene	Styrene	×5	Benzene (no O_2)	Rate constant of deactivation of triplet states k_q^T varies in same way as the electron-donating properties of quenchers	$V \approx I^{0.5}[P]^1$	Free-radical		[11, 92]
2	^{1}Naphthalene* and its derivatives			Dimethyl formamide (no O_2)	k_q of fluorescence varies in the same way as the electron-donor properties of the photoinitiator, % conversion of monomer to polymer varies in the same way	$V \approx I^{0.57}[P]^{0.2-0.4} \times [M]^{1.1-1.5}$	"	Inhibition with oxygen	[93, 94]
	^{1}Anthracene* + monomer ^{1}Pyrene* ^{1}Fluorenone* ^{1}Diphenyl*	Acrylonitrile	×2–6						
3	^{3}Phenazine* ^{3}Acridine* + ^{3}Anthracene* monomer	Butylmethacrylate	×4–6	Toluene tetrahydrofuran (no O_2)	k_q^T of quenching varies in proportion to EA of photoinitiators ($k_q \approx 10^5-10^7$ litre mol^{-1} s^{-1})	$V = I^{0.5}[P]^{0.4-0.6}[M]^{1.0}$	"	"	[95, 138]
4	^{1,3}*N*-Vinylcarbazole* + triethylamine	*N*-Vinylcarbazole		Benzene (no O_2), acetone (in the presence of O_2)	k_q of fluorescence of *N*-vinylcarbazole with amines varies in the same way as their electron-donating capacity		Free-radical (α-aminoalkyl radical causes polymerisation)	1. Inhibition of polymerisation with O_2 2. Proton transfer from TEA to monomer takes place	[91, 96]
5	^{1}*N*-Vinylcarbazole* + CBr_4	"		Dichloroethane, nitrobenzene, benzene	Quenching of fluorescence of *N*-vinylcarbazole CCl_4 and CBr_4. Fluorescence band of exciplex appears		Free-radical and cationic	Bromine free radical and active cationic sites with C–Br bond occur	[97, 98, 140, 141]
6	^{3}*N*-Vinylcarbazole* + azobutyronitrile	"	more than 10 times	Dichloromethane, benzene	Excited triplet complex of *N*-vinylcarbazole with the solvent rate constant of quenching diffusion controlled	$V_p = \frac{k_p}{k_t^{0.5}} I^{0.5}[A]^{0.5}[M]^{1.5}$ $V_{cat} = \frac{k_p}{k_t} I[A]^{1.0}[M]^{1.0}$	Free-radical and cationic mechanism (at high concentrations of monomer)	Cationic polymerisation is terminated in the presence of dimethylformamide—a trap of cationic sites. Distribution of polymerisation products varies according to the polarity of the solvent	[27]
7	^{1}*N*-Vinylcarbazole* + fumaronitrile	"		Dichloromethane, benzene	Band of exciplex in fluorescence spectrum; rate constant of fluorescence quenching of the same order as the diffusion constant		Cationic and free-radical		[99, 123]
8	^{1}*N*-Vinylcarbazole* + diethyl fomarate	"		Acetone, acetonitrile, dimethyformamide	Fluorescence quenching, band of exciplex in fluorescence spectrum		Free-radical and cationic	Ratio of polymerisation products varies in solvents of different basicity	[100]
9	*N*-Vinylcarbazole* + benzoyl peroxide	*N*-vinylcarbazole		Benzene, dichloromethane	Cation radicals of *N*-vinylcarbazole detected using pulsed methods in dichloromethane but not in benzene		Free-radical and cationic	Agreement between effect of basicity on formation of radical cations and ocurrence of corresponding polymerisation products	[101]
10	*N*-Vinylcarbazole* + chloranil	"					Free-radical	Inhibition with oxygen	[102]
11	^{1}Thiobenzophenone* + *N*-vinylcarbazole	"		Benzene, toluene, acetonitrile (in a current of argon)	Forms singlet exciplex		Cationic	Polymerisation occurs in the presence of thiobenzophenone, which is a free radical trap	[90, 103]
12	^{3}α-Methylstyrene* + tetracyanobenzene	α-Methylstyrene		Dichloroethane (no O_2)	Singlet and triplet exciplex formed. Photoconductivity recorded		"	Water and amines inhibit polymerisation	[18, 104, 105]
13	^{3}α-Methylsytrene* + pyromellitic dianhydride	"		"	Exciplex formed		"	"	[106]
14	Styrene* + maleic anhydride	Styrene		Acetonitrile	Radical cation of styrene observed in absorption spectra (pulsed excitation)		"	Addition of tertiary amines terminates polymerisation	[107]
15	Styrene* + acrylonitrile	Styrene and acrylonitrile (copolymer)		Dichloromethane			"	Addition of water and amines inhibits polymerisation	

Table 2 (continued).

No.	Initiating system	Monomer	Acceleration effect	Solvent	Evidence for ET or exciplex	Expression for initial rate of polymerisation	Polymerisation mechanism	Evidence for initiation mechanism	Refs.
1	2	3	4	5	6	7	8	9	10
16	Nitroethylene* + cyclohexene oxide	Nitroethylene	more than 10 times	Tetrahydrofuran	Band of weak charge-transfer complex in absorption spectrum		Cationic and anionic simultaneously	Traces of HCl inhibit polymerisation by 20%. Polynitroethylene (0.73) and polycyclohexene (0.27) identified by fractional analysis	[109]
17	Maleic anhydride* + tetrahydrofuran	methyl methacrylate	×2–4	Tetrahydrofuran	Photocurrent recorded		Anionic and free-radical	Polymerisation occurs in the presence of free-radical traps—1,1-diphenyl-2-picrylhydrazyl. It slightly lowers the rate of polymerisation	[110]
18	^{1}Benzyl-1,4-dihydronicotinamide* + monomer	Styrene, methyl methacrylate	×10	Dichloromethane, acetonitrile, methanol	Fluoroescence quenching of photoinitiator varies in the same way as the donor-acceptor properties of partners	$V \approx [P]^{0.5}$	Free-radical	Polarity of medium has virtually no effect on rate of polymerisation. Linear dependence of reverse polymerisation stage on inhibitor concentration	[111]
19	^{3}Benzophenone* + triethylenetetramine	Methyl methacrylate		Benzene, toluene, acetone, methanol (in a current of nitrogen)		$V \approx [P]^{0.5}[A]^{0.5}$	"	With an increase in ε of the medium the rate of polymerisation decreases, $k_p^2/k_t = 1.06 \times 10^{-2}$ litre mol^{-1} s^{-1}	[22]
20	^{3}Benzophenone* + tertiary amines	Methyl methacrylate		t-Butyl alcohol (no O_2)	Deactivation of triplet state of benzophenone with amine, formation of a radical ion pair	$V = k[M]^{1-1.5}[A]^{0.5}$	Free-radical	Higher rate of proton transfer $k_{PT} \geqslant 10^9$ s^{-1}	[24, 75, 114]
21	^{3}Benzophenone* + triethylamine (tributylamine, di-n-butylamine, n-butylamine)	Acrylonitrile	×11	Benzene dimethylformamide (in a current of nitrogen)	Deactivation of triplet states of benzophenone by amines with $k_q^T = 2.3 \times 10^9$ litre mol^{-1} s^{-1}	$V \approx [P]^{0.3-0.4}[M]^{1.3}$		Rate of polymerisation remains almost the same on going from benzene to dimethylformamide	[115]
22	^{3}Benzophenone* + aliphatic amines (primary, secondary, tertiary)	Methyl methacrylate	×10	Benzene, carbon tetrachloride, dimethylformamide	Triplet exciplex formed	$V \approx [P]^{0.38}[A]^{0.5}[M]^{1.5}$	Free-radical	Induction period occurs in the presence of O_2. Hydroquinone inhibits polymerisation. $k_p^2/k_t = 1.54 \times 10^{-3}$ litre mol^{-1} s^{-1}	[116, 117]
23	^{3}Fluorenone* + triethylamine (*N,N*-dimethylethanolamine)	"	×7–10	Benzene	Quenching of singlet and triplet states of fluoroenone by amines with $k_q^T \geqslant 10^{10}$ litre mol^{-1} s^{-1}		"	With an increase in ε of the medium the rate of polymerisation decreases. $k_p^2/k_t = 1-4 \times 10^{-3}$ litre mol^{-1} s^{-1}	[20]
24	^{1}Anthracene* (Phenanthrene, naphthalene, acetonaphthone)* + (di- and tri-ethylamine, aniline, *N*-methyl- and *N,N*-dimethylaniline	Methyl methacrylate, acrylonitrile	×15 to 16	Dimethylformamide (in a current of nitrogen)	Fluorescence quenching of photoactive components by amines with $k_q > 10^9$ litre mol^{-1} s^{-1}	$V \approx [P]^{0.5}[A]^{0.5}[M]^{1.0}$	Free-radical or ionic		[15]
25	Fluorenone* (acetophenone, Michler Ketone) + aliphatic amines	Acrylonitrile	×5–10	Dimethylformamide, benzene (in a current of nitrogen)	Quenching of triplet states of photoactive components by amines with $k_q \geqslant 10^9$ litre mol^{-1} s^{-1}	$V \approx [P]^{0.35}[M]^{2.20}$	"	Polymerisation does not occur in a nonpolar solvent	
26	^{3}Thioxanthone* + aliphatic amines	Methyl methacrylate		Benzene, acetonitrile	Quenching of triplet state of photoactive component by amines with $k_q^T \geqslant 10^9$ litre mol^{-1} s^{-1}. Polarity of medium did not affect k_q^T		Free-radical	Formation of free radicals—partners of initiating mixture—detected. Lack of dependence on polarity	[118]
27	^{3}Benzophenone salts* + triethylamine (triethanolamine, methylethanolamine)	Acrylamide	×3–15	Water (in a current of nitrogen)	Quenching of triplet states of photoinitiator by amines with $k_q^T \geqslant 10^9$ litre mol^{-1} s^{-1}	$V \approx I^{0.5}[P]^{0.5}[A]^{0.5}[M]^{1.5}$	Free-radical, but anionic not excluded	Ketyl radical of benzophenone occurs	[119]
28	Iron tetraphenyl porphin* + aliphatic amines + carbon tetrachloride	Methyl methacrylate	×5–10	Methanol (no O_2)			Free-radical		[120]

Table 2 (continued).

No.	Initiating system	Monomer	Acceleration effect	Solvent	Evidence for ET or exciplex	Expression for initial rate of polymerisation	Polymerisation mechanism	Evidence for initiation mechanism	Refs.
1	2	3	4	5	6	7	8	9	10
29	Dyes* (thiazine, xanthine, acridinone) + activator (amines, enolates, organometallic compounds, thiols)	Acrylamide, vinyl alcohol, cellulose acetate, vinyl chloride	more than 10 timees	(no O_2)	Quenching of triplet states of photoactive component by activator with $k_q \geqslant 10^9$ litre mol^{-1} s^{-1}. Correlation between k_q and value of Δq_{ET}		"		[13]
30	^{3}Fluorenone* (benzanthrone, acridine, 9-phenylacridine)* + hetero aromatic thiols	Methyl methacrylate derivatives	more than 10 times	In thin layers	Quenching of triplet states of photoinitiators with activators by electron and energy transfer mechanism		Free-radical		[121]
31	^{3}Phenazine and its derivatives* + benzophenone and its derivatives	Butyl methacrylate	more than 200 times	Toluene, acetonitrile (no O_2)	Quenching of triplet stages of phenazine with benzophenone derivatives. Correlation between k_q^T and Hammett σ-constants of substituents in benzophenone molecule. Photocondutivity in acetonitrile	$V_{exp} = I^{0.5}[P]^{0.3-0.5} \times [A]^{1.0}[M]^{1.8}$ $V_{calc} = k[P]^{1.0}[A]^{1.0} \times [M]^{>1.5}$	Ionic (involving radical ion pairs)	Rate of polymerisation increases sharply with ε of medium. In a nonpolar solvent polymerisation does not occur, $k_p/k_t \approx 3-3.8 \times 10^2$ litre mol^{-1} s^{-1}. Solvent-separated radical ions detected in acetonitrile	[26, 122]
32	^{1}Acridine* (^{1}phenazine, 1anthracene)* + *N,N*-dimethylaniline	"	× 15 to 30	Toluene, acetonitrile (no O_2)	Formation of singlet fluorescing exciplexes between partners. Photodissociation in acetonitrile (photoconductivity occurs)	$V = I^{0.5}[P]^{0.5}[A]^{0.5}[M]^{2.0}$	Ionic (involving radical ion pairs and ionic triads)	Rate of polymerisation increases sharply with ε of medium. Free radicals are absent. Solvent-separated radical ions and ternary complexes detected in acetonitrile	[123]
33	^{1}Perylene* + dicyanobenzene	*N*-Vinyl carbazole	× 6	Acetone, dimethyl sulphoxide (in the presence of O_2)	Fluorescence quenching of perylene by dicyanobenzene with $k_q > 10^9$ litre mol^{-1} s^{-1}. It increases as ε increases			Sharp increse in rate of polymerisation with ε of medium	[23]
34	^{3}Benzophenone (benzaldehyde)* with acceptor substituents + 4,4-bis-*N,N*-diethylaminobenzophenone	Methyl methacrylate		In a current of nitrogen	Quenching of triplet-excited states of photoinitiator with activator		Free-radical	Induction period in the presence of O_2	[124]
35	^{3}Benzophenone* + benzaldehyde + triethylamine	"	more than 10 times				"		[125]
36	^{3}Benzophenone* + tri-, di-, and monoethylenediamine + maleic acid		× 10		Quenching of triplet states of benzophenone with amines			Induction period occurs	[126]
37	^{3}Benzophenone* + diethanolamine + O_2	Hexane diol acrylate					"	"	[159,127]
38	^{3}Benzophenone* + 2-ethylhexyl *p*-(*N,N*-dimethylamino)benzoate + O_2	Epoxy acrylate	× 10 to 20	Films (in the presence of O_2)	Quenching of triplet states of benzophenone with amines		"		[128]
39	^{3}Benzophenone* + *N,N*-dialkylaminoethyl methacrylate	*N,N*-dialkylaminoethyl acrylate		Benzene (in the absence of O_2, in its presence, and in a current of argon)	Formation of excited charge-transfer complex		"	Induction period occurs. Free radicals detected	[129]
40	Benzoin isobutyl ether* + tetramethyl-*p*-phenylenediamine + O_2								[130]
41	^{3}(Xanthene, triazene, anthracene, phenanthrene)* + onium compounds	Cyclic ethers, epoxy compounds		In the presence of O_2, acetonitrile, water			Cationic mechanhism	No induction period	[162,163, 131,132]

act as donors of a hydrogen atom detached from a CH group at the α-position relative to the nitrogen atom. The α-aminoalkyl radical formed as a result of deprotonation is responsible for generating the polymerisation chain. The presence of nitrogen atoms in the polymer provides proof of this.[134]

It should be noted that there is a dependence of the rate of polymerisation on the size of the alkyl substituents in the aminoalkyl group that is similar to the dependence of the rate constant of proton transfer on the same parameters, as discussed in Section II.[83] Thus the rate of polymerisation V for system 25 is higher when triethanolamine is used as the activator than when tributylamine is used, while for system 24 it is higher when dimethylaniline is used compared to the use of diethylaniline and it varies in the same way as the rate constant of proton transfer.[15] The experiments conducted in parallel with two activators—triphenyl- and triethylamine in combination with benzophenone—showed that only in the second case, in which proton transfer occurs, does the polymerisation of methyl methacrylate occur (systems 20–22).[114] Meanwhile, electron transfer in both systems occurs at a rate that is higher than the diffusion rate. All of these facts suggest that proton transfer between the components of the initiating mixture plays a role in the generation of active radicals.

The same reaction of proton transfer with the formation of semi-reduced radical products forms the basis of the interaction of the photoactive components of a number of aromatic, heteroaromatic, and carbonyl compounds with proton-donating solvents.[135,136] However, the rate of polymerisation in this case is low, in contrast to systems in which the same photoinitiators are used in combination with amines.[15,135,137] As in fact the polymerisation mechanism (free-radical) does not change, why is there a preference for the latter?

In actual fact the rate of initiation of polymerisation with primary active products depends on the efficiency factor of the initiator β and the concentration of the primary radicals [R$^{\cdot}$]:[24,90]

$$V_i = \beta[R^{\cdot}]. \qquad (14)$$

The efficiency factor of the initiator β is governed by the proportion of radicals formed that participate in initiation of polymerisation. It is usually considerably less than unity, as a result of radicals participating in side reactions, and it is determined by the nature of both the initiator and the monomer. The concentration of primary radicals, [R$^{\cdot}$] depends on the rate constant for their formation, in these particular cases—on the rate constant of proton transfer k_{PT}. In the presence of photoinitiation mixtures in which proton transfer occurs rapidly, such as in benzophenone–triethylamine systems (18–19), $k_{PT} = 10^{12}$ s^{-1};[77] even with a comparatively low value of β for the α-aminoalkyl radical equal to $1-5 \times 10^{-3}$,[24] the polymerisation of methyl methacrylate is very active. On the other hand, when polymerisation is initiated by a deprotonated tetrahydrofuran radical, which has a value of $\beta = 5 \times 10^{-2}$,[24] because of the low value of $k_{PT} = 4.2 \times 10^6$ mol^{-1} s^{-1} its rate is considerably lower.[115] The very slow polymerisation initiated by the system aromatic hydrocarbon–propanol is apparently related to this.[15] It is known that in this system $k_{PT} = 6 \times 10^5$ mol^{-1} s^{-1}.[178] As has already been mentioned in Section II, an unfavourable geometry for proton transfer of the components in exciplexes of aromatic or heteroaromatic compounds with *N,N*-dimethylaniline (DMA) is responsible for the low value of k_{PT} in benzene. As a result, a low rate of polymerisation of butyl methacrylate is recorded in it (system 32), although in this system in a non-polar solvent the α-aminoalkyl radical of DMA should be present with almost the same efficiency as the α-aminoalkyl radical of triethylamine.[15]

Aminyl radicals which are formed as a result of deprotonation of primary and secondary amines are less effective than the α-aminoalkyl radical because of their increased tendency to undergo a disproportionation reaction.[103]

The least effective were protonated radicals of the photoactive components of the initiation system (ketyl radicals of benzophenone, semi-reduced radicals of phenazine, acridine, anthracene, etc.). Generation of a polymerisation chain in their presence occurs either at a very low rate or not at all (systems 20 and 32). On the contrary, in a number of cases they have an inhibitory effect by participating in chain termination reactions.[140] This accounts for the appearance of a descending curve on graphs of the rate of polymerisation against the concentration of photoinitiator.[15,94,115] Moreover, the semi-reduced radicals are consumed to form final products of the destructive bleaching of the photoabsorbent compound accompanying polymerisation.

The adoption of a free-radical photopolymerisation mechanism for the systems examined above is consistent with the ideas about the effect of the polarity of the medium on these processes (Table 2). In fact, in systems 19, 21, 23, 29, and 36 polymerisation occurs more rapidly in benzene than in any polar solvent. Careful analysis of the active products initiating polymerisation, their precursors—exciplexes or other intermediates of electron transfer—and the kinetics of electron and proton transfer also support the idea of a free-radical mechanism of polymerisation in these systems.

Unfortunately, a detailed study of the mechanism of polymerisation with identification of the intermediate stages of initiation has only been carried out for a narrow range of reactions (systems 19, 20, 23, 26). For the remaining systems given in Table 2, a free-radical mechanism of polymerisation has only been established from its similarity with the above systems. Meanwhile, such similarities are not always consistent. Thus, although for a number of systems such as 24, 25 and 27 a free-radical mechanism is maintained by the authors, the experimental evidence for such conclusions is insufficient. The study of polymerisation was conducted with the use of a polar solvent—dimethylformamide, acetonitrile, or water. The nature of the radicals generating the polymerisation chain was not verified. The authors did not take into account the fact that the photoactive components of the initiating systems studied by them—aromatic compounds (24) or carbonyl compounds (25, 27) with a $^3\pi^*$ lowest excited state—on reacting with amines have a greater tendency to undergo complete electron transfer reactions than to undergo secondary proton transfer reactions, especially in polar media[77,80] (see Section II). It cannot be excluded that it is this fact which accounts for the acceleration by a factor of 3–5 of the polymerisation of acrylonitrile in systems 24 and 25 on going from benzene to acrylonitrile. In adhering to their view of a free-radical mechanism, Kubota and Ogiwara[15] cannot account for the effect of the polarity of the medium on the rate of polymerisation.

There is no doubt that many factors such as the nature of the photoinitiator (the type of electronic transition responsible for excitation, its multiplicity), the activator, and monomer can affect the mechanism of initiation of polymerisation. It is therefore interesting to consider the behaviour of two photoinitiators from the class of aromatic ketones—benzophenone and fluorenone. They differ according to the electronic nature of the lowest excited states. In benzophenone the $^1S^*$ and $^1T^*$ states have an $n\pi^*$ electronic configuration.[141] The majority of reactions, including electron and proton transfer, occur in the $^1T^*$ state. The polarity of the medium does not affect the quantum yields of formation of triplet states,

formation of ketyl radicals, or the quantum yield of the overall reduction process.[141,142] In contrast to benzophenone, the $^1S^*$ and $^1T^*$ states of fluorenone have a $\pi\pi^*$ electronic configuration.[143] However, in view of the proximity of the $^2S^*_{\pi\pi^*}$ and $^1S^*_{\pi\pi^*}$ state and also the $^2T^*_{\pi\pi^*}$ and $^1T^*_{\pi\pi^*}$ states, the contribution of the $n\pi^*$ electronic configuration to the lowest $^1S^*$ and $^1T^*$ states is quite evident. Therefore the polarity of the medium has a substantial effect on the kinetics of the photophysical processes. With an increase in ε the quantum yield and duration of fluorescence increase by a factor of almost 10^2 and the quantum yield of intersystem crossing is halved.[144] The quantum yields of formation of ketyl radicals and the overall reduction reaction decrease by the same order of magnitude.[145]

The lowest triplet state of benzophenone participates in electron and proton transfer from amines. The latter reaction, as has aleady been mentioned, occurs with a high rate constant ($k_{PT} \approx 10^9$ s^{-1}).[19,77] The resulting free radicals generate the polymerisation chain. The polarity of the medium has virtually no effect on the rate of polymerisation[15,22,24] (systems 19–21, 26 in Table 2).

Fluorenone behaves in a similar manner in the initiation of the polymerisation of MMA (system 23).[113] The maximum rate V of photopolymerisation has been recorded in benzene. In acetonitrile V decreases by a factor of almost 5,[114] which is an argument in favour of a free-radical mechanism of polymerisation. However, an alternative explanation for this phenomenon is also possible. With an increase in ε the quantum yield of intersystem crossing decreases and the quantum yield of formation of ketyl radicals of fluorenone and deprotonated amine radicals correspondingly decreases.[144]

Fluorenone behaves quite differently in the polymerisation of acrylonitrile (system 25). The rate of polymerisation of this monomer, initiated with system 25, increases by a factor of 4 on going from benzene to acetonitrile, although the yield of radical products in this case is halved,[144] as in the example considered above. It is known, however, that with an increase in ε the lifetime of the $^1S^*$ state increases. It is sufficiently long for fluorenone in the $^1S^*$ state to interact with amines by a charge-transfer mechanism.[146] The rate constants of quenching of the $^1S^*$ state of fluorenone with triethylamine in benzene and acetonitrile are equal to 1×10^9 and 7×10^9 litre mol^{-1} s^{-1} respectively, whereas the rate constants of deactivation of the $^1T^*$ state with the same amine is two orders lower ($1.7-2.3 \times 10^7$) litre mol^{-1} s^{-1}.[145] Apparently at concentrations of amine greater than 10^{-2} mol $litre^{-1}$, which is commonly used in polymerisation, the excited fluorenone molecules mainly in the $^1S^*$ state interact with amines. Since with an increase in ε the probability of proton transfer decreases sharply in the system fluorenone–amine because of electron transfer competing with it,[145] the quantum yield of formation of free radicals must decrease. It can be expected that in system 25, where $\varepsilon \approx 20$, the photoinitiating mixture will exist as radical ion pairs as a result of light absorption. It is possible that acrylonitrile, being a stronger electron acceptor than MMA, can interact with such an ion pair to form a "loose" ternary complex. This will generate the polymerisation chain. Such a possibility has also not been excluded for MMA.[10] Similar views about the initiation of polymerisation of acrylontrile by means of radical ions have also been expressed.[113]

3. Photoinitiation of polymerisation with the final products of electron phototransfer

In this section we shall examine the polymerisation processes that are initiated by the products of complete electron transfer in redox systems of radical ions. This applies to polymerisation initiated by EPT.[147,148] It has a specific nature which at the present time is still far from understood.

The possibility of initiation of polymerisation by radical ion species is influenced by a considerable effect from the polarity of the medium, its acidity or basicity. Thus, polymerisation initiated with radical anions occurs preferentially in more basic solvents while that initiated with radical cations is preferred in more acidic solvents.[91,149]

No less important a factor is the stability of solvent-separated radical ions. Depending on this, either the rapid combination of radical ions or the formation of a neutral radical producing a polymerisation chain by a free-radical mechanism is possible.

a) Photoinitiation systems of monomer–activator

Table 2 lists a number of binary systems (1–18), one component of which is the monomer. In the majority of cases the latter functions as the photoactive partner of the mixture. *N*-Vinylcarbazole (VC) and α-methylstyrene, which participate in cationic polymerisation, are good electron donors. Their ionisation potentials are equal to 7.42 and 8.35 eV respectively.[114] Systems with styrene,[110] *p*-methoxystyrene,[152] and phenyl vinyl ether[153] which as a result of electron phototransfer form radical cations that cause cyclodimerisation have not been included in Table 2. The latter may be regarded as a chain reaction that differs from polymerisation in the length of the chain.

Cyclohexene oxide is a weaker electron donor. As a result of interacting with strong electron acceptors it forms a radical cation and causes polymerisation by a cationic mechanism. Interestingly, in the presence of nitroethylene (system 16) polymerisation occurs simultaneously by cationic and anionic mechanisms.[109] Weak electron acceptors such as maleic anhydride and methyl methacrylate in the ternary system tetrahydrofuran–maleic anhydride–monomer (system 17) cause polymerisation by an anionic mechanism.

Indirect evidence for the ionic polymerisation route and the presence in these systems of the respective radicals ions is given in Table 2. Direct evidence has only been obtained for two monomers—α-methylstyrene (systems 7 and 8) and VC (systems 5–7, 12, 13). Singlet and triplet exciplexes of α-methylstyrene with tetracyanobenzene and pyromellitic dianhydride have been detected using pulsed spectroscopic methods.[104, 105] In methylene dichloride and n-amyl alcohol these exciplexes dissociate to radical ions that have been recorded using pulsed photoconductivity. However, the rate of recombination of the radical ions which are formed from singlet-excited molecules is so high that they can only be reliably observed at low temperatures (below −40 °C).[121] The lifetime of ion radicals formed in a triplet route is considerably longer (of the order of tens of microseconds). This time is sufficient for the resulting cation radicals to undergo a chain propagation reaction. The sequence of reactions of a monomeric radical cation of α-methylstyrene to dimeric and trimeric forms, etc. has been observed from the respective absorption spectra. Introduction of air caused an almost complete cessation of the photocurrent and termination of polymerisation. Since the generation of cation radicals of α-methylstyrene capable of initiating a polymerisation chain has been carried out using a triplet route, these systems are unfortunately also sensitive to oxygen, like the photoinitiating components for free-radical polymerisation.

VC behaves differently. On excitation with light at $\lambda \geqslant 350$ nm it forms fluorescing exciplexes with dimethyl terephthalate, diethyl fumarate (system 8),[9] and with thiobenzophenone (system 11) (in the latter case, however, the thiobenzophenone molecule is excited).[90,103]

The rate constant of formation of exciplexes is of the same order as the diffusion constant. Radical cations of VC that are formed by photodissociation of singlet exciplexes have been recorded by pulsed methods.[154] They are involved in the generation of a polymerisation chain in systems 6–11. Arguments in favour of a cationic mechanism of polymerisation are provided by the results when it is carried out in nitrobenzene, which serves as a free radical "trap" (see Table 1) and by its inertness towards oxygen. Furthermore, it was established that in a number of cases oxygen assists the cationic polymerisation of VC. It can act as a co-initiator, interacting with VC to form a stable radical anion, being a counterion for the radical cation of monomer. Moreover, it promotes chain transfer during cationic polymerisation.[91,155]

The ability of VC in the presence of electron acceptors to initiate polymerisation by a cationic mechanism was discovered in the 1970s.[99,102] Before then it was assumed that it could only cause polymerisation by a free-radical mechanism. However, polymerisation, as a rule, was carried out in solvents with a high basicity (acetone, tetrahydrofuran, dimethylformamide). The generation of free radicals in this case was achieved from a triplet-excited state of VC. By changing to solvents with a higher acidity it was possible to alter the mechanism of polymerisation when mixtures of VC and acceptor-type activators were used. It appeared that the charge-transfer complexes and exciplexes formed by these mixtures could generate charged primary active products. At the same time the efficiency of initiation of cationic polymerisation with exciplexes is higher than with charge-transfer complexes.[104] The reason for this is not clear. One of the explanations put forward by the authors is the more favourable geometry for electron transfer in an exciplex than in a charge-transfer complex.

b) Initiation systems of photoinitiator – activator

The advantage of these over the systems examined above is obvious. Firstly, with a wide series of photoinititors and activators being available, it is possible to select those systems which achieve a high probability of free electron transfer and the formation of active products. Secondly, by using suitable photosensitive compounds it is possible to extend the spectroscopic sensitivity and increase the total sensitivity of the polymerising system. Unfortunately, the mechanism of the action of most photoinitiating systems of initiator–activator is so far unclear. However, as was mentioned above, it is highly probable that these systems (24 and 25) can generate radical ions that are capable of initiating and producing a polymerisation chain.

More definite information indicating a change in mechanism of initiation from free-radical to radical-ion has been obtained for the binary systems 31 and 32. The photoactive components in these are heteroaromatic (phenazine, acridine, and their derivatives) or aromatic (anthracene and its derivatives) compounds. Depending on their partner they act as an electron donor (system 31) or electron acceptor (system 32). Redox systems that include them initiate the polymerisation of butyl methacrylate. The latter can participate in chain propagation by both a free-radical and an anionic mechanism.[90] However, in benzene photopolymerisation occurs at an extremely slow rate. When acetonitrile is added the rate of polymerisation increases by a factor of 10^1-10^3. The dependence of $\lg V$ on the Kirkwood polarity function is linear and has a positive gradient.[122,123] With an increase in ε, semi-reduced radicals of heteroaromatic or aromatic compounds were not detected in any of these systems, nor were ketyl radicals of benzophenone, which would suggest proton transfer. On the other hand in acetonitrile a photocurrent developed, that was induced by excitation of photoactive mixtures with a pulsed laser. It originates from the solvent-separated radical ions formed as a result of complete electron transfer between the partners of the mixture.

Interestingly, in system 31 the signal due to the photocurrent disappeared after the introduction of atmospheric oxygen while in system 32 it persisted under these conditions.

There are other arguments that suggest the electron donor-acceptor nature of the interactions in these mixtures. Thus for system 31 there was a correlation between the rate constant for deactivation of triplet-excited molecules of phenazine derivatives and the Hammett σ-constants of substituents in the benzophenone molecule acting as an electron acceptor. The reaction constant $\rho = 1.1$ (Fig. 1*a*). It is significant that a value of $\rho = 1.0$ (Fig. 1*b*), which is similar to it, was obtained for the correlation between the rate of polymerisation V and the same parameters.[122] This is one of the most serious arguments in favour of the electron donor-acceptor interactions of triplet-excited phenazine molecules with electron acceptors playing a decisive role in the overall photopolymerisation process.

It was established for system 32 that the partners of photoinitiating mixtures form singlet fluorescing exciplexes with a considerable degree of charge transfer.[156,157] It is these which take part in the subsequent chemical reactions that are responsible for the generation of primary active products. As well as binary exciplexes, ternary singlet photoinitiator–activator–monomer exciplexes were detected, having a characteristic fluorescence band that is shifted towards the "red" end of the spectrum relative to the fluorescence of the binary exciplex (Fig. 2). Since charge-transfer interactions also make a considerable contribution to the stabilisation energy of a ternary exciplex, it may be assumed that with an increase in polarity of the medium it will be converted to a "loose" ionic triad occurring in a solvent cage.[160]

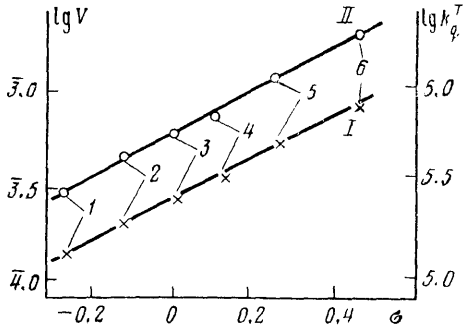


Figure 1. Dependence of the rate constant of deactivation of triplet states of 2-dimethylaminophenazine (line *I*) and the rate of polymerisation initiated with 2-dimethylaminophenazine in the presence of benzophenone (line *II*) on Hammett σ-constants of substituents in the acceptor molecule: *1*) 4-OCH_3; *2*) 4-CH_3; *3*) 4-H; *4*) 4-C_6H_5; *5*) 4-Cl; *6*) 4,4′-$(Cl)_2$.

From what has been stated it may be concluded that in systems 31 and 32 the primary active products in polar media are radical ion pairs, solvent-separated radical ions, and also "loose" ionic triads rather than neutral radicals which are mainly formed in a non-polar medium. They initiate polymerisation, which was taken into account in a kinetic scheme of initiation with systems 31 and 32. A whole

series of relationships confirming the experimental results follows from the expression for V obtained on the basis of this scheme. These are primarily the agreement between the values of the exponents in the equation for V (see Table 2) and the series of rate constants of the fundamental stages that are determined from this expression and by using independent experimental methods.[122] Consideration should be given to the value of the ratio k_p/k_t determined from this expression. It is equal $(3.1-3.8) \times 10^2$, which corresponds to values that are typical for the anionic polymerisation of vinyl monomers, in which generation of the chain involves radical ion pairs (see Table 1).[162] An argument in favour of the involvement of radical ion pairs rather than solvent-separated radical ions in initiation is the low reaction constant $\rho = 0.18$ for the correlation dependence of $\lg(k_p/k_t)$ on the Hammett σ-constants of substituents in the benzophenone molecule (system 31). In fact, by conducting the polymerisation in acetonitrile it is not possible to achieve a value of $\varepsilon > 20$. With such a value of ε it is doubtful whether the ionic "triads" can be converted to solvent-separated radical ions (we should note that the values of k_q are equal to 10^7-10^8 litre mol^{-1} s^{-1} for the quenching of fluorescence from the binary exciplexes with a monomer in this case).

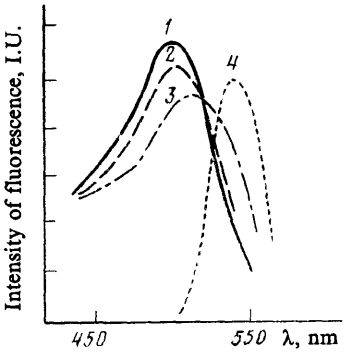


Figure 2. Effect of addition of butyl methacrylate (BMA) on the fluorescence intensity of the exciplex of anthracene with *N,N*-dimethylaniline. *1*) $C_{BMA} = 0$; *2*) $C_{BMA} = 1$ mol litre^{-1}; *3*) $C_{BMA} = 2.5$ mol litre^{-1}; *4*) differential fluorescence spectrum of ternary complex on a scale of 1 : 4.

From the expression obtained for V (Table 2) it is possible to account for the effect of the electronic structure of the photoactive components of system 32 on the rate of polymerisation. It results from the different thermodynamic and kinetic conditions of electron transfer between the components of the photoactive mixtures of system 32.[123]

The latter system is also of intereest in that for the first time the formation of a ternary excited complex involving a monomer has been detected in it. The possibility that it is formed followed logically from the results of more recent studies, including also those for system 31.[10,26,113] The advantage of agglomerates of this type is that polymerisation initiated and carried out with their participation is less sensitive to the effect of inhibitors.[89,147] Moreover, systems 31 and 32 demonstrate the real possibility of a change in the multiplicity of the excited state of the photoactive component participating in photoinitiation through a suitable choice of partners. This in turn suggests the possible ways of conducting polymerisation in the presence of oxygen during photogeneration of the primary active products in a singlet route and generation of the polymerisation chain by a cationic mechanism.

These conditions are met when photoinitiation system 33 is used, which is involved in polymerisation that occurs in the presence of oxygen. Perylene, which absorbs light with $\lambda \geqslant 436$ nm, serves as the photoactive component in it, dicyanobenzene is the activator, and VC is the monomer. As a result of light absorption the singlet-excited molecules of perylene donate an electron to dicyanobenzene. The rate constant of fluorescence quenching of perylene, which results from this process, is of the same order as the diffusion constant.[23] The resulting radical cation of perylene initiates polymerisation of vinylcarbazole through electron transfer from the latter. Photopolymerisation in acetonitrile in this case takes place under mild conditions—at room temperature in air. In strongly polar solvents with well-defined basic properties (dimethylformamide, dimethyl sulphoxide) it does not take place. A sixfold increase in the rate of photopoymerisation initiated with the binary mixture perylene–dicyanobenzene relative to initiation with perylene is recorded. It is likely that in the system perylene–activator–monomer an effective separation of charges is achieved, producing a marked acceleration of polymerisation.

IV. Conclusion

Thus photoinitiation systems whose action is based on electron phototransfer that occurs in an exciplex or another of its intermediates are highly effective. Neutral protonated and deprotonated radicals, radical ion pairs or solvent-separated radical ions can initiate polymerisation. In the first case the polymerisation chain is generated by a free radical mechanism while in the second case an ionic mechanism occurs. With all of the systems it is possible to carry out polymerisation by exposure to low-energy light quanta.

Radical polymerisation. The advantage of these initiating systems lies in the fact that by forming exciplexes or other electon transfer intermediates they create favourable conditions for the subsequent transfer of a proton between the partners. With a suitable choice of the components of photonitiating mixtures, based on an analysis of their thermodynamic and kinetic properties, it is possible to optimise their composition. Thus, for example, if tertiary aromatic amines that generate α-aminoalkyl radicals are used as activators, the latter can both initiate polymerisation and retard the inhibitory action of oxygen by reacting with it (see systems 37 and 38 in Table 2). In a number of cases systems that form a ternary complex with oxygen are used. The oxygen in them acts as an intermediate agent in electron transfer. Here, as in the previous case, peroxide radicals are formed, which also take part in the generation of the polymerisation chain (system 40).[130] The use of a monomer containing an amino group as the activator has future potential. The undesirable effect of oxygen can be inhibited in this way (system 40).[129]

Polymerisation initiated by electron phototransfer. In this case the choice of partners of the initiating mixture must guarantee a high probability of complete electron transfer followed by charge separation. An important condition for this to be fulfilled is $k_{ET} \gg k_{PT}$. It is necessary to bear in mind, however, that if anionic polymerisation occurs, whatever the multiplicity of the excited state of the photoinitiator it is not possible to exclude the inhibitory effect of oxygen.

If polymerisation occurs by a cationic mechanism and the photoinitiator "operates" in a singlet-excited state, oxygen does not

as a rule suppress it. The rate of polymerisation will depend to a large extent on the polarity of the medium and its acid-base properties. The latter influence the effectiveness of anionic polymerisation to the same extent.

Special requirements should be imposed on the choice of photoinitiator dictated by the mechanism of polymerisation. In this case it is mainly necessary to take into account the electronic configuration of the lowest excited states that take part in reaction and their multiplicity. Thus, if the formation of active primary radicals is based on secondary proton transfer reactions, the use of photoinitiators that have a considerable contribution of the $n\pi^*$ electronic configuration to the lowest excited state is preferred. This assists rapid proton transfer. When the secondary reaction is complete electron transfer with a passage of radical ions into the surroundings, systems with a significant or complete contribution of the $\pi\pi^*$ electronic configuration to the lowest excited state are more advantageous.

Finally, in order to improve the efficiency of initiation of polymerisation with radical ions it is necessary to ensure a more complete separation of charges. This can be achieved as a result of the formation of ternary initiating systems of photoinitiation–activator–monomer. In these one of the components acts as an electron transfer agent (mediator) between the second partner and the monomer (systems 31, 32, 35, 36). The second method involves the use of photoinitiators that have quaternary ammonium salts as a secondary substituent[164] or the use of activators connected to the π-electron skeleton of the molecule by a methine bridge.[165] Finally, very effective systems in which onium compounds are used as the partners of the photoinitiator (system 41) [131,132] have recently been developed.

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Translated from *Uspekhi Khimii* **60** 241–284 (1991) U.D.C. 47.422.127

Asymmetric epoxidation

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ABSTRACT. **The data on asymmetric epoxidation that have been obtained in recent years are correlated. Particular attention is given to the epoxidation of allylic alcohols with Sharpless reagent, which is a chemical complex of a titanium alkoxide with dialkyl tartrate. The structure of the catalyst, a model of the transition state, and the reaction mechanism are examined.**

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I. Introduction

In recent years the epoxidation of olefins—an important and frequently used reaction in organic synthesis—has acquired increasing significance as a method for the synthesis of chiral compounds. Enantioselective epoxidation, which results in the formation of two chiral sites in a single stage, yields optically active oxiranes, which are synthons for the preparation of natural compounds and their analogues. Of particular importance is the use of oxiranes in an optically pure form in the production of drugs, pheromones, etc.[1,2]

Chiral oxiranes play a significant role in the active processes of plants and animals. They are intermediates in biological synthesis. For example, the important function of 2,3-epoxysqualene in the biosynthesis of terpenes and steroids is well-known. By studying asymmetric epoxidation (AE) it is possible to establish the mechanism of many biological processes. Epoxidation is one of the fundamental stages during the exchange of substances in plant cells and animal organisms.[3] In many cases oxiranes participate in the catabolism of pesticides, drugs, and other xenomorphic comounds.[3,4] Hydroxylation, which is a key stage in the metabolism of aromatic amino acids, drugs, and vitamins in living organisms, occurs via an epoxidation reaction.[5] Intermediates containing an oxirane ring that are formed during the oxidation of aromatic hydrocarbons function as carcinogenic, mutagenic, and cytogenic agents.[5] Some natural epoxy compounds have juvenile hormonal activity.[6–8]

The physiological activity of many natural compounds containing an epoxide ring and the important role of oxiranes in the synthesis of natural compounds have determined the need for research into effective methods and a study of the mechanism of enantioselective epoxidation. A survey of the methods of AE is the aim of the present review, in which epoxidation using Sharpless reagent, which has been studied the most comprehensively in direct relation to the mechanism of this reaction, occupies a central position.

II. Methods of asymmetric epoxidation

AE was first reported to have been carried out by Henbest in 1965.[9,10] By epoxidising olefins with an isolated double bond with (+)-peroxycamphoric acid it was possible to obtain oxiranes with an enantiomeric excess (EE) of less than 5%. Despite the low optical purity of the compounds obtained, this reaction played an important role since for the first time the possibility of synthesising chiral oxiranes from achiral precursors was demonstrated. The attempts made subsequently to carry out AE using other peroxides were not successful in increasing the optical purity of oxiranes above 10%.[11–18] In 1977 Pirkle again studied this method and found that the peroxycamphoric acid which had been used in previous experiments was insufficiently pure.[19] As a result of purifying the oxidising agent it was possible to increase the enantioselectivity of the reaction by a factor of more than 2. By using the purified peroxyacid in the epoxidation of imines it was possible to obtain oxaziridines with an EE of >60%. In the majority of the cases mentioned above the low asymmetric induction at the stage involving oxygen transfer is probably due to the considerable distance of the electrophilic atom of the peroxide oxygen from the asymmetric centre and hence to the weak interaction between this centre and the double bond in the transition state (Fig. 1*a*).[20]

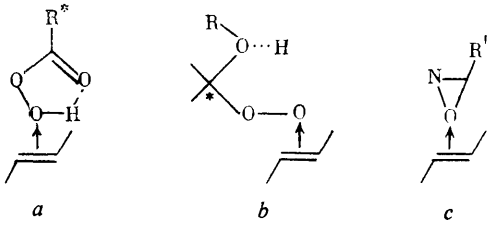


Figure 1. Transition state in the epoxidation of olefins with chiral peroxyacids (*a*), α-substituted hydroperoxyketals (*b*), oxaziridines (*c*).

The epoxidation of olefins with different chiral α-substituted hydroperoxyketals occurs with low asymmetric induction (EE <5%).[21] This value, in the opinion of Finn and Sharpless,[22]

could be increased since in this case the chiral centre is closer to the reaction site than for chiral peroxyacids (Fig. 1*b*).

Considerable success was achieved in the epoxidation of olefins with oxaziridines. In the transition state (Fig. 1*c*) the interaction between the chiral centre and the double bond is greater than when peroxyacids are used.[23–25] The maximum EE of these reactions was 65%.[24,25]

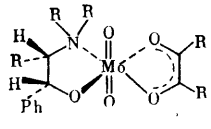
Use of the dioxiranes obtained by reaction of potassium peroxomonosulphate with chiral ketones for asymmetric induction in the epoxidation of olefins results in the formation of epoxy compounds with a low enantioselectivity (EE 4–13%).[26]

Epoxidation with hydrogen peroxide, t-butyl hydroperoxide (TBHP), or with hypochlorite of α,β-unsaturated acids, aldehydes, ketones, and other olefins whose double bond is conjugated with strongly electronegative substituents gives chiral epoxy compounds when a two-phase system and an optically active phase-transfer catalyst are used. In this case the enantioselectivity of the reaction varies from 1.2–5.4% EE (quaternary salts of quinone added to a polystyrene matrix comprise the phase-transfer catalyst),[27] 11% EE in the presence of cyclodextrins,[28–30] up to values of 55–78% EE when phase-transfer catalysts based on cinchona alkaloids[31] and quinine derivatives[32–37] are used. Much more effective phase-transfer catalysts are the so-called synthetic enzymes—polyamino acids—which can be used to epoxidise prochiral olefins with a high enantiomeric purity (EE up to 100%).[38–43] Epoxidation in this case takes place in a three-phase system—α-amino acid/aqueous phase/organic phase.

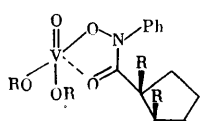
AE with hydrogen peroxide in an aqueous solution of sodium hydroxide under phase-transfer conditions using optically active solvents as the organic phase has been reported.[44] Chiral crown ethers have been used for asymmetric induction under phase-transfer conditions.[45] Epoxidation of olefins with aromatic substituents by hydrogen peroxide in the presence of (+)- or (−)-cyanoheptohelicene gives chiral oxiranes with an optical purity of 97–100%.[46]

Oxiranes with an EE of about 10% have been obtained by Darzens condensation in the presence of chiral compounds such as quinine salts.[47,48] Quinine salts have also been used for asymmetric induction in the epoxidation of prochiral olefins with molecular oxygen.[49]

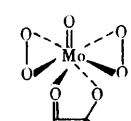
During the last twenty years there has been increased interest in transition metal complexes as catalysts for AE.[50,51] One of the advantages of processes catalysed by transition metals is the possibility of varying the structure of the ligands for modifying catalytic processes. In the case of chiral ligands, the substituents will in all probability be arranged asymmetrically about the chiral centre. On the basis of this assumption, Yamada[52] and Sharpless et al.[53] used chiral complexes of molybdenum (I) and vanadium (II) for the first time in order to carry out the asymmetric epoxidation of allylic alcohols with organic hydroperoxides.



(I)



(II)



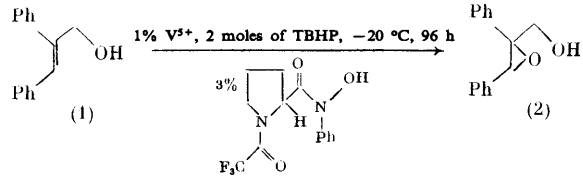
(III)

R = CH_3

A number of reports were later published on the epoxidation of prochiral olefins with various chiral molybdenum oxodiperoxo complexes used in stoichiometric amounts[54–59] [this reaction was carried out for the first time using complex (III)] and on the asymmetric epoxidation of olefins with organic hydroperoxides when a catalytic quantity of chiral dioxomolybdenum complexes [similar to complex (I)] were used.[60–63] On treatment of molybdenum oxodiperoxo complexes in the presence of chiral diols it was possible to obtain an oxirane with an EE of 95.4% in the epoxidation of olefins with an isolated double bond.[59] Lower asymmetric induction occurred in the epoxidation of olefins with an isolated double bond by hydrogen peroxide in the presence of chiral platinum complexes modified with diphosphines (EE 41%)[64] and also chiral complexes of iron porphyrin (EE about 51%).[65] In the latter case oxo compounds obtained by oxidation of iron porphyrin with iodosylbenzene constitute the epoxidising agent. Chiral complex iron compounds have also been used for AE of styrene derivatives (EE about 50%).[66–68]

The use of aluminium alkoxides and chiral hydroxamate ligands for carrying out the AE of allylic alcohols with TBHP has been reported (EE 30–40%).[69]

The AE of substituted allylic alcohols catalysed by vanadium complexes involving more than 20 chiral hydroxamate ligands has been studied.[70–72] The maximum enantioselectivity was achieved in the epoxidation of (*E*)-α-phenylcinnamic alcohol (1) [EE of epoxyalcohol (2) was 80%]:



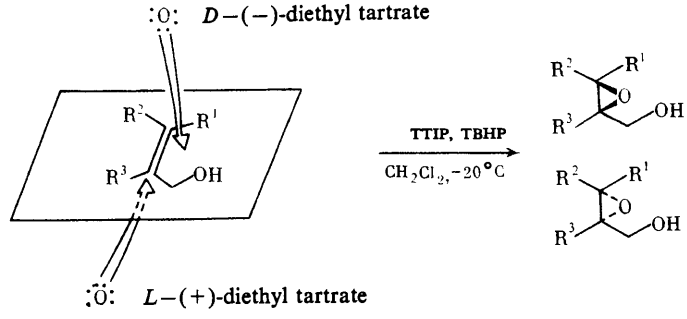


Figure 2. Asymmetric epoxidation of prochiral allylic alcohols.

In addition to chemical methods, other ways of obtaining chiral oxiranes are also known. One of these is the microbiological epoxidation of olefins.[73–82] The enantioselectivity of the reactions catalysed by the enzymes secreted by microorganisms depends on metabolic by-products of the microorganisms, which can cause inhibition of the reaction. Enzymatic epoxidation has been used to obtain oxiranes with a high EE.[83–87] For example, a high degree of enantioselectivity can be achieved when globular proteins such as bovine serum albumin (BSA) are used as catalysts.[88–91] In particular, AE of 2-substituted naphthoquinones with hydrogen peroxide and TBHP in a buffer solution containing an organic

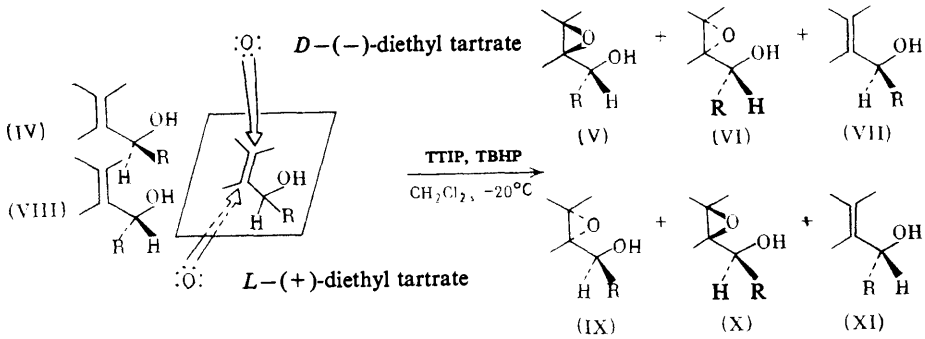


Figure 3. Kinetic resolution of racemic secondary allylic alcohols.

solvent and BSA results in the formation of chiral oxiranes with an EE of up to 100%. Asymmetric induction in this case is due to BSA occurring in the form of α-helices with hydrophobic groups capable of bonding with water-insoluble substrates situated between the helices. It should be noted that AE catalysed by enzymes is only suitable for a narrow range of substrates and its effectiveness is determined to a considerable extent by the reaction conditions.

III. Asymmetric epoxidation in the presence of a chiral titanium−tartrate complex

Directed research on chiral ligands was carried out in order to obtain an effective AE catalyst based on titanium and vanadium compounds.[71,72] This culminated in 1980 with the publication of the first report on an unusually effective method of enantioselective epoxidation that gave chiral oxiranes, the absolute configuration of which depended only on the configuration of the tartrate used and not on the structure of the substrate.[92,93] Soon afterwards Sharpless et al found that this unique combination of titanium alkoxide, optically active tartrate ester, and TBHP was sensitive to chirality existing in the substrate and could be used for the kinetic resolution of racemic allylic alcohols.[94,95]

AE has been used quite frequently and at the present time it is the most successful means of obtaining optically active oxiranes with high enantiomeric purity. Since the publication of the first report on AE using Sharpless reagent, a large number of studies and several reviews devoted to the use of this reaction and an investigation of its mechanism have been published.[20,22,96–106]

1. Reactivity of substrates and enantioselectivity of asymmetric epoxidation

A scheme for AE of allylic alcohols with Sharpless reagent is shown in Fig. 2. As a result of coordination of the titanium atom of a chiral complex consisting of titanium tetraisopropoxide (TTIP), dialkyl tartrate, and TBHP with the hydroxyl group of the compound undergoing epoxidation, the faces of the plane of the double bond become nonequivalent. For this reason attack by the oxygen atom of the peroxide occurs preferentially from one of these faces depending on the absolute configuration of the tartrate used, resulting in the preferred formation of one of the two possible enantiomers of the epoxy alcohol. By studying the stereochemical structure of a large number of α-hydroxyepoxides obtained by AE of allylic alcohols, it was possible for Sharpless et al[22] to develop a rule for the enantioselectivity of this reaction. If the allylic alcohol is drawn in a plane as shown in Fig. 3, attack by the oxygen atom on the double bond when *L*-(+)-tartrate is used occurs from below, while when *D*-(−)-tartrate is used attack occurs from above. This rule has no known exceptions amongst prochiral substrates at the present time. It can be used to predict easily and accurately the absolute configuration of the resulting epoxyalcohol, which is one of the significant merits of this reaction.

By comparing the results of epoxidation of allylic alcohols with different structures it is possible to establish the mechanism of AE.

1. The rate of the reaction, as when epoxidation is carried out by other methods, increases with an increase in electron density on the double bond of the olefin.[22,107] For example, a comparison of the rates of epoxidation of unsubstituted (4) and substituted cinnamic alcohols (Table 1) shows that the introduction of an electron-withdrawing nitro group reduces the rate of epoxidation [compound (3)] while an electron-donating methoxy or chloro group increases the rate of reaction [compounds (5) and (6)].

2. The rate of epoxidation of (*Z*)-allylic alcohols [compounds (7)−(24), Tables 2 and 3] with a substituent on the C(3)† carbon atom (Tables 2 and 3) is lower than for (*E*)-allylic alcohols [compounds (1), (4), (25)−(42), Tables 4 and 5].[108]

At the same time the enantioselectivity of the reaction is also somewhat less. For example, (*E*)-allylic alcohol (30) with a t-butyl substituent on the C(3) carbon atom is epoxidised with high optical purity, whereas the enantioselectivity of AE of (*Z*)-allylic alcohol (12) is low.

3. The optical purity of the α-hydroxyepoxides obtained from (*Z*)-allylic alcohols with a substituent on the C(3) carbon atom depends on the steric structure of the substituent (Table 2).[108] In compounds (7)−(9), (11), (15)−(20), containing an unbranched substituent, the enantioselectivity is high (EE 80−95%). In the case of compounds with a secondary [e.g. (10)] or tertiary [e.g. (12)] C(4)

† Here and subsequently, if the name of the compound according to the IUPAC nomenclature is not given, the carbon atom bearing the hydroxy group is designated C(1).

carbon atom, the optical purity of the α-hydroxyepoxide obtained is reduced. The same pattern is observed in the epoxidation of 2,3-, 3,3- and 2,3,3-substituted allylic alcohols [compounds (22)–(24), (43)–(49), Tables 3 and 6].

Table 1. Relative rates of asymmetric epoxidation of substituted cinnamic alcohols.[107]

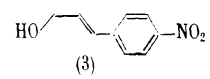
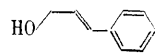
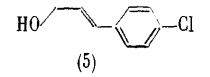
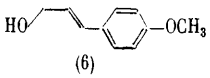
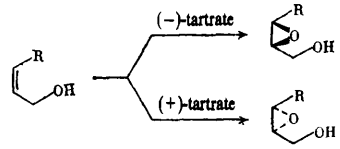
Substrate	Rate constant, s^{-1}	Relative rate
 (3)	0.579	0.42
 (4)	1.38	1.00
 (5)	1.65	1.20
 (6)	6.06	4.39

Table 2. Asymmetic epoxidation of (*Z*)-allylic alcohols with a substituent on the C(3) atom

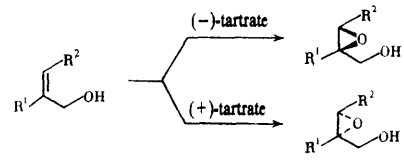


Compound	R	Catalyst: tartrate	Catalyst: Ti/tartrate, mol%	Reaction time, h	Temperature, °C	Yield, %	EE, %	Refs.
(7)	CH_3	(+)-DIPT	5/6	–	–	68	92	[109]
(8)	C_2H_5	(+)-DET	–	–	−20	60	80	[110]
(9)	n-C_3H_7	(−)-DIPT	stoichiometric	72	−20	56	80	[111, 112]
(10)	iso-C_3H_7	(+)-DET	–	–	−23	54	66	[113]
(11)	iso-C_4H_9	(+)-DET	–	–	–	80	95	[114] [115,
(12)	t-C_4H_9	(+)-DET	120/150	192	–	77	25	116]
(13)	C_5H_{11}	(−)-DET	stoichiometric	–	−20	78	–	[112]
(14)	C_6H_{13}	(+)-DET	–	–	–	64.3	80	[117]
(15)	n-C_8H_{19}	(−)-DET	100/100	–	–	80	91	[92]
(16)	n-C_7H_{15}	(+)-DET	10/14	29	−10	74	86	[109]
(17)	n-C_8H_{17}	(+)-DIPT	5/74	42	−12	63	80	[109]
(18)	$CH_2CH{=}CHC_5H_{11}$	(+)-DMT	110/110	–	–	70	94	[118]
(19)	$(CH_2)_3COOCH_3$	(+)-DET	–	–	−50 – −20	57	95	[119, 120]
(20)	CH_2OBz	(−)-DET	100/100	–	–	84	92	[121]
(20)	CH_2OBz		14/14	24	−20	–	95	[109]
(21)	Ph	(+)-DET	100/120	120	−30	61	78	[122]

DIPT = diisopropyl tartrate; DET = diethyl tartrate; DMT = dimethyl tartrate.

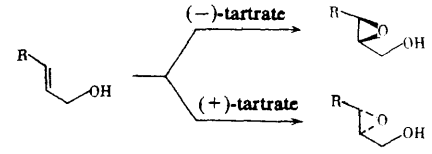
As in the case of (*Z*)-allylic alcohols with a substituent on the C(3) carbon atom, steric factors have the effect of slightly reducing the EE in the epoxidation of alcohols with a branched substituent on the C(2) carbon atom [Table 7, compounds (55) and (56)] in comparison with the results of epoxidation of alcohols [compounds (50)–(54), (58–(60)] with an unbranched substituent.[108] For the same reason the EE of stilbene α-hydroxyepoxide decreases by 20% when a chlorine atom is introduced into the *ortho*-position of the aromatic group on the C(2) carbon atom.[159]

Table 3. Asymmetric epoxidation of (*Z*)-allylic alcohols with a substituent on the C(2) and C(3) carbon atoms

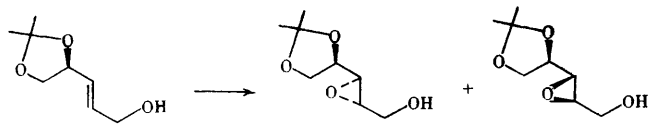


Compound	R^1	R^2	Yield, %	EE, %	Refs.
(22)	$C(CH_3)_3$	CH_3	43	60	[115, 116]
(23)	CH_3	n-C_4H_9	80	89	[92]
(24)	CH_3	CH_2Ph	90	91	[123]

Table 4. Asymmetric epoxidation of (*E*)-allylic alcohols with a substituent on the C(3) atom

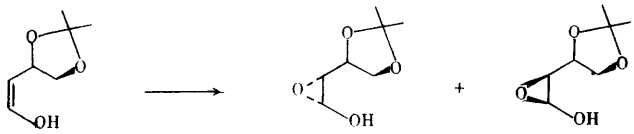


Compound	R	Catalyst: tartrate	Catalyst: Ti/tartrate, mol%	Reaction time, h	Temperature, °C	Yield, %	EE, %	Refs.
(25)	CH_3	(−)-DIPT	100/100	16	−20	48–50	95	[125–127]
(25)	CH_3	(+)-DIPT	5/6	2	−20	70	92	[109]
(26)	C_2H_5	(−)-DIPT	stoichiometric	–	–	80	>95	[128]
(27)	n-C_3H_7	(+)-DET	100/104	14	−20	64	93	[129]
(27)	n-C_3H_7	(+)-DET	5/6	2.5	−20	85	94	[109]
(28)	iso-C_3H_7	(+)-DET	100/104	–	–	66	98	[129]
(28)	iso-C_3H_7	(−)-DET	stoichiometric	–	–	59	–	[130]
(29)	n-C_4H_9	(+)-DET	»	–	−23	75	–	[131]
(30)	t-C_4H_9	(+)-DET	120/150	96	–	52	>95	[115, 116]
(31)	n-C_5H_{11}	(+)-DET	–	–	–	78	95	[134]
(4)	C_6H_{13}	(+)-DET	–	–	–	47.3	90	[117]
(32)	n-C_8H_{17}	(+)-DET	5/6	1.5	−10	78	94	[109]
(33)	n-$C_{10}H_{21}$	(+)-DET	100/100	72	−75	79	>95	[92]
(34)	Ph_3Si	(+)-DIPT	–	–	–	–	90	[138]
(34)	Ph_3Si	(−)-DIPT	–	–	–	–	90	[138]
(35)	$(CH_3)_3Si$	(−)-DIPT	–	–	–	–	95	[139]



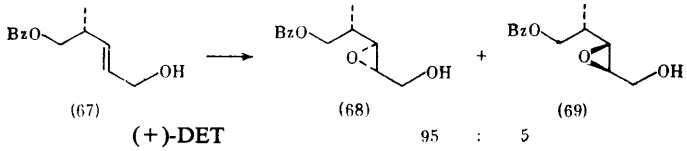
(61) (62) (63)

(+)-DET 15 h, 85% 20 : 1
(−)-DET 15 h, 78% 1 : 20



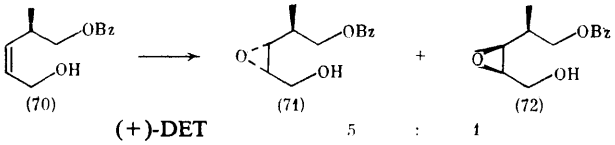
(64) (65) (66)

(+)-DET 336 h, 55% 30 : 1
(−)-DET 264 h 3 : 2



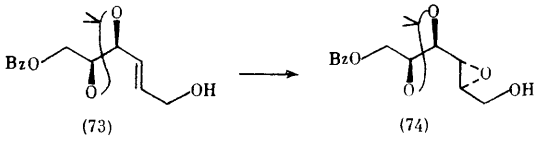
(67) (68) (69)

(+)-DET 95 : 5
(−)-DET 5 : 95

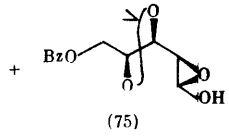


(70) (71) (72)

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(−)-DET 1 : 1

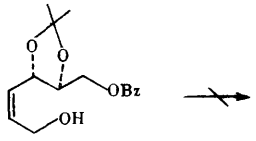


(73) (74)



(75)

(+)-DIPT 36 h, 70% 20 :
(−)-DIPT 36 h, 70% 1 :

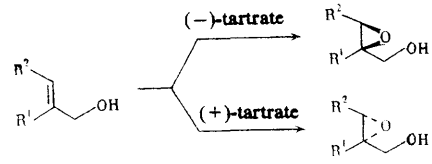


(76)

(+)-DET
(−)-DET

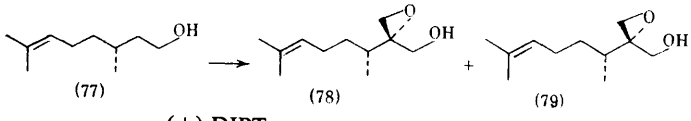
4. The results of epoxidation of optically active (*Z*)- and (*E*)-allylic alcohols with a chiral substituent on the C(3) carbon atom differ. While for (*E*)-isomers (61), (67), and (73)[121,160,161] the presence of a chiral centre has virtually no effect on the results of AE (EE is high whatever the absolute configuration of the tartrate used), in the epoxidation of a (*Z*)-isomer (64) and (70)[160,161] as a result of the interaction between the chiral substituent and the catalyst the stereoselectivity of the reaction depends on the absolute configuration of the catalyst—for one enantiomer of tartrate the diastereoselectivity is high while for the other it is virtually absent because of steric hindrance. (*Z*)-Allylic alcohol (76) is hardly epoxidised at all when either (+)- or (−)-DIPT is used,[121] since in this case the presence of a bulky substituent on the C(3) carbon atom has a substantial effect on the results of AE. It is clear from the examples given that AE of optically active (*Z*)-allylic alcohols can only be successfully achieved when the selected tartrate directs oxygen to the face of the plane of the double bond that is opposite to that in which the bond with the chiral substituent is situated.

Table 5. Asymmetric epoxidation of (*E*)-allylic alcohols with a substituent on the C(2) and C(3) atoms



Compound	R¹	R²	Tartrate	Reaction time, h	Temperature, °C	Yield, %	EE, %	Refs.
(36)	CH_3	CH_3	(+)-DET	–	–	77	94	[140]
(37)	CH_3	C_2H_5	(+)-DMT	16	−20	79	95	[125]
(38)	CH_3	CH_2OBz	(−)-DIPT	–	−15	87	90	[141]
(39)	CH_3	Ph	(+)-DIPT	2	−35	79	98	[109]
(1)	Ph	Ph	(+)-DET	–	–	70	96	[92, 109]
(40)	CH_3	$CH_2CH=C(CH_3)_2$	(+)-DET	12	−23	64	96	[144]
(40)	CH_3	$CH_2CH=C(CH_3)_2$	(−)-DET	12	−23	59	91	[144]
(41)		$-(CH_2)_3-$	(+)-DET	–	–	38	95	[145]
(42)		$-(CH_2)_4-$	(+)-DET	–	–	77	93	[109]

Like optically active (*Z*)-allylic alcohols with a substituent on the C(3) carbon atom, the diastereoselectivity of AE of an allylic alcohol with a chiral substituent on the C(2) carbon atom depends on the absolute configuration of the tartrate used, which follows from an analysis of the results of AE of (3*R*)-3,7-dimethyl-2-methylene-6-octan-1-ol (77):[162]

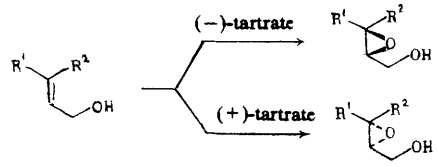


(77) (78) (79)

(+)-DIPT 96 : 1
(−)-DIPT 1 : 3

5. With an increase in reactivity of the allylic alcohols, the sensitivity of the resulting α-hydroxyepoxides towards opening of the oxirane ring increases, which in the presence of different nucleophiles (TBHP, isopropyl alcohol, titanium alkoxides) results in a decrease in effectiveness of the catalytic complex (the resulting diol is a catalyst inhibitor) and a reduction in yield of α-hydroxyepoxide.[102,107] For example, even with complete conversion of the substrate it is not possible to isolate an α-hydroxyepoxide in the AE of 4-methoxycinnamic alcohol (6), whereas 4-nitro- and 4-chlorocinnamic alcohols (4) and (5) are epoxidised in good yield. Glycidol

Table 6. Asymmetric epoxidation of (*E*)- and (*Z*)-allylic alcohols with substituents on the C(3) carbon atom



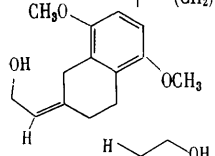
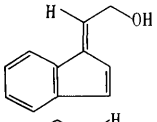
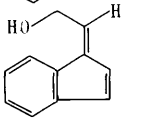
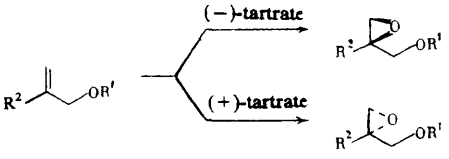
Compound	R¹	R²	Catalyst: tartrate	Catalyst: Ti/tartrate, mol%	Temperature, °C	Yield, %	EE, %	Refs.
(43)	CH_3	CH_3	(−)-DBT	100/100	−20	25	90	[147]
(44)	$CH_2CH=C(CH_3)_2$	CH_3	(+)-DET	200/200	–	67	95	[148]
(45)	$(CH_2)_2CH=C(CH_3)_2$	CH_3	(+)-DET	100/100	–	77	95	[92]
	$(CH_2)_2CH=C(CH_3)_2$	CH_3	(+)-DET	5/74	–	95	91	[109]
(46)	CH_3	$(CH_2)_2CH=C(CH_3)_2$	(+)-DET	100/100	−23	79	94	[92]
(47)			(+)-DET	10/15	–	97	93	[151]
(48)			(+)-DET	100/110	–	–	84	[152]
(49)			(+)-DET	100/110	–	–	88	[152]

Table 7. Asymmetric epoxidation of allylic alcohols with a substituent on the C(2) carbon atom

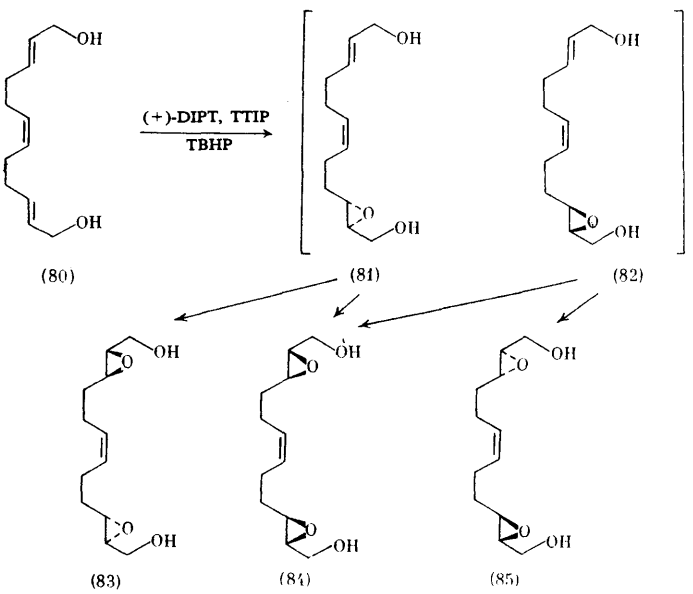


Compound	R¹	R²	Catalyst: Tartrate	Catalyst: Ti/tartrate, mol%	Reaction time, h	Temperature, °C	Yield, %	EE, %	Refs.
(50)	H	CH_3	(+)-DET	100/100[a]	72	−20	78	85	[153]
(50)	H	CH_3	(−)-DET	27/27	40	−30	32	94	[154]
(50)	H	CH_3	(−)-DET	7/6/10[a]	12	−45 ÷ −20	47	95	[155]
(51)	*p*-nitrobenzene	CH_3	(+)-DIPT	5/6	–	–	78	92 (98)[b]	[109]
(52)	tosyl	CH_3	(+)-DIPT	5/6	–	–	69	95	[109]
(53)	2-naphthalenesulphonyl	CH_3	(+)-DIPT	5/6	–	–	60	(92)[b]	[109]
(54)	H	n-C_3H_7	(+)-DET	4.7/5.9	11	−12	88	95	[109]
(55)	H	iso-C_3H_7	(+)-DET	65/120	68	−30	56	86	[156]
(56)	H	t-C_4H_9	(+)-DET	120/150[a]	15		42	86	[115, 116]
(57)	H	C_5H_{11}	(+)-DET	100/100	40	−20	81	95	[92]
(58)	H	n-C_9H_{19}	(+)-DET	100/110	–	−40	53	96	[157]
(59)	H	n-$C_{14}H_{29}$	(+)-DET	100/110[a]	–	−20	51	95	[158]
(59)	H	n-$C_{14}H_{29}$	(+)-DET	10/13	11	−12	91	96	[109]
(60)	H	CH_2OBz	(−)-DET	7.6/10[a]	12	−45 ÷ −20	74	95	[155]

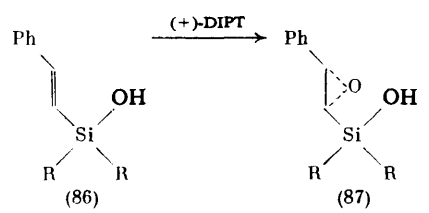
[a] Reaction carried out in the presence of $Ti(O-t-C_4H_9)_4$; [b] values of EE after recrystallisation are given in brackets.

and α-hydroxyepoxides with a substituent on the C(2) carbon atom [compounds (50), (55), (56), (58), (59), Table 7] are particularly sensitive towards opening of the epoxide ring.[92,158]

An interesting sequence of AE occurs for symmetric diallylic alcohol molecules. These results were first reported for the AE of (2*Z*, 6*E*, 10*Z*)-dodeca-2,6,10-triene-1,12-diol (80).[163,164] In the epoxidation of alcohol (80), α-hydroxyepoxide (81) is formed with high enantioselectivity together with a small quantity of epoxyalcohol (82). Epoxidation of the second double bond of enantiomers (81) and (82) occurs with the same enantioselectivity as takes place in the first epoxidation reaction. The three epoxides (83)–(85) are obtained as a result of double AE. Since the *meso*-compound (84) can be separated from the mixture and compound (85) is formed in insignificant quantity, the enantiomeric purity of the main product (83) is very high.



1,1-Substituted allylic alcohols are not effectively epoxidised by a titanium-tartrate complex. For example, AE of 2-methylbut-3-en-2-ol takes place very slowly and it was not possible to isolate the epoxyalcohol.[108] Epoxidation of 2-methyloct-3-en-2-ol results in the formation of the corresponding α-hydroxyepoxide in 67% yield and with an EE of 4%.[117] By replacing the C(1) carbon atom with a silicon atom it is possible to increase the optical purity of the resulting oxirane (87) because of the longer Si=C bond compared to the C=C bond.[165] The lower EE of compound (87b) compared to (87a) is probably due to the steric effect of the phenyl groups.



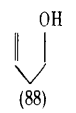
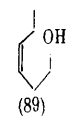
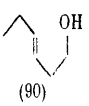
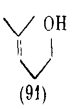
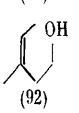
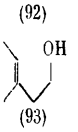
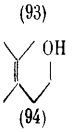
When R = CH_3, the yield of (87) is 50% and EE is 95%; when R = Ph, the yield of (87) is 70% and the EE is 20%.

The AE of homoallylic alcohols has several characteristic features when compared with the epoxidation of allylic alcohols (Table 8).[166]

1. The reactivity of homoallylic alcohols (88)–(94) is lower.

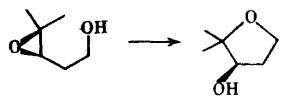
2. The absolute configurations of the hydroxyepoxides obtained by AE of allylic and homoallylic alcohols when the same tartrate ester enantiomer is used are of opposite sign.

Table 8. Asymmetic epoxidation of homoallylic alcohols.[166]

Substrate	Configuration of epoxyalcohol	Yield, %	EE, %
 (88)	(3*R*)	11–25	[55]
 (89)	(3*T*, 4*S*)	30–50	[36–50]
 (90)	(3*R*, 4*R*)	34–50	[41]
 (91)	(3*R*)	41	[27]
 (92)	–	60	[23]
 (93)	–	15	[23]
 (94)	–	62	[48]

3. The enantioselectivity of AE of homoallylic alcohols is lower than the enantioselectivity of AE of the corresponding allylic alcohols (EE 20–55%). Since the reduction in enantioselectivity of AE of homoallylic alcohols is due to the lengthening of the carbon chain by one methylene unit, in order to study the possibility of increasing the EE of an α-hydroxyepoxide chiral complexes based on zirconium, hafnium, and tantalum, which have a longer metal–oxygen bond than in a titanium complex, were used.[20] It was shown that AE of homoallylic alcohols in the presence of a zirconium tetraisopropoxide complex and (+)-dicylohexyl tartramide occurs with the same enantioselectivity as for epoxidation using the titanium–tartrate catalyst and epoxidation of a (*Z*)-homoallylic alcohol takes place with an even greater EE (up to 77%).[20]

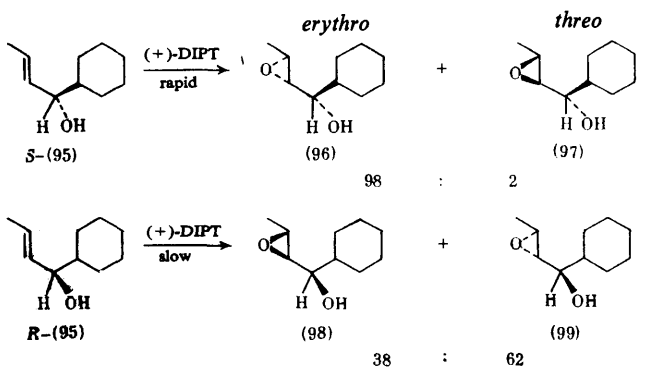
4. β-Hydroxyepoxides are more prone to isomerisation than α-hydroxyepoxides:



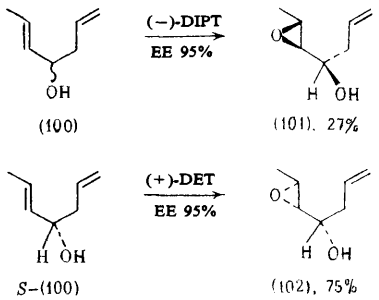
2. Kinetic resolution of racemic allylic alcohols by asymmetric epoxidation

In studying AE of racemic compounds with a secondary hydroxyl group, it is necessary to consider at the same time the enantioselectivity and diastereoselectivity of the reaction. As a result of coordination of the titanium atom of the chiral complex with the hydroxyl group of the compound undergoing epoxidation, two diastereomers of the intermediate complex are formed, AE of which occurs at a different rate, resulting in kinetic resolution of the racemate (Fig. 3).

As in the AE of prochiral allylic alcohols, the direction of attack by the oxygen atom on the double bond of the racemic allylic alcohol is determined by the absolute configuration of the tartrate selected, resulting in the preferential formation of one of the two possible *erythro*-(V) and (IX) or *threo*-(VI) and (X) diastereomers of α-hydroxyepoxide from each enantiomer of the racemate of alcohol (IV) and (VIII). However, as a result of the different orientation of the chiral substituent relative to the direction of attack by the oxygen atom the rates of epoxidation of the enantiomers differ; that enantiomer whose chiral substituent does not cause steric hindrance for attack by oxygen reacts rapidly, and hence its epoxidation leads to the formation of the *erythro*-epoxyalcohol (V) or (IX). For example, in the epoxidation of the allylic alcohol (95) in the presence of *L*-(+)-dialkyl tartrate attack on the double bond form below predominates in accordance with the proposed scheme (Fig. 3).[94,95] In this case the (*S*)-isomer of the allylic alcohol (95), whose chiral substituent does not hinder attack by the oxygen atom, reacts rapidly to form *erythro*-epoxyalcohol (96). For the (*R*)-isomer, because of the interaction between the substituent on the C(1) carbon atom and the catalyst, attack from below is inhibited so the reaction occurs slowly and with low selectivity, the *threo*-diastereomer (99) being predominant. The use of *D*-(−)-dialkyl tartrate gives the opposite result—the (*R*)-isomer of the allylic alcohol (95) is the rapidly reacting one and its epoxidation lead to the formation of *erythro*-epoxyalcohol (98).



Thus, for the reaction of AE with kinetic resolution of racemic allylic alcohols, a high *erythro* selectivity occurs since the isomer that gives an *erythro*-epoxyalcohol is the rapidly reacting one, while the isomer which forms a *threo*-diastereomer is epoxidised slowly and with a correct choice of reaction conditions remains in the mixture as unreacted (VII) and (XI) (Fig. 3). For example, the use of (−)-DIPT in the epoxidation of allylic alcohol (100) results in the formation of epoxyalcohol (101) with an EE of 95%.[167–169] The (*S*)-enantiomer of allylic alcohol (100) remains unreacted and can be epoxidised again in the presence of (+)-DET to form *erythro*-epoxyalcohol (102) with a high yield and EE.



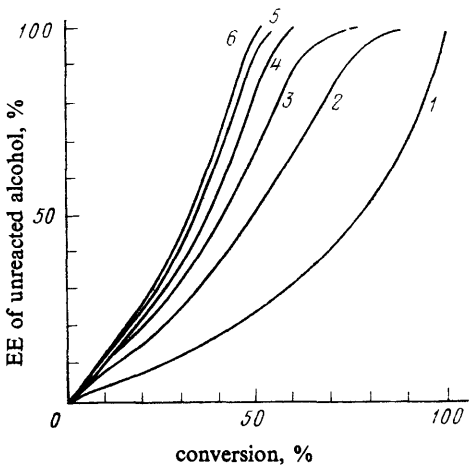
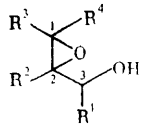


Figure 4. Graph of dependence of EE on conversion for different values of K_{rel}: *1*, 2; *2*, 5; *3*, 10; *4*, 25; *5*, 200; *6*, ∞.

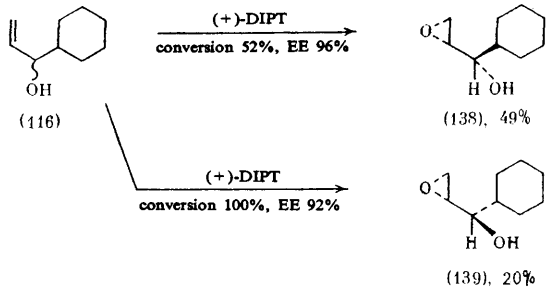
The considerable difference in the rates of epoxidation of the two enantiomers of a racemic allylic alcohol [compounds (103)–(137)] makes it possible to obtain both the α-hydroxyepoxide (Table 9) and the unreacted alcohol (Table 10) with high optical purity. The efficiency of resolution is determined by the relative rate of epoxidation of the allylic alcohols (K_{rel}), which constitutes the ratio of rates of epoxidation of the rapidly reacting to slow reacting enantiomers ($K_{rel} = K_r/K_s$) and varies over a wide range (Table 11).[22] When $K_{rel} = 100$ the reaction is almost as effective as when $K_{rel} = \infty$. Even when $K_{rel} = 15-25$ good results can be obtained.[103] The dependence of the EE of the allylic alcohol remaining in the reaction mixture on the conversion of substrate for different values of K_{rel} is shown in Fig. 4.[94] Analysis of the graph shows that when $K_{rel} = 25$, in order to reach 100% EE of unreacted alcohol, conversion should be less than 60%, which is achieved by reducing the quantity

Table 9. Asymmetric epoxidation of secondary allylic alcohols.

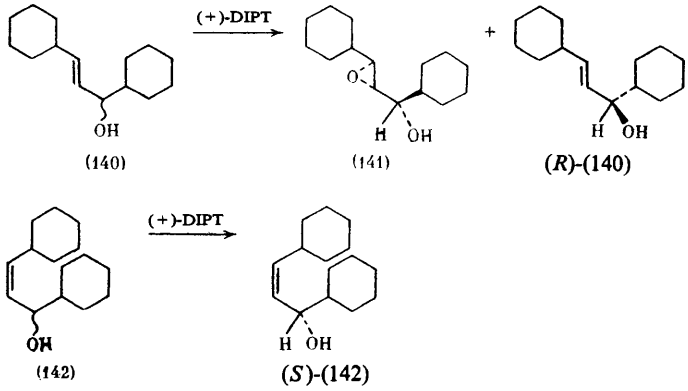


Compound	R^1	R^2	R^3	R^4	Configuration		Yield, %	EE, %	Refs.
					DIPT	epoxyalcohol			
(103)	C_2H_5	H	H	H	+	(2*R*, 3*S*)	–	–	[170]
(104)	n-C_5H_{11}	H	H	H	–	(2*S*, 3*R*)	47	91	[171]
(105)	$(CH_2)_6COOCH_3$	H	H	H	+	(2*R*, 3*S*)	36	95	[172]
(106)	$CH_2C=CSi(iso\text{-}C_3H_7)_3$	H	H	H	–	(2*S*, 3*R*)	40	90	[173]
(107)	C_2H_5	CH_3	H	H	+	(2*R*, 3*S*)	82	92	[174]
(108)	$CH(OBz)CH=CHCH_3$	H	CH_3	H	+	(1*S*, 2*S*, 3*S*)	35	95	[175]
(109)	CH_3	H	$CH_2CH=CH_2$	H	–	(1*R*, 2*R*, 3*R*)	40	90	[168]
(110)	CH_3	H	$C_2H_3(OCH_3)_2$	H	+	(1*R*, 2*S*, 3*S*)	74	98	[176]
(111)	CH_3	H	$C_2H_3(OCH_3)_2$	H	–	(1*S*, 2*R*, 3*R*)	78	97	[176]
(112)	CH_3	H	H	$C_2H_3(OCH_3)_2$	+	(1*R*, 2*S*, 3*S*)	34	97	[176]
(113)	CH_3	H	H	$C_2H_3(OCH_3)_2$	–	(1*S*, 2*R*, 3*R*)	34	96	[176]
(114)	$C_2H_3(OCH_3)_2$	H	H	CH_3	+	(1*S*, 2*R*, 3*R*)	55	93	[176]
(115)	$C_2H_3(OCH_3)_2$	H	H	CH_3	–	(1*R*, 2*S*, 3*S*)	60	95	[176]

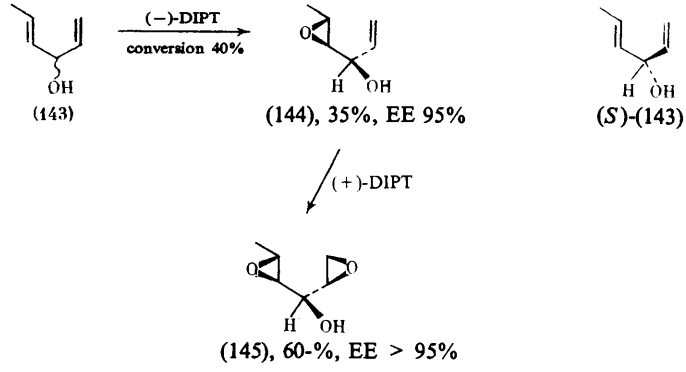
of oxidising agent. If the required reaction product is the optically active epoxyalcohol, a high EE can be achieved at 45% conversion.[108] For example, when AE with kinetic resolution of allylic alcohol (116) is carried out with a conversion of 52%, the *erythro*-epoxyalcohol (138) is formed with an EE of 96%, and with 100% conversion *threo*-epoxyalcohol (139) is isolated with an EE of 92%:[94,95]



For some substrates [compounds (126), (134), (135), and (137), Table 11] the rate of epoxidation of the rapidly reacting enantiomer is low, and the reaction takes quite a long time.[108] In the majority of cases the difference in the rates of epoxidation of the two enantiomers in the resolution of (*Z*)-allylic alcohols is less than for (*E*)-allylic alcohols and the efficiency of kinetic resolution is lower (Table 11).[94,95,107,176] In this case the optical purity of the preferentially formed (*Z*)-*erythro*-epoxyalcohol may be high, whereas (*Z*)-*threo*-epoxyalcohols are similar to racemates.[176] If the substituent on the C(3) carbon atom of the (*Z*)-allylic alcohol is branched, resolution of the enantiomers becomes virtually impossible, which is consistent with the general tendency towards a reduction in rate and enantioselectivity of AE for the analogous prochiral allylic alcohols. For example, asymmetric epoxidation with kinetic resolution of (*E*)-allylic alcohol (140) is complete after 15 h and results in the formation of α-hydroxyepoxide (141) and allylic alcohol (*R*)-(140) with a high EE (>96%), the (*Z*)-isomer (142) is ineffectively resolved (EE 10%):[94,95]



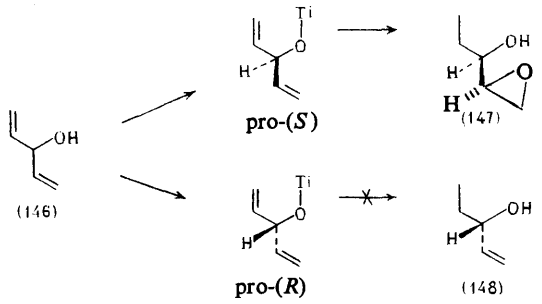
An interesting case of diastereoselectivity and enantioselectivity in AE with kinetic resolution of the racemic diene (143) using a titanium–tartrate system has been described by Sharpless:[123]



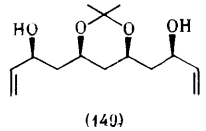
In this case it is possible to obtain eight monoepoxides. The

mechanism of AE of secondary allylic alcohols causes the preferential formation of a single monoepoxide. Firstly, from the dependence of the rate of epoxidation of allylic alcohols on the electron density of the double bond, it is to be expected that the reactivity of the disubstituted double bond is higher than that of the monosubstituted double bond. Secondly, the choice of tartrate enantiomer dictates the direction of attack on the double bond by the oxygen atom of the peroxide. And finally, the *erythro*-selectivity in AE with kinetic resolution of secondary allylic alcohols gives rise to the formation of a single monoepoxide. Thus, when (−)-DIPT is used, as a result of AE with kinetic resolution of the racemic diene (143), the (*R*)-*erythro*-epoxycarbinol (144) is mainly formed. A second asymmetric epoxidation of (144) using (+)-DIPT leads to the formation of the diepoxide (145).

Secondary allylic alcohols that have two identical substituents, such as divinylcarbinol (146), do not contain a chiral centre, but when they react with a chiral titanium complex the two double bonds become stereochemically nonequivalent (diastereotopic).[108,189–193] In this case AE occurs selectively on one double bond, the choice of which is dictated by the same factors as in the process of AE with kinetic resolution. The same factors that determine the selectivity of AE of chiral allylic alcohols cause the preferential formation of the pro-(*S*)-conformation. Hence, epoxidation of divinylcarbinol (146) gives (2*R*,3*S*)-epoxyalcohol (147).



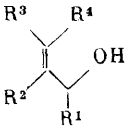
It should be noted that as a result of AE of the divinylcarbinol a small amount of epoxyalcohol (148), which is enantiomeric to the main epoxyalcohol (147), is also formed, resulting in a reduction in optical purity of the final compound. However, the configuration of the unreacted group of the allylic alcohol in this isomer is favourable for a second epoxidation to take place, and this isomer is converted to the diepoxide at a high rate, so the optical purity of α-hydroxyepoxide (147) increases as a result.[192,194] For divinylcarbinols a mathematical equation relating the optical purity of the product with the rate of epoxidation was obtained. A similar analysis can also be used in the AE of prochiral compounds such as (149).[195]



(149)

The efficiency of kinetic resolution increases when iodo-, chloro-, stannyl-, or silicon-containing substituents are present on the C(3) carbon atom of secondary (*E*)-allylic alcohols [compounds (150)–(167), Table 12].[184–188,196,197] AE of these substrates was used for the first time to obtain compounds such as (2*S*,3*S*)-3-trimethylsilylglycidol from (*E*)-3-trimethylsilylallylic alcohols and 2-trimethylsilylglycidols from 2-trimethylsilylallylic alcohols (124) and (125) (Table 10),[183] and in the latter case it was shown that it occurs with a satisfactory difference in rates of epoxidation of the two enantiomers, although it is less than in the case of kinetic resolution of (*E*)-3-trimethylsilylallylic alcohols.

Table 10. Kinetic resolution of secondary allylic alcohols



Compound	R¹	R²	R³	R⁴	Recovered allylic alcohol, %		Refs.
					yield	EE	
(109)	CH_3	H	$CH_2CH{=}CH_2$	H	39	90	[177]
(116)	cyclo-C_6H_{11}	H	H	H	32	98	[178]
(107)	C_2H_5	CH_3	H	H	–	98	[179]
(117)	n-C_4H_9	H	H	H	43	98	[180]
(118)	C_2H_5	H	Ph	H	–	99	[123]
(119)	CH_2CH_2Ph	H	H	H	–	99	[123]
(120)	n-$C_{12}H_{25}$	H	CH_3	H	44	97	[182]
(121)	CH_3	$C(CH_3)_3$	H	H	–	30	[115, 116]
(122)	$C(CH_3)_3$	H	CH_3	H	–	5	[115, 116]
(123)	$C(CH_3)_3$	H	H	H	–	10	[115, 116]
(124)	n-C_5H_{11}	$(CH_3)_3Si$	H	H	–	87.4	[183]
(125)	CH_3	$(CH_3)_3Si$	n-C_4H_9	H	–	95.4	[183]

A study of the effect of steric and electronic properties of the silyl group on the rate of epoxidation showed that the decrease in the overall rate of the process on replacing a carbon substituent by a silyl group was due to differences in the composition of the electron shells of carbon and silicon atoms while the increase in K_{rel} is due to the steric effect of the bulky trimethylsilyl group.[184] The same increase in K_{rel} occurs when a t-butyl group is introduced into the C(3)-position.[184] By studying the AE with kinetic resolution of the racemates of fluoroalkyl-(*E*)-vinylcarbinols (163)–(166) (Table 12), Hanzawa et al[198] were able to conclude that the electronegativity of the fluorine atom plays an important part in this process.

Kinetic resolution during the AE of secondary allylic alcohols with the hydroxyl group in a ring[94,108,123,200–203] occurs with lower optical purity than for acyclic allylic alcohols.

Although asymmetric epoxidation with kinetic resolution has been used most frequently for the resolution of allylic alcohols with a substituent on the C(1) atom, this reaction can be used to resolve the racemate of allylic alcohols (168)–(175) with chiral substituents on other carbon atoms (Table 13). AE of allylic alcohols with a chiral centre that is remote from the hydroxyl group can lead to results that do not conform to the general rules that apply in the epoxidation of secondary allylic alcohols. For example, the efficiency of kinetic resolution of the (*E*)-allylic alcohol (168) is low (although the enantioselectivity of epoxidation is high) while resolution of the (*Z*)-isomer (170) is effective (EE of unreacted alcohol is 95%).

Table 11. Relative rates (K_{rel}) of kinetic resolution of secondary allylic alcohols.

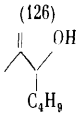
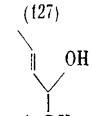
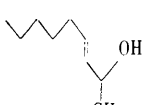
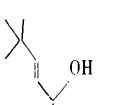
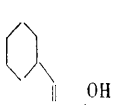
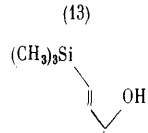
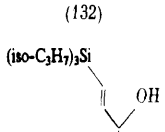
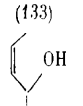
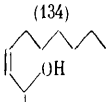
Substrate	Reaction time, h	K_{rel}, −20 °C, DIPT	EE, %	K_{rel}, 0 °C			Refs.
				DIPT	DET	DMT	
 (126)	288	83	96	60	–	–	[22, 94]
 (127)	15	138	96	96	52	–	[22, 94]
 (128)	15	104	96	74	28	15	[22, 94]
 (129)	24	160	98	–	–	–	[184]
 (130)	–	300	–	–	–	–	[184]
 (13)	–	330	–	–	–	–	[184]
 (132)	–	700	–	–	–	–	[184–188]
 (133)	–	300	–	–	–	–	[184]
 (134)	144	20	91	–	–	–	[22, 94]
 (135)	48	16	82	13	–	–	[22, 94]

Table 11 (continued).

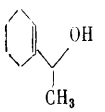
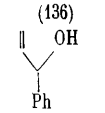
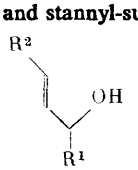
Substrate	Reaction time, h	K_{rel}, −20 °C, DIPT	EE, %	K_{rel}, 0 °C			Refs.
				DIPT	DET	DMT	
 (136)	15	83	96	60	38	–	[22, 94]
	–	4–10	–	–	–	–	[22, 94]

Table 12. Kinetic resolution during asymmetric epoxidation of silyl-, halo-, and stannyl-substituted allylic alcohols



Compound	R^1	R^2	Yield, %		EE, %		Refs.
			allylic alcohol	epoxy-alcohol	allylic alcohol	epoxy-alcohol	
(150)	n-C_5H_{11}	$(CH_3)_3Si$	42	42	99	99	[185, 186]
(151)	iso-C_3H_7	$(CH_3)_3Si$	40	41	99	99	[186]
(152)	Ph	$(CH_3)_3Si$	44	42	99	97	[186]
(153)	CH_2OPh	$(CH_3)_3Si$	47	46	99	99	[186]
(154)	CH_2OCH_2Ph	$(CH_3)_3Si$	43	48	99	99	[186]
(155)	n-C_6H_{11}	I	49	49	99	99	[196]
(156)	C_2H_5	I	40	–	98	–	[196]
(157)	cyclo-C_5H_9	I	44	–	99	–	[196]
(158)	C_6H_6	I	43	–	98	–	[196]
(159)	n-C_5H_{11}	Cl	43	–	99	–	[196]
(160)	n-C_5H_{11}	$Sn(C_4H_9)_3$	40	–	99	84	[197]
(161)	cyclo-C_6H_{11}	$Sn(C_4H_9)_3$	41	–	99	–	[197]
(162)	CH_2OPh	$Sn(C_4H_9)_3$	40	–	99	–	[197]
(163)	CF_3	n-C_6H_{13}	46	50	60	–	[198]
(164)	CF_2H	n-C_5H_{11}	39	52	98	–	[198]
(165)	CFH_2	n-C_5H_{11}	49	56	98	–	[198]
(166)	CF_3	n-C_5H_{11}	45	52	14	–	[198]

3. Mechanism of asymmetric epoxidation

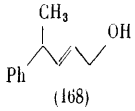
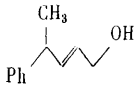
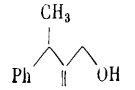
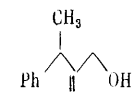
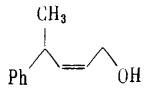
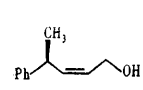
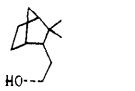
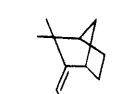
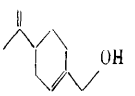
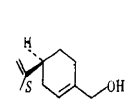
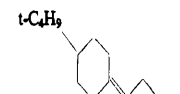
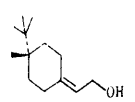
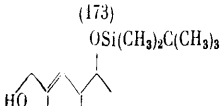
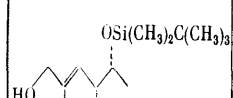
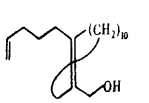
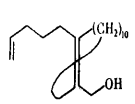
The mechanism of AE and the structural features of the catalyst that govern the high degree of enantioselectivity of reaction for allylic alcohols with different structures have been examined in several studies.[22,107,108,206]

a) Advantage of complex titanium compounds as catalysts for the asymmetric epoxidation of allylic alcohols

Asymmetric epoxidation of allylic alcohols with Sharpless reagent takes place in a similar manner to epoxidation reactions catalysed by other transition metal complexes (Fig. 5).[22,53,70,107,207–216]

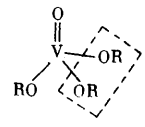
The $ML_n(OR)_m$ catalyst [L = oxo ligand, (OR) = alkoxide ligand, $n = 0-2$, $m = 2-4$ depending on the metal M][106,213,214] bonds covalently with the alkyl hydroperoxide and allylic alcohol, thus activating the peroxide. Epoxidation of the substrate occurs via the intermediate complex (XIV).[22,53,70,207-216] Although titanium alkoxides are not the most effective of the known epoxidation catalysts, these compounds have a high catalytic activity in the Sharpless method of AE. The success of AE using titanium alkoxides is determined by several properties of these systems.[107]

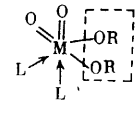
Table 13. Kinetic resolution of primary allylic alcohols.

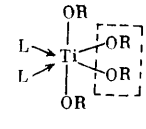
Substrate (configuration)	Recovered allylic alcohol		Refs.
	configuration	EE, %	
 (168)		6	[123]
 (169)		80	[123]
 (170)		95	[123]
 (171), (+)-enantiomer		85	[123]
 (172)		48	[123]
 (173)		70	[123]
 (174)		95	[204]
 (175), (+)-enantiomer		>95	[205]

1. Exchange of monodentate alkoxide ligands in solution takes place rapidly, which is also typical for other epoxidation catalysts such as complex compounds of vanadium, molybdenum, and tungsten.

2. In contrast to other highly active catalysts acting as complexing agents, titanium has the four covalent bonds needed for carrying out AE (two for bonding of divalent chiral tartrate, one for TBHP, and one for the allylic alcohol). Formation of a Ti=O bond is difficult, whereas the vanadium complex (XVII) is stable with one and complexes of molybdenum or tungsten (XVIII) are stable with two oxo ligands, which reduces the number of potential sites for bonding chiral ligands.[71,72]


(XVII)


(XVIII)
M = Mo, W


(XIX)

Thus, these compounds can covalently bond three (for vanadium) and two (for molybdenum and tungsten) alkoxide ligands and hence cannot be coordinated simultaneously with allylic alcohol, TBHP, and a bidentate chiral ligand, thus accounting for the low degree of enantioselectivity when AE is carried out in the presence of complexes of these metals.[52-70]

3. Titanium alkoxides are weak Lewis acids and hence to a certain extent they activate the coordinated alkylperoxo ligand for nucleophilic attack on the olefin.[210]

4. The coordination number of the titanium atom can vary.[213-215] This property is also typical for other transition metals, but when they are used as complexing agents for the preparation of chiral catalysts with dialkyl tartrates, AE of allylic alcohols using TBHP takes place slowly and with a low symmetric induction. The absolute configuration of the α-hydroxyepoxides thus obtained is usually the opposite of that which occurs when titanium is used (Table 14).[52-70,106] Evidently the formation of an effective chiral catalyst is determined by titanium's unique set of properties.

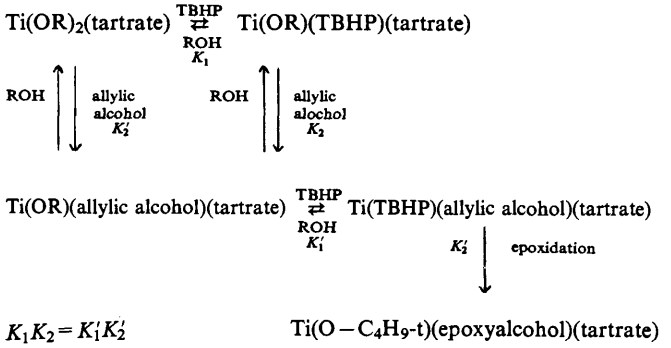
b) Reaction kinetics

On mixing equimolar solutions of titanium alkoxide and dialkyl tartrate, an equilibrium is established, as given by equation (1):[107]

$$Ti(OR)_4 + \text{tartrate} \rightleftarrows Ti(\text{tartrate})(OR)_2 + 2ROH. \quad (1)$$

In the majority of cases this system rapidly reaches equilibrium. However, when bulky alkoxides or tartrates are used to form a complex considerable time may be needed. For example, not less than 20 min is needed from a mixture of $Ti(O-C_4H_9\text{-}t)_4$ and (+)-DIPT, otherwise the EE of the epoxyalcohol obtained is significantly reduced.[22] The equilibrium in Eqn. (1) is considerably shifted to the right, since the binding constant of the diol with the titanium atom is much higher than that with monodentate alcohols. NMR spectroscopic and gas chromatographic data suggest that two moles of aliphatic alcohol occur in solution.[22,107,108] The rapid exchange of ligands continues when peroxide and allylic alcohol are introduced into the reaction medium. In this case the concentration of aliphatic alcohol increases, resulting in a shift of the equilibrium

in solution to the left [Eqn. (1)]. In the majority of cases this shift is insignificant and is suppressed by the addition of excess tartrate. On introducing the substrate and oxidising agent equilibrium is rapidly established, being represented by constants K_1 and K_2, which are equal to ~1 for TBHP and the majority of allylic alcohols.

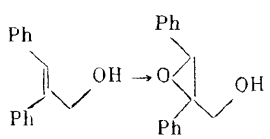


When TBHP and allyl alcohol replace the two remaining alkoxide ligands of the same titanium atom [as for example in compound (XX)],[210] the oxygen is transferred and t-butanol and a chiral epoxyalcohol are formed, which are again replaced by available allylic alcohol and TBHP. The catalytic cycle is complete when complex (XX) is regenerated.[107] A study of the kinetics of AE showed that the rate of reaction is first order with respect to the concentration of catalyst, peroxide, and allylic alcohol:[107]

$$V_{\text{reaction}} = \frac{k[\text{Ti(tartrate)(OR}_2)][\text{TBHP}][\text{allylic alcohol}]}{[\text{OR}]^2}$$

Transfer of oxygen is the rate-limiting stage.[107]

Table 14. Asymmetric epoxidation with TBHP in the presence of transition metal alkoxides



$M(OR)_n$	Configuration		EE, %
	tartrate	C(2)	
$Al(O-C_4H_9\text{-}t)_3$	(+)-DET	(*R*)	5
$MoO_2(acac)_2$	(+)-DIPT	(*R*)	15
$V(O-C_3H_7\text{-}n)_3$	(+)-DET	(*R*)	17
$Zr(O-C_3H_7\text{-}iso)_3$	(+)-DET	(*R*)	10
$Hf(O-C_3H_7\text{-}iso)_3$	(+)-DET	(*R*)	3
$Nb(O-C_2H_5)_3$	(+)-DET	(–)	0
$Ta(O-C_3H_7\text{-}iso)_5$	(+)-DIPT	(*R*)	39
$Ta(O-C_2H_5)_5$	(+)-DET	(*S*)	47
$Sr(O-C_3H_7\text{-}iso)_4$	(+)-DET	does not react	—
$Ti(O-C_3H_7\text{-}iso)_4$	(+)-DET	(*S*)	95

c) Structure of the catalytic complex

Studies on the kinetics of AE made it possible to reach general conclusions about the reaction mechanism. However, these results do not explain the high enantioselectivity of the process, since there is no information on the structure and characteristics of the titanium–tartrate complex that cause the high enantioselectivity of the reaction for a large number of substrates. A determination of the structure of the complex is, in addition to purely theoretical interest, of practical significance since it can serve as the basis for the development of novel chiral catalysts.[217] For these reasons much attention has been given to studying the structure of the titanium–tartrate complex.[22,107,108,218–225]

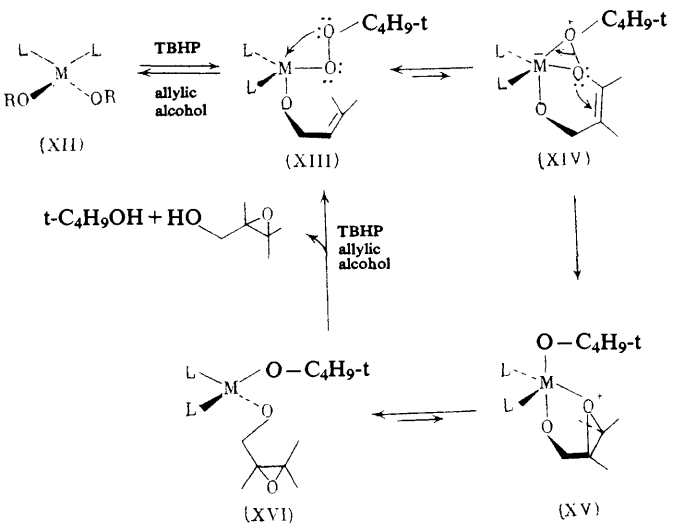


Figure 5. Epoxidation catalysed by transition metal complexes.

The complexity of the problem lies in the fact that because of the rapid exchange of ligands it is not possible to determine the structure of the titanium–tartrate complex participating in the catalytic cycle. Moreover, attempts to isolate the catalyst in crystalline form have proved unsuccessful. Some information about the structure of the complex in solution was obtained by physicochemical methods—mass spectrometry, osomometry, light dispersion, NMR and IR spectroscopy, and isopiestic methods.[22,107,108] In particular, it was shown that in solution a chiral catalyst with a 1:1 ratio of titanium alkoxide to dialkyl tartrate is mainly in the form of the dimer $Ti_2(tartrate)_2(OR)_4$. The formation of a dimeric chiral complex is supported by the nonlinear dependence of the EE of α-hydroxyepoxide on the EE of dialkyl tartrate. Since the enantiomeric purity of the epoxyalcohol is substantially higher than that expected from a linear dependence of the EE of the reaction product on the EE of the chiral ligand, it may be assumed that the high efficiency of the chiral catalyst is due to the inclusion of more than one tartrate ligand in the catalytic complex.[218] A dimeric structure for the catalyst was supported by the results obtained in a study of catalytic complexes containing novel tartrate, tartrate-like, and other ligands.[220–225] From the results of X-ray diffraction analysis of one of these complexes—Ti_2(dibenzyltartramide)$_2(OR)_4$—and assuming the similarity of this compound with the titanium–tartrate complex

$[Ti_2(tartrate)_2(OR)_4]$, the latter was suggested as having the equilibrium structure of a bisymmetric tricyclic dimer consisting of two residues of dialkyl tartrate, each of which is covalently bonded via the oxygen atom of a hydroxyl group with the two titanium atoms (Fig. 6)[224] (in contrast to the previously proposed ten-membered ring).[107] This structure has a C_2 axis of symmetry with the two titanium atoms in the same stereochemical environment. Each titanium atom (coordination number six) is bonded to six oxygen atoms: O(1) and O(2) are the oxygen atoms of the two alkoxy groups, O(3) and O(4) are the oxygen atoms of the hydroxyl groups, O(5) is from the ester group of the first tartrate ligand, and O(6) is the oxygen atom of a hydroxyl group of the second tartrate ligand. Thus, a bridging bond occurs between the two titanium atoms via the two oxygen atoms of hydroxyl groups of the two tartrate molecules, resulting in the formation of a dimeric pseudo-octahedral complex. At room temperature the signals from all of the tartrate groups in the NMR spectrum are identical. When the temperature is lowered the signals undergo a resolution that is typical of a system with asymmetrically bonded tartrate groups of a single type. From the results Finn and Sharpless[22] assumed that an equilibrium is established in solution between the two structures of the complex as depicted in Fig. 6. It should be noted that the geometric configuration of the ligands about each titanium atom in Fig. 6 is depicted for a complex with *L*-(+)-tartrate.[22] It is clear that when the *D*-(−)-enantiomer is used, the configuration of the ester groups of the tartrate will be a mirror image of the structure shown in Fig. 6. Sharpless et al.[22,108] have proposed that only one of the two titanium atoms is involved in the catalytic cycle of AE, but the possibility of both titanium atoms participting is not excluded.

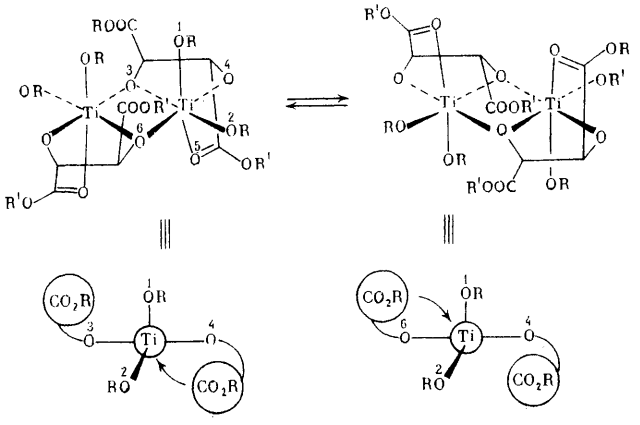


Figure 6. Equilibrium structure of a titanium–tartrate complex in solution.

d) Model of the transition state

The structure of catalyst proposed by Sharpless et al.[22,108] was the basis for a model of the transition state formed by the introduction of peroxide and substrate (Fig. 7). The frontier orbitals on the equatorial oxygen atom of the peroxide make it possible for the allylic alcohol to have four different orientations (Fig. 8).[22,219] The preferred orientation is determined by both stereochemical and stereoelectronic requirements.[22] The structures of (XXIII) and (XXIV) are sterically hindered because of the interaction between the ester group of the tartrate and the C(1) atom of the allylic alcohol. For the remaining structures (XXI) and (XXII) attack by the oxygen atom occurs from opposite sides of the plane of the double bond and hence the exclusion of conformations (XXIII) and (XXIV) does not account for the enantioselectivity of AE. However, the preferred formation of structures (XXI) and (XXII) governs the high stereoselectivity of kinetic resolution of secondary allylic alcohols. The conformation of the intermediate complex in which R^1 = H, R^2 = alkyl substituent is preferred to the conformation in which R^1 = Alk and R^2 = H because of greater steric hindrance in the latter case. For the same reason AE of tertiary allylic alcohols is ineffective.[108,117]

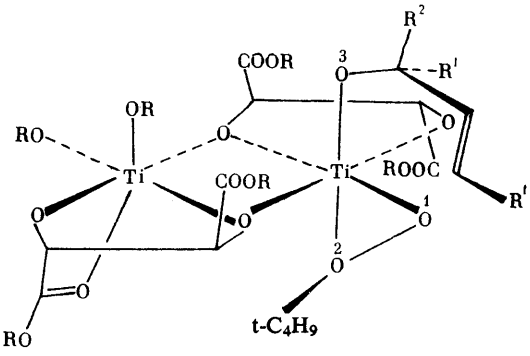


Figure 7. Model of intermediate complex; O(1) and O(2) are oxygen atoms of bidentate peroxide (by analogy with the coordination of TBHP with vanadium)[22,226] and O(3) is the oxygen atom of the allylic alcohol.

The preferred formation of one out of the two possible conformations of the intermediate complex (XXI) and (XXII), which gives rise to the high enantioselectivity of AE, is determined by stereoelectronic factors rather than by steric interactions.[22] An analysis of these factors shows that the *spiro*-orientation (XXI) of olefin and alkoxide with a small O–C/C=C dihedral angle (~30°) is the most probable one, rather than the planar orientation (XXII). The model of the transition state of complex (XXI) is confirmed by calculations using the frontier orbital method.[219] The enantioselectivity rule of AE is satisfactorily accounted for by the proposed structure of the transition state.

By choosing structure (XXI) as the preferred model of the transition state it is possible to account for the other rules of AE.[22] For example, the reduction in enantioselectivity that occurs for (*Z*)-allylic alcohols with a substituent on the C(3) atom is due to steric interactions between the substituent and the C–O bond of the allylic alcohol in conformation (XXI) (dehedral angle O–C/C=C is ~30°). This interaction is small when the substituent is hydrogen and increases as R becomes larger. When R = CH_3 or CH_2R, the

steric interactions result in a decrease in reaction rate while asymmetric induction remains high.



With a bulkier substituent (for example, R = cyclohexyl or phenyl) the rate decreases even more and there is a considerable reduction in EE.[22] The considerable efficiency of kinetic resolution of (*Z*)-allylic alcohols with a chiral substituent on the C(3) carbon atom (in contrast to a secondary (*Z*)-allylic alcohol) can be accounted for in the same way. For example, in the AE of allylic alcohol (170) (see Table 13), depending on the absolute configuration of the tartrate used the position of the phenyl and methyl groups is determined by the steric interactions when the oxygen atom of the hydroxyl group converges with the hydrogen atom on the C(4) carbon atom in the preferred conformation of the allylic alcohol in the transition complex. Thus, it is to be expected that the enantiomer remaining behind after kinetic resolution in the presence of (+)-DIPT will be the S-configuration. In the experiment this enantiomer was obtained with an EE of 95%.[123] The data given are consistent with the results on the dependence of enantioselectivity of AE of optically active (*Z*)-allylic alcohols (64) and (70) on the correspondence between the absolute configurations of the chiral substituent on the C(3) carbon atom and the tartrate used.

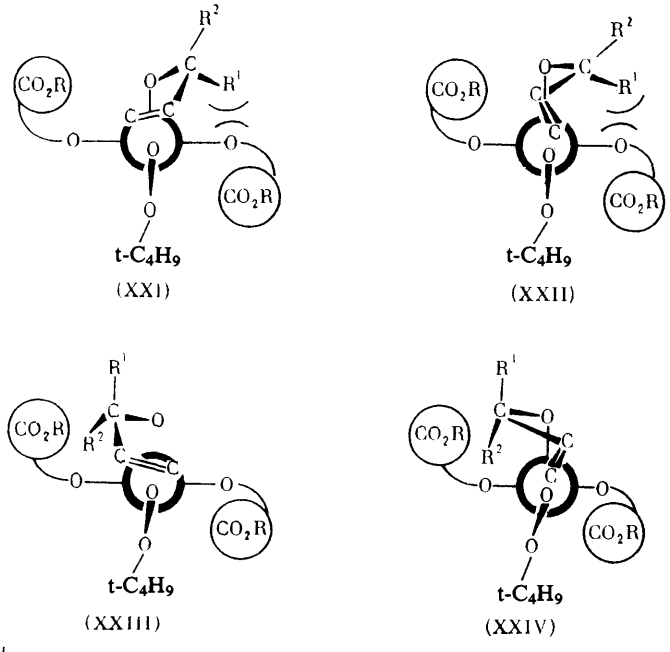


Figure 8. Possible orientations of ligands about the titanium atom in the transition state.

By using the model of the transition state (XXI) it is possible to account for other results of kinetic resolution of primary allylic alcohols with chiral substituents that are remote from the C(1) carbon atom. Thus, 2-(1′-phenylethyl)-2-propen-1-ol (169) (Table 13) in the intermediate complex exists in a conformation in which the hydrogen atom of the chiral site is directed towards the titanium–tartrate catalyst (Fig. 9).[22] By taking into account the steric interactions between the phenyl group (greater) or methyl group (smaller) with the substituent on the C(3) carbon atom of the (*E*)-allylic alcohol, a preferential formation of structure (XXV) is to be expected (Fig. 9). In fact, it was found that during AE with kinetic resolution of the racemate of (169), the (*S*)-isomer remains in the reaction mixture with 80% EE.[123]

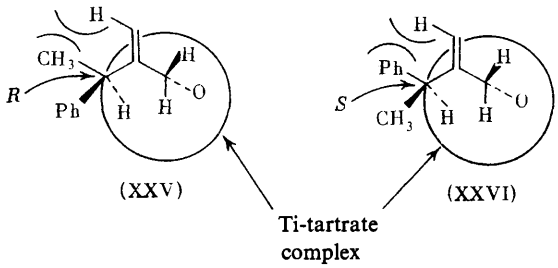


Figure 9. Kinetic resolution of 2-(1′-phenylethyl)-2-propen-1-ol.

Having created a model for the transition state similar to that given in Fig. 8, the low efficiency of kinetic resolution with high enantioselectivity of AE of the (*E*)-allylic alcohol of the α-phenylethyl group on the C(3) carbon atom (168) (Table 13) can be attributed to the spatial remoteness of this substituent from the chiral catalyst. This conclusion is consistent with the data obtained during AE of optically active alcohols when the chiral substituent on the C(3) carbon atom of (*E*)-allylic alcohols (61), (67) and (73) does not affect the results of epoxidation.

4. Reaction conditions

The unique feature of epoxidation with Sharpless reagent is the combination of high enantioselectivity of the reaction with the simplicity in carrying it out, the availability of all of the reagents, the uniformity of the reaction conditions, its preparative and technological significance, and the constancy of the results obtained. Nevertheless, in order to achieve the optimum results in each specific case it is necessary to control some process parameters. A detailed description of the conditions used in conducting AE has been given in several studies.[93,106,123,227–230]

a) Oxidising agent

TBHP is almost always used in AE as the oxidising agent; in certain cases cumyl hydroperoxide has been used.[109] Secondary hydro-peroxides such as phenyl and cyclohexyl hydroperoxides can serve as effective oxidising agents.[22] For enantioselective epoxidation of prochiral allylic alcohols and the kinetic resolution of secondary allylic alcohols, hydroperoxides with bulky tertiary groups such as trityl and tris(*p*-nitrophenyl)methyl have been successfully used.[22,130] The use of primary hydroperoxides is ineffective for AE.[22] For example, *n*-butylhydroperoxide gives rise to a substantially lower EE than does TBHP.

In order to achieve a high rate of AE of prochiral allylic alcohols, it is usual to employ 1.5–2.0 equivalents of oxidising agent. So as to ensure a large difference in the rates of epoxidation of the enantiomers of a racemic allylic alcohol during AE with kinetic resolution a smaller quantity of peroxide is used (~0.6 equivalents). Through careful control of the degree of conversion of alcohol to epoxide, it is possible to use >0.6 equivalents of peroxide, thus reducing the time of reaction.[106,108]

Normally AE using TBHP is carried out in a nonaqueous solution of methylene dichloride.[108] The absence of even trace amounts of water is an important factor, since water inhibits the rate of reaction and reduces the enantioselectivity of epoxidation.[22,53,70,208–212,227] This is because water in the presence of TBHP reacts rapidly with titanium alkoxide to form titanium peroxides and bridging compounds of the type Ti–O–Ti.[213] This results in a decrease in the number of coordination sites of the titanium atom participating in the formation of the intermediate complex and poisoning of the catalyst occurs. A study of the effect of adding water on the AE of (*E*)-α-phenylcinnamic alcohol showed that in the absence of water the EE is 99% and it decreases to 48% when one equivalent of water is added.[195] A detailed description of the methods of preparation, storage, and use of a nonaqueous solution of TBHP appears in three studies.[106,109,232]

An interesting case has been reported in which the source of oxygen for epoxidation is provided by the allyl hydroperoxide which is obtained from 2-t-butylpropene by photooxidation. The hydroperoxide is subsequently converted in the presence of the titanium–tartrate catalyst to 2-t-butoxy-2,3-epoxypropanol with an EE of 72% and yield of 79%.[116]

b) Catalyst

TTIP is used most frequently as a catalyst for AE, but other titanium compounds are used for special purposes. For example, in order to prevent the opening of an epoxide ring formed by AE which is unstable to nucleophilic attack, titanium tetraisobutoxide is used (see Table 7). Thus it was found that replacement of isopropoxide by the less nucleophilic t-butoxide makes it possible to increase the yield of hydroxyepoxide significantly (from 15–51%) in the AE of allylic alcohol (59).[153]

In certain cases $Ti(O-iso-C_3H_7)_2Cl_2$ is used instead of TTIP to obtain epoxyalcohols that are unstable under the reaction conditions.[158] In this case opening of the oxirane ring of the intermediate epoxyalcohol results in the formation of 3-chloro-1,2-diols in 60–80% yield and good regioselectivity. Treatment of the chlorodiols with a base gives epoxyalcohols with low enantioselectivity (20–70%). The absolute configuration of the intermediate epoxyalcohol is the opposite of that which occurs during traditional AE. Finn and Sharpless[22] relate the inversion of configuration of the enantiomer obtained to a strengthening of the titanium–carbonyl group interaction. The same pattern occurs when added quantities of electron-withdrawing monodentate ligands are introduced into the traditional catalyst (Table 15).[22]

The preparation and storage of a catalyst for AE has been described in three studies.[108,213,214]

Dialkyl tartrates and tartramides are used as ligands of the AE catalyst. Most frequent use is made of DMT, DET, and DIPT, which in the majority of cases are equally effective for carrying out AE.[106] It should be noted, however, that by using a tartrate with a bulkier ester group it is possible to increase the yield and rate of reaction when the epoxyalcohols formed are unstable under the reaction conditions. This is probably related to the fact that a bulkier ligand protects the epoxide ring from opening and formation of a diol.[106] For example, epoxidation of cinnamic alcohol when using DIPT occurs more rapidly and with a higher yield than when DET is used.[109] On the other hand, on changing from DIPT to DET there is a small increase in enantioselectivity (from 93 to 95%) in the epoxidation of (*E*)-substituted allylic alcohols such as (*E*)-2-hexen-1-ol.

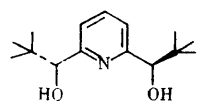
Table 15. Asymmetric epoxidation of *E*-α-phenylcinnamic alcohol.[22]

Added component	Ti	Tartrate	Added component	Configuration of epoxyalcohol	EE	Yield
	mol%				%	
–	2	2	0	(2*S*, 3*S*)	98	90
–	2	1	0	(2*S*, 3*S*)	80	90
O_2N–C$_6$H$_4$–OH	2	1	2	(2*R*, 3*R*)	80–85	50–70
$(F_3C)_2CH$–OH	2	1	2	(2*R*, 3*R*)	85	90
F_5C_6–OH	2	1	2	(2*R*, 3*R*)	90	93
PhOH	2	1	2	(2*R*, 3*R*)	6	90

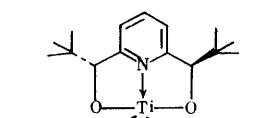
In contrast to the AE of prochiral primary allylic alcohols, the choice of dialkyl tartrate has a substantial effect on the efficiency of AE with kinetic resolution. In this case DIPT provides a better resolution in comparison with DET and DMT, which is of particular importance for substrates with only a small difference in rates of epoxidation of the enantiomers.[22] When dicyclohexyl and dicyclododecyl tartrates are used in the kinetic resolution of a number of allylic alcohols the EE of the products obtained is higher than when DIPT is used, but the yield is slightly lower.[109]

When diadamantyl and di-t-butyl tartrates are used as ligands in AE, the reaction takes place slowly and with a low EE of the resulting products.[22,106] Other dialkyl tartrates substantially reduced the efficiency of the catalytic system.[106]

Hawkins and Sharpless[225] carried out the AE of (*E*)-α-phenylcinnamic alcohol (1) in the presence of TTIP and the chiral reagent (*R*,*R*)-(XXVII).

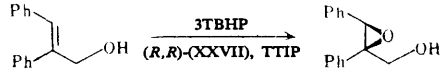


(*R*,*R*)-(XXVII)

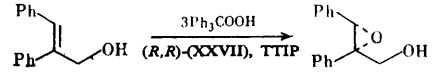


(XXVIII)

The use of TBHP resulted in the formation of the corresponding epoxyalcohol in high yield and with an EE of the predominant (2*S*)-enantiomer of ~40%.

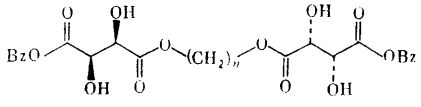


The use of trityl hydroperoxide resulted in the preferential formation of the (2*R*)-enantiomer with an EE of 64%:



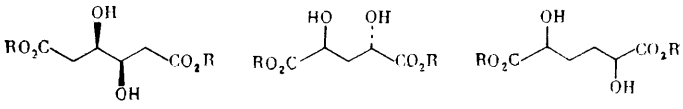
In these cases the epoxidation catalyst is the optically active complex (XXVIII), which exists in solution as a monomer.[225] Asymmetric induction during epoxidation in the presence of complex (XXVIII) depends on the size of the alkyl group of the peroxide, in contrast to reactions in the presence of the titanium–tartrate complex, in which TBHP and trityl hydroperoxide have no effect on the absolute configuration of the resulting epoxyalcohol.

Catalysts based on the novel esters of tartaric acid (XXIX) (n = 3–5) which incorporate two equivalents of titanium tetraisobutoxide provide a high enantioselectivity of AE but are ineffective for kinetic resolution.



(XXIX)

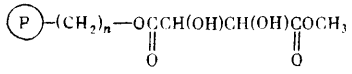
More recently the three tartrate-like ligands (XXX)–(XXXII) have been synthesised.[223] It was shown that (3*R*,4*R*)-diisopropyl 3,4-dihydroxyadipate (XXX) and (2*S*,4*S*)-diisopropyl 2,4-dihydroxyglutarate (XXXI) mainly form dimeric titanium–ligand complexes in the same way as the titanium–tartrate complex, while (2*S*,5*S*)-diisopropyl 2,5-dihydroxyadipate (XXXII) gives seven complexes.



(XXX) (XXXI) (XXXII)

Thus epoxidation in the presence of a titanium–diol (XXX) complex takes place very slowly and inactively; the titanium–diol (XXXI) complex is as effective as the titanium–tartrate complex in the epoxidation of primary allylic alcohols (EE > 93%, but is ineffective as a catalyst of kinetic resolution; and epoxidation in the presence of a titanium–diol (XXXII) complex, which probably consists of several active catalysts, occurs with low selectivity.[223]

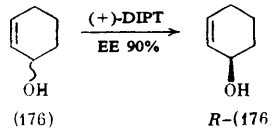
In order to establish the possibility of the repeated use of a chiral tartrate, the tartrate ester (XXXIII) was synthesised, being bonded via the ester with a hydroxymethyl (n = 1) or hydroxyethyl (n = 2) group of a polymer.[233]



(XXXIII)

The epoxidation of geraniol using TBHP in the presence of compound (XXXIII) and TTIP results in the formation of an epoxyalcohol with an EE of 49% (n = 1) and 65% (n = 2). The tartrate bonded to the polymer can be returned to the catalytic cycle and used again, although with reduced efficiency. Although the enantioselectivity of AE using (XXXIII) is less than for a homogeneous catalyst, this reaction has played an important role as it was the first attempt to use a heterogeneous catalyst that made possible the use of a chiral tartrate ester for the second time.

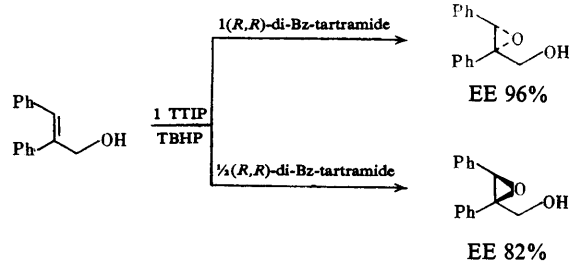
An important factor that determines the successful realisation of AE is the ratio of TTIP : tartrate in the complex catalyst. In contrast to the previously suggested ratio of 1 : 1,[92,93] in order to obtain the maximum possible EE Sharpless recommends the use of the tartrate in at least 10% excess relative to the titanium alkoxide.[94] This is because in the presence of a lesser quantity of tartrate in the system unsubstituted titanium alkoxide remains, which, like the complex Ti(tartrate)$(OR)_2$, is an active epoxidation catalyst and because of its achirality even a small percentage of it in the reaction mixture results in a reduction of enantioselectivity of AE. Of particular importance is the use of excess tartrate in AE reactions of substrates with low reactivity. For example, AE with kinetic resolution of compounds (142) and (176) does not occur when a ratio of titanium : tartrate equal to 1 : 1 is used; with a ratio of 1 : 1.5 the EE of compounds (*S*)-(142) and (*R*)-(176) is 10 and 30% respectively.[94,95]



(176) *R*-(176)

Thus, for reducing the content of titanium alkoxide to a minimum it is necessary to use more than one molecule of tartrate per titanium atom. However, when the excess of tartrate is increased by more than 10–20% the rate of reaction decreases, which is due to the formation of a $[Ti(tartrate)_2]_x$ structure, which is catalytically inactive because of the impossibility of displacing the bidentate tartrate with monodentate allylic alcohol and TBHP.[106] Hence in selecting the ratio of titanium : tartrate for carrying out AE, it is necessary to bear in mind that an increase in the tartrate content will lead simultaneously to an increase in enantioselectivity and a reduction in the rate of reaction.

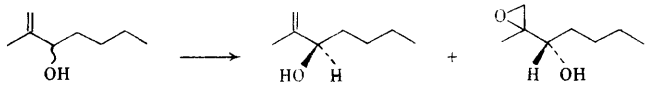
As has already been mentioned, a titanium–tartramide complex is an effective catalyst of AE. When this complex is used asymmetric induction is determined by the ratio of the components in the catalytic complex.[22] For example, AE of allylic alcohols using a TTIP–dibenzyltartramide system in the ratio 1 : 1 as the catalyst takes place with the same enantioselectivity as occurred when a titanium–tartrate complex was used.[158] It should be emphasised that on changing the ratio of titanium : dibenzyltartramide to 2 : 1 inversion of the absolute configuration of the α-hydroxyepoxide occurs:



c) Ratio of substrate to catalyst. Heterogeneous catalysis

Until 1986 a stoichiometric quantity of the catalytic system was used in the majority of cases to carry out AE, and only for a small number of allylic alcohols did AE give good results in the presence of a catalytic amount (5–10%) of titanium–tartrate complex.[106] Thus, the yield of AE of cinnamic alcohol under stoichiometric conditions was 65% and under catalytic conditions it was 80%. For epoxidation of 4-chloro- and 4-nitro-cinnamic alcohol only 5% catalyst is required. The epoxidation of less reactive substrates was also successfully carried out under catalytic conditions. For example, the epoxidation of (*Z*)-2-hexen-1-ol with < 10% catalyst takes place with high enantioselectivity, although at the same time the rate of reaction is slower than with a stoichiometric quantity of catalyst and it is difficult to achieve 100% conversion of the initial compound.[228]

Catalytic quantities of titanium–tartrate complex can also be used to carry out AE with kinetic resolution of allylic alcohols.[94,95] For example, allylic alcohol (127) is effectively resolved when 0.25 equivalents of the TTIP–(+)-DIPT complex is used. It should be noted that the enantioselectivity of kinetic resolution decreases slightly in the presence of the titanium–tartrate complex in catalytic amount as compared to a stoichiometric reaction. To obtain the best results with a catalytic quantity of complex, dicyclohexyl tartrate and dicyclododecyl tartrate are used instead of DIPT.[108]



(127)

A substantial improvement in AE was achieved by introducing molecular sieves into the reaction medium, making it possible to carry out virtually all of the reactions with catalytic quantities of titanium–tartrate complex.[109,232] For example, epoxidation of many simple allylic alcohols (such as 2-hexanol, cinnamic alcohol, 2,4-pentadien-1-ol) using a 5 mol.% titanium–tartrate complex in the absence of molecular sieves occurs with partial conversion (5–50%), while in their presence (3 or 4 Å sieves) reaction moves rapidly to complete consumption of the initial alcohols. When molecular sieves are used the EE decreases slightly (to 85–95%) but it can be increased by subsequent purification. For example, 4-nitrocinnamic alcohol is epoxidised in the presence of 2 mol.% TTIP–DIPT and molecular sieves with an EE of 90%. The resulting α-hydroxy-epoxide is crystallised to give an EE equal to 100%.[22]

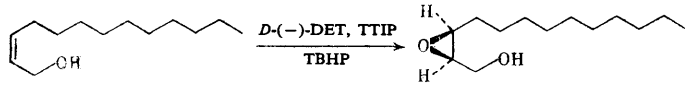
It should be noted that it is possible to reduce the concentration of catalyst to a given limit, after which a decrease in the optical purity of the resulting epoxyalcohol occurs, which is probably due to replacement of tartrate in the catalytic complex, without which asymmetric induction is impossible, by allylic alcohol or hydroxy-peroxide residues.[108] Thus, a study of the epoxidation of cinnamic alcohol showed that there was a substantial decrease in EE on reducing the catalyst content below 5 mol.% (Table 16).[108] At the present time it is recommended to use 5–10% mol.% TTIP and 6–12% mol.% tartrate to carry out AE in the presence of molecular sieves.[109]

In all probability the role of the molecular sieves is to protect the catalyst from water that could penetrate the reaction medium or could be formed in small quantities in side reactions during epoxidation.[108] A detailed description of the principles that should be followed when molecular sieves are used during AE is given in several studies.[22,106,108,109]

Asymmetric epoxidation in the presence of catalytic quantities of titanium–tartrate complex has the following advantages:[109]

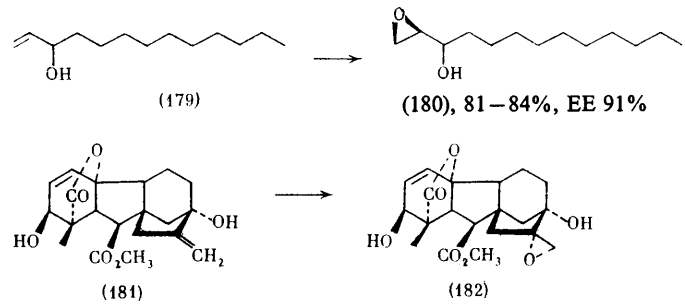
1. The quantity of reagent used is reduced while the rate of reaction is kept at the same level.
2. The reaction is carried out under milder conditions.
3. The yield of the reaction increases (Tables 4, 6, and 7).
4. In contrast to stoichiometric conditions substrates with a low molecular weight are effectively epoxidised.
5. Isolation of the reaction product is simplified.
6. The possibility of obtaining epoxyalcohol derivatives arises.
7. The concentration of substrate can be increased (as in contrast to AE with a stoichiometric amount of catalyst an increase in concentration of the allylic alcohol when there is a catalytic amount of chiral complex does not result in the increased probability of side reactions occurring).

In a number of cases the use of AE is limited by the long reaction time, which can amount to several weeks. It is possible to reduce the reaction time substantially by introducing a catalytic quantity of calcium hydride and silica gel into the reaction mixture.[234–237] For example, the time of epoxidation of (*Z*)-2-tridecen-1-ol (177) in the presence of 5–10 mol.% calcium hydride and 10–15 mol.% silica gel can be reduced from 96 to 8 h, whereas the yield and EE of the epoxyalcohol (178) remains unchanged.[234]



(177) (178)

The time of kinetic resolution of 1-tridecen-3-ol (179) in the presence of 5–10 mol.% calcium hydride and 10–15% mol.% silica gel decreased from 360 to 25 h.[234] AE of methyl giberellate (181) using traditional methods is ineffective. The use of calcium hydride and silica gel results in the formation of the corresponding epoxyalcohol (182) in 70–80% yield and with an EE of 75–80%.[235]



(179) (180), 81–84%, EE 91%

(181) (182)

Table 16. Effect of catalyst concentration on enantioselectivity of asymmetric epoxidation of cinnamic alcohol.[108]

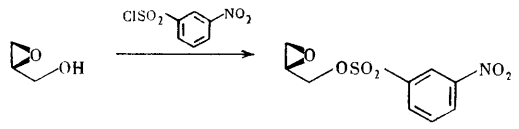
TTIP, mol%	(+)-DIPT, mol%	EE, %
5.0	6.0	92
4.0	5.2	87
2.0	2.5	69

When the reaction is carried out in the presence of calcium hydride alone (or sodium or potassium hydride), the reaction time is reduced but at the same time the optical purity of the product is also reduced. The use of silica gel alone does not reduce the enantioselectivity but shortens the time of epoxidation.[234,236]

d) Preparation of epoxyalcohol derivatives *in situ*

Because of the sensitivity of a number of epoxyalcohols to the action of nucleophiles and their solubility in water, isolation of the reaction product can be difficult. Of particular importance in this case is the preparation of epoxyalcohol derivatives *in situ*, which can be used to carry out AE with a catalyst content of 5–10 mol.%. For example, low molecular-weight alcohols such as glycidol (183) are

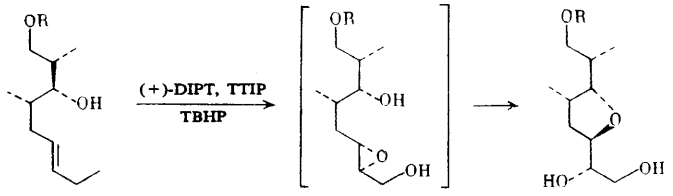
readily isolated from the reaction mixture as their ester derivatives, such as *p*-nitrobenzoate or 3-nitrobenzenesulphonate (184).[109,238]



(183) (184)

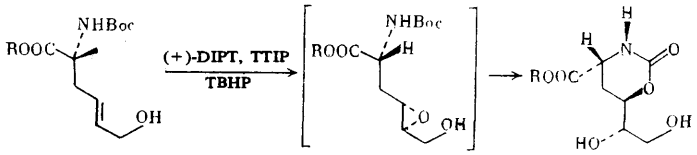
The increase in yield of 2,3-epoxypropanol in the preparation of derivatives *in situ* can be seen from the data of Table 7. With a stoichiometric quantity of titanium–tartrate complex the 2-methylallylic alcohol is epoxidised with an EE of 90% but in low yield. By carrying out the reaction under catalytic conditions and preparing derivatives *in situ* it is possible to isolate the *p*-nitrobenzoate in 70% yield and an EE of 98% and the 3-nitrobenzenesulphonate (184) in 55% yield and an EE of 93%.[108]

It is possible to obtain derivatives *in situ* by nucleophilic opening of the epoxide ring using the TTIP which is already contained in the reaction medium and is an effective reagent that accelerates regioselective attack by nucleophiles on 2,3-epoxyalcohols.[239] In this case the required compounds can be obtained with a given configuration of the functional groups relative to the double bond of the allylic alcohols. In particular, compound (187) is formed as a result of AE of allylic alcohol (185) followed by intramolecular cyclisation.[158]



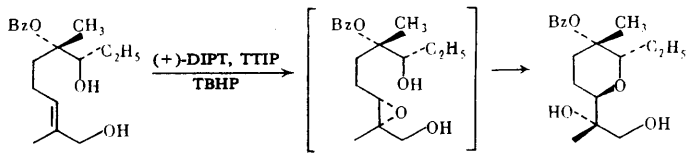
(185) (186) (187)

In the same way, in the epoxidation of alcohol (188) cyclisation of the intermediate epoxyalcohol (189) occurs during reaction and results in the formation of the cyclic urethane (190).[240]



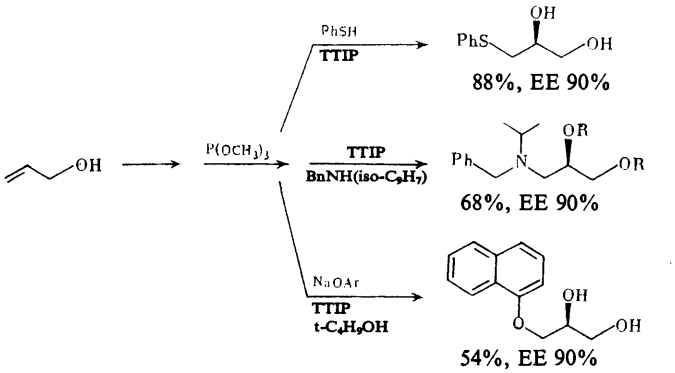
(188) (189) (190)

Epoxyalcohol (192), obtained from allylic alcohol (191), gives the ether (193) as a result of intramolecular cyclisation.[174]

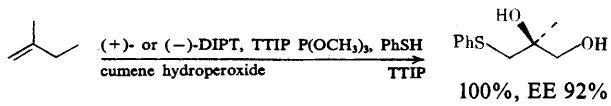


(191) (192) (193)

The preparation of derivatives *in situ* not only assists the isolation of the reaction product, but it can also be used to obtain chiral compounds in a suitable form for further synthesis. For example, *in situ* opening of the epoxide ring of glycidol using nucleophiles such as thiols, secondary amines, and phenols results in the formation of intermediates in the synthesis of adrenalin blockers, antidepressants, etc.[162,241,242]



Thus, methallylic alcohol gives a diol that is used in the synthesis of important organic compounds:



Sulphonation, silylation, and esterification *in situ* result in the formation of derivatives that are intermediates in the synthesis of natural derivatives.

- - -o0o- - -

This literature survey on AE has shown that the most effective method of obtaining optically active oxiranes is the Sharpless reaction, which has the following main advantages.

1. Simplicity, availability, and economical price of all components.
2. Reliability (AE of the majority of prochiral and optically active allylic alcohols, and also the AE with kinetic resolution of the racemate of allylic alcohols occur successfully).
3. High enantioselectivity (EE of 90–95% or more in many cases).
4. Preparation of oxiranes with a given absolute configuration.

The possibility of regioselective opening of the epoxide ring could be used for Sharpless epoxidation in a number of multistage syntheses of optically active compounds, amongst which natural compounds such as sugars, pheromones, and products used as drugs are of the greatest importance. The number of studies devoted to a directed synthesis of natural compounds using the Sharpless asymmetric epoxidation as the key stage continues to grow.

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Translated from *Uspekhi Khimii* 60 285–316 (1991) U.D.C. 547.7.07:547.241

Synthesis of heterocycles by the aza-Wittig reaction

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ABSTRACT. **This review is devoted to the synthesis of *N*-heterocyclics by the interaction of phosphazo groups (either preformed or prepared *in situ*) with carbonyl or thiocarbonyl groups. Examples are presented systematically only for syntheses by an intramolecular aza-Wittig reaction or where the latter is incorporated in a multi-step route. The feasibility of preparing various types of heterocycle by this method has been examined.**

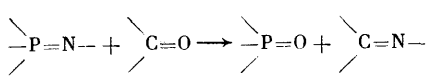
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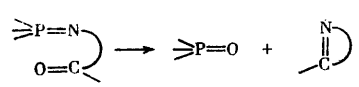
I. Introduction

Phosphazo compounds (phosphine imines) can react with carbonyl compounds in the same manner as phosphonium ylids, i.e. as aza-analogues of the latter. The reaction is thus analogous to the Wittig synthesis,[1] the end product being the corresponding imine.



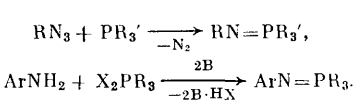
Because of this analogy, it is generally referred to nowadays as the aza-Wittig reaction, although, in fact, it was first discussed by Staudinger and Meyer[2] independently of the work of Wittig.

If the phosphazo and carbonyl groups are in the same molecule, intramolecular condensation can take place to give a nitrogen-containing heterocycle:



Many types of five-, six- and unusual seven-membered *N*-heterocylics, including natural products and their analogues, have been prepared by this route, notably in the last two decades. However, up to now, there has been no systematic survey of literature data on this reaction, except in Zbiral's review[3] of 1974, in which there is a small section on the synthesis of heterocyclics with phosphine imines.

The mild conditions of the cyclisation and the ready availability of the starting materials are normally considered as the principal advantages of the aza-Wittig synthesis. Azides and aromatic amines are very often used as precursors of phosphazo compounds, the first being converted into the latter by treatment with the corresponding phosphine or phosphite, while aromatic amines afford phosphazo compounds by treatment with dihalogenotriorganophosphoranes in the presence of base:

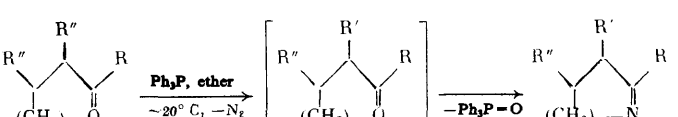


In many cases, reaction can be undertaken with *in situ*-generated phosphazo compounds.

II. Syntheses by aza-Wittig reaction

1. Cyclisation of phosphazoketones and phosphazoaldehydes

Ketones and aldehydes are normally used as the carbonyl function in the aza-Wittig reaction. Reaction with phosphazo groups proceeds under comparatively mild conditions—in many instances at room temperature. Notably, this reaction has been applied with readily available ω-azidoketones, from which five-, six-, and seven-membered cyclic imines (I) can be obtained. Such compounds are intermediates for alkaloids. There are a number of advantages of this method over other known procedures. For example, as reaction can be conducted in non-aqueous media under non-reductive conditions, the method can be applied to ring systems with substituents which are sensitive to reductants and water.[4,5]

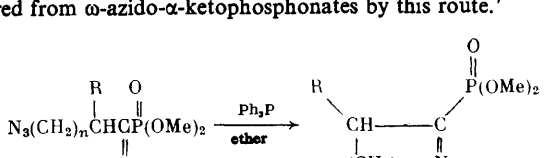


(I), 60–92%

$n = 1–3$; R, R′, R″ = H, Me, Et, PhS, 4-BrC$_6$H$_4$.

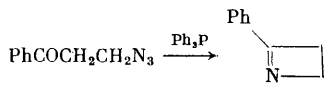
The synthesis of 1-pyrrolines (I, n = 1) by the aza-Wittig reaction has already been discussed.[6]

2-Phosphonyl-Δ^1-pyrrolines and -Δ^1-piperideines have been prepared from ω-azido-α-ketophosphonates by this route.[7]

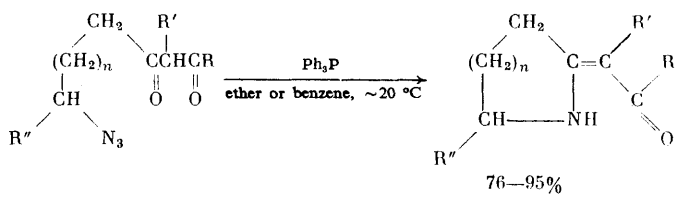


n=2,3; R=H, Me, allyl.

Azetines cannot be obtained by the aza-Wittig reaction in preparative yield.[8] Thus, 4-azidobutan-2-one and methyl 3-azidopropionate do not cyclise on treatment with triphenylphosphine, even under harsh conditions. However, it is possible to prepare 2-phenyl-1-azetine in very low yield by reaction of β-azidopropiophenone with triphenylphosphine.



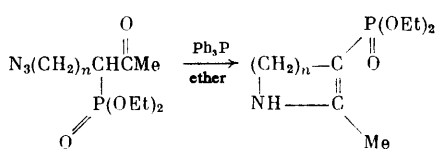
The reaction of ω-azido-β-diketones or ω-azido-β-ketoesters with triphenylphosphine is accompanied by migration of a labile hydrogen atom from carbon to nitrogen to provide heterocyclics with an exocyclic double bond. Such products, obtainable in quantitative yield, may be regarded as vinylogous amides or urethans.[6,7,9]



$n = 1-3$

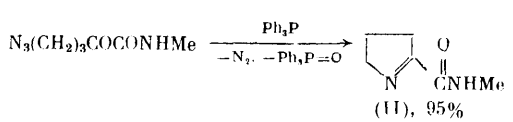
Attempts to prepare eight-membered heterocycles in this way failed when the starting materials were heated in toluene.[9]

Transfer of hydrogen from carbon to nitrogen also takes place on intramolecular aza-Wittig cyclisation of ω-azido-α-(diethoxyphosphinyl)ketones, there affording 3-diethoxyphosphinyl-2-pyrrolines and -2-piperideines in ~75% yield.[6]

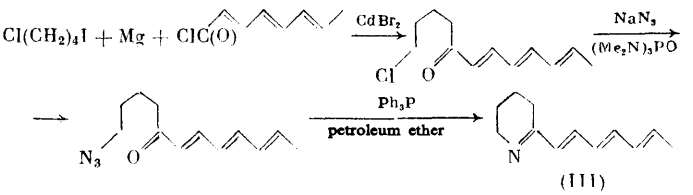


$n = 2, 3$

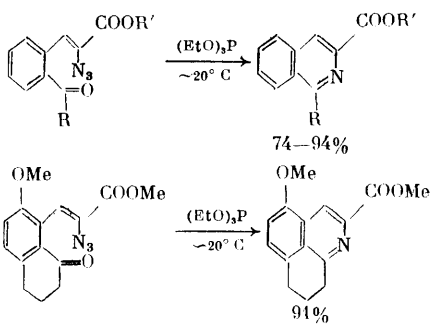
The amide (II) is obtained in high yield by interaction of *N*-methyl-5-azido-2-ketovaleramide with triphenylphosphine in benzene. It is reported that this method is suitable for preparing the relatively inaccessible 1,2-dehydroproline system. However, it is not possible to prepare seven-membered heterocyclics by such ring closure of ketoamides.[10]



The method has also been applied in the final step of a multistage route to the alkaloid nigrifactine (III), which possesses high physiological activity. The intermediate chloro- and azido-ketones, with four double bonds in conjugation, and nigrifactine itself, are all very unstable and are isolated in low yield.[11]

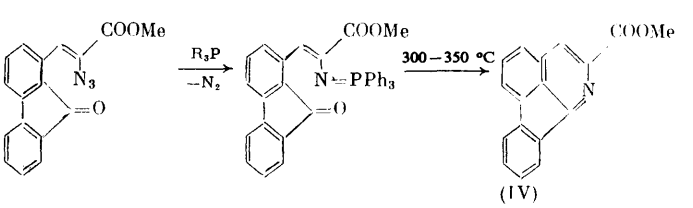


Intramolecular aza-Wittig reaction with *o*-carbonyl-substituted α-azidocinnamates and analogous 1-tetralone derivatives readily cyclise at room temperature to isoquinolines without isolation of intermediate phosphazo compounds.

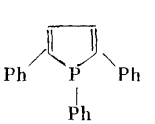


R = H, Me, Ph; R′ = Me, Et.

The phosphazo compounds obtained from fluorenone and triphenylphosphine or triethyl phosphite do not cyclise on heating in xylene; however, the azafluoranthene (IV) is obtained at 300–350 °C in 12 and 19% yield, respectively. The product can be obtained in somewhat higher yield (34%) by cyclisation of the phosphazo compound obtained by reaction of the starting azide with 1,2,5-triphenylphosphole (see p. 152). In this case reaction is complete within two minutes at 300 °C.[12,13]

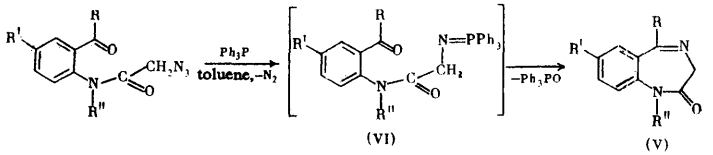


R = Ph, EtO or R$_3$P =



Benzodiazepine derivatives, including the psychotherapeutic drugs diazepam and nitrazepam (Va, b),[14] as well as the analogues (Vc–e),[15] have also been prepared by intramolecular aza-Wittig reaction. The intermediate phosphazo compound (VIe), formed by reaction of triphenylphosphine with 2-(azidoacetylamino)4-chlorobenzophenone, is stable at room temperature and may be isolated as

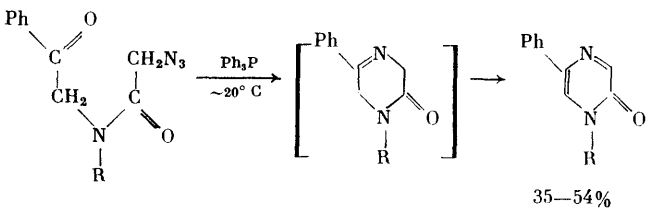
the hydrochloride; on heating in toluene it is converted into the corresponding benzodiazepine (Ve) in 80% yield.[15]



(VI) (V)

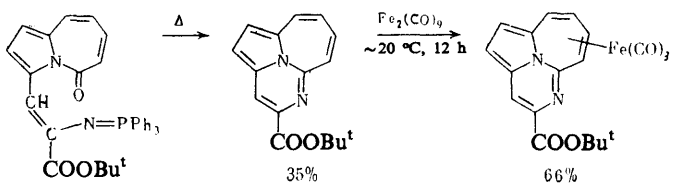
	a	b	c	d	e
R	Ph	Ph	H	Ph	Ph
R′	Cl	NO_2H	H	Cl	
R″	Me	H	H	Me	H

The analogous cyclisation of azidoacetyl(phenacyl)amines leads to 2-pyrazinones, even on conducting the reaction under argon, rather than the corresponding dihydro derivatives as would have been anticipated for an intramolecular aza-Wittig reaction.[15]



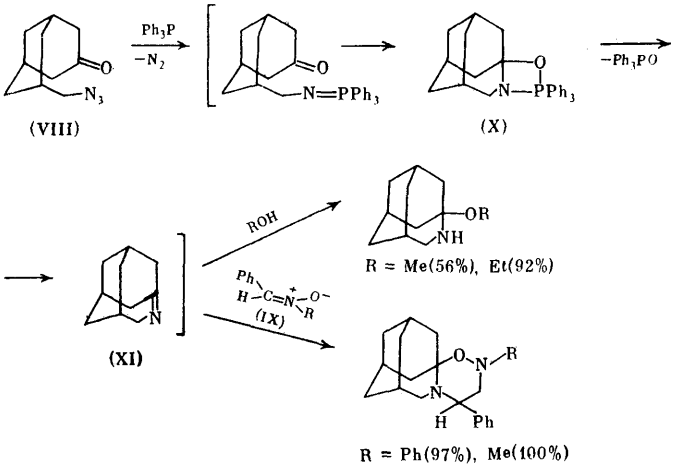
35—54%

The tricyclic system, 5,9-diazabenz[*c*,*d*]azulene, is formed by heating the phosphazo compound (VII) in toluene. The product is very unstable, but may be characterised as an iron tricabornyl complex.[16]



(VII) 35% 66%

Similarly, heating 3-azidomethylbicyclo[3.3.1]nonan-7-one (VIII) with triphenylphosphine in alcoholic media gave alkoxy-4-azahomoadamantanes, while reaction with triphenylphosphine and nitrones (IX) in benzene afforded compounds having the oxadiazinohomodamantane skeleton. By following the reaction of azide (VIII) with triphenylphosphine in deuteriochloroform with the aid of ^{1}H- and ^{13}C-NMR spectroscopy, it was shown that the conversion of the intermediate phosphazo compound into the oxazaphosphetane (X) is a rapid process by virtue of a favourable entropy factor, while the cleavage of (X) to the highly strained imine (XI) is slow. As a consequence, it is possible to characterise compound (X) spectroscopically.

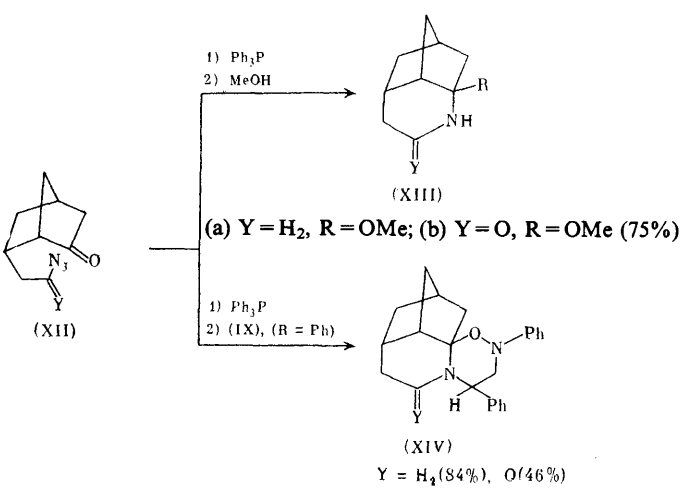


(VIII) (X) (XI)

R = Me(56%), Et(92%)

R = Ph(97%), Me(100%)

Azide (XII) affords 4-aza-4-homobrendane derivatives (XIII, XIV) in high yield with the same reagents under the same conditions. The unstable aminoacetal (XIIIa) was reduced with $LiAlH_4$ to the stable imine (XIII; Y = H_2, R = H) in 87% yield.[17]

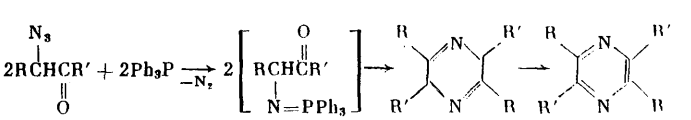


(XII) (XIII) (XIV)

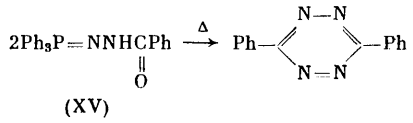
(a) Y = H_2, R = OMe; (b) Y = O, R = OMe (75%)

Y = H_2(84%), O(46%)

A number of heterocyclic systems has been obtained by double aza-Wittig reaction. Thus, pyrazine derivatives can be prepared conveniently by reaction of α-azidoketones with triphenylphosphine. In this case, two molecules of phosphazo compound, formed in the initial step of the reaction, participate in a "head-to-tail" double aza-Wittig coupling providing dihydropyrazines which undergo dehydrogenation to pyrazines during the reaction.[18]

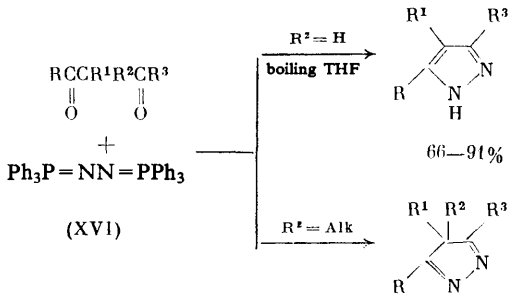


A similar sequence is involved in the preparation of 2,6-diphenyl-*s*-tetrazine from phosphazo compound (XV).[19]



(XV)

An original method has also been reported for the preparation of pyrazoles by condensation of β-ketones with phosphazine (XVI).[20] If there is one hydrogen atom on the α-carbon atom of the β-diketone, the reaction provides 1*H*-pyrazoles, but if the α-carbon is disubstituted by alkyl groups a double aza-Wittig reaction takes place to give 4*H*-pyrazoles.



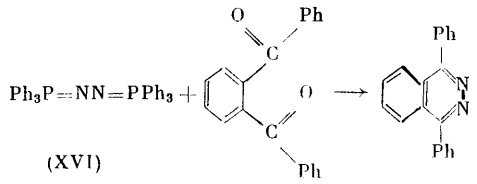
(XVI)

66—91%

R = Me, Ph; R^1 = H, Me; R^2 = H, Me; R^3 = Me, Ph.

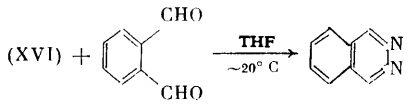
R = R^1 = R^2 = R^3 = Me, 38,4%

Treatment of *o*-dibenzoylbenzene with phosphazine (XVI) affords 1,4-diphenylphthalazine,[20] while *o*-phthalaldehyde gives phthalazine itself.[21]



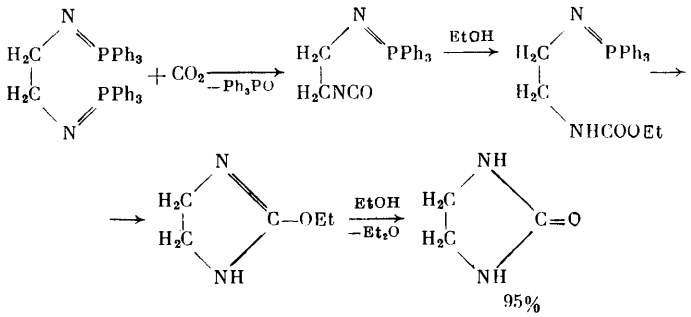
(XVI)

55%



77%

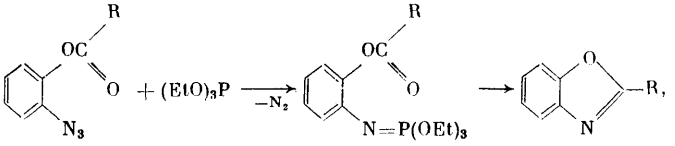
An excellent yield of 2-imidazolidone was obtained by passing carbon dioxide into an alcoholic solution of 1,2-*bis*(triphenylphosphazo)ethane. It is likely that reaction proceeds via isocyanate and urethan intermediates.[20]



95%

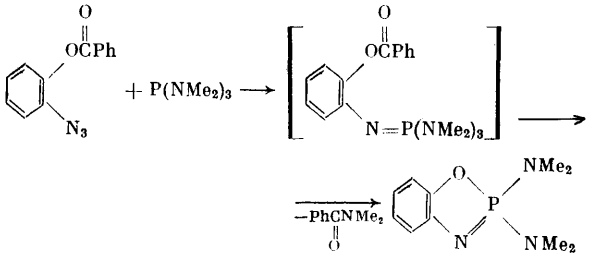
2. Cyclisation of phosphazoesters (of carboxylic acids)

The intramolecular condensation of phosphazo groups with esters requires somewhat harsher conditions than the condensation with ketones. Thus, cyclisation of the phosphazo compounds obtained by the exothermic reaction of *o*-acoxyazides with triethyl phosphite proceeds by prolonged heating in cyclohexane to give 2-substituted benzoxazoles.[22]

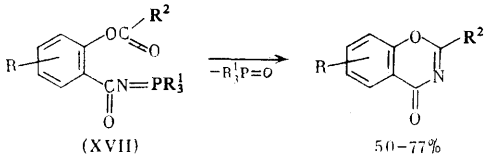


R = Me (69%), Ph (71%).

Interestingly, heating *o*-azidophenyl benzoate with hexamethylphosphorous triamide in cyclohexane for 24 h is accompanied by evolution of *N,N*-dimethylbenzamide, rather than hexamethylphosphoramide, to give 1,3,2-benzoxazaphosphole derivatives.[23]



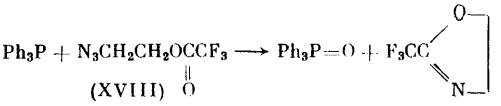
With salicyclic acid derivatives (XVII), intramolecular aza-Wittig reaction proceeds at room temperature in toluene, or on heating in a mixture of acetone and petroleum spirit, to give 4*H*-1,3-benzoxazin-4-ones, including the previously unknown 2-alkoxy derivatives.[24,25]



(XVII)

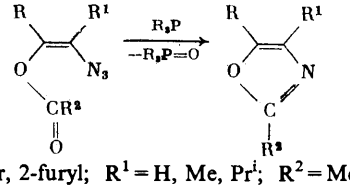
50—77%

At the same time, the azidoester (XVIII) reacts immediately with triphenylphosphine in the cold to give a high yield of 2-trifluoromethyl-2-oxazoline.[26]



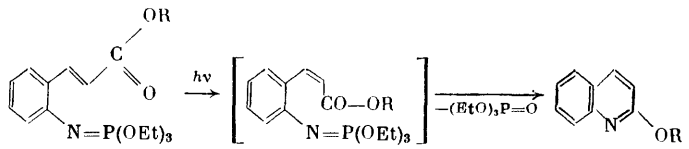
80%

The cyclisation of β-acoxyvinyl azides with trivalent phosphorus compounds (preferably triethyl phosphite) provides a suitable method of preparing oxazoles, which are used not only as blocking groups, but also as intermediates and as key components of alkaloids and macrocyclic antibiotics.[27]



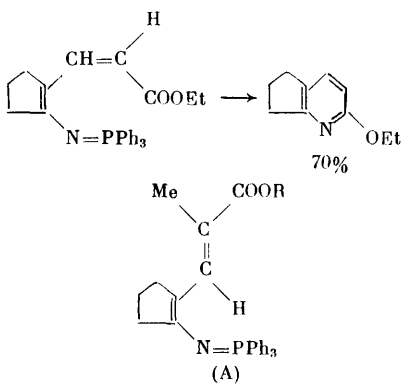
R = Ar, 2-furyl; R^1 = H, Me, Pr^i; R^2 = Me, Et, cyclopropyl, 2-furyl, 3-pyridyl.

Heating is not necessary for the cyclisation of *o*-phosphazocinnamic acids and their esters. Reaction takes place on irradiation (365 nm) for 30 minutes to give a high yield of 2-hydroxy-, 2-alkoxy- or 2-phenoxy-quinolines, probably as a result of an initial *trans*→*cis*-isomerisation.[28]

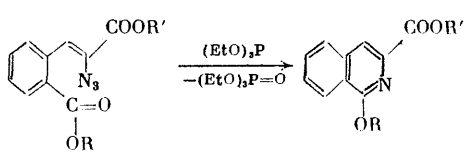


R = H, Me, C_6H_{11}(>75%), Ph(95%).

By studying the analogous cyclisation of 3-(2-triphenylphosphazocyclopent-1-enyl)-acrylates and -methacrylates, it was found that the ethyl acrylates react under harsh conditions (at 207 °C in boiling tetralin) to give a high yield of 2-ethoxycyclopenteno[*b*]pyridine. The corresponding methacrylate derivative did not cyclise under these conditions, probably as a result of the steric repulsion between the methyl and the phosphazo group. This stabilises the structure in the (*E*)-form (A) which is unfavourable for cyclisation.[29]

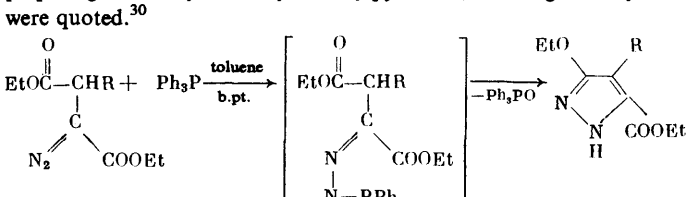


α-Azido-*o*-carboxy- and α-azido-*o*-carbethoxycinnamates react with triethyl phosphite at 20–50 °C to give the corresponding esters of 1-hydroxy- or 1-ethoxy-isoquinoline-3-carboxylic acid esters.[12]



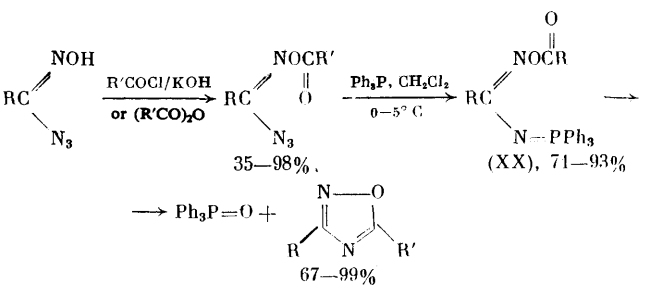
70—90%

The reaction of β-diazoesters with triphenylphosphine in heated toluene may be used for the preparation of 3-ethoxypyrazoles. The phosphazine (XIX) is an intermediate in this conversion. The authors of this work consider this to be a general method of preparing 3-ethoxy-5-ethoxycarbonylpyrazoles, although no yields were quoted.[30]



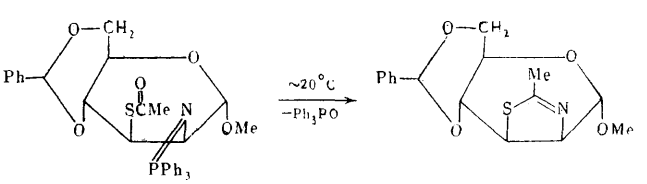
R = H, NHCOOEt. (XIX)

The carbonyl group of *O*-acyloximes may also participate in the aza-Wittig reaction. This has been incorporated as the final step in a convenient synthesis of 3,5-disubstituted 1,2,4-oxadiazoles, based on acylation of 1,1-azido-oximes, treatment of the intermediate with triphenylphosphine, and then heating the resulting phosphazo compound in toluene.[31] It was not possible to prepare 5-alkylamino-1,2,4-oxadiazoles by this route because the intermediate 1,1-phosphazo-oxime carbamates (XX, R′ = MeNH, EtNH) give a complex mixture of compounds on heating in toluene.



R = Ar; R′ = Me, EtO, Ar.

Ring closure of acetylthio compounds to give acid-resistant thiazole derivatives can be achieved by condensation with a neighbouring phosphazo group. This has been adapted for the protection of the 2-aminomercaptan function in the synthesis of thiosugars with potential biological activity. The phosphazo compound (XXI), obtained from the corresponding azidodeoxy-mannose derivative, has been shown to be stable in ether but is immediately converted into the thiazoline (XXII) on dissolution in chloroform.[32]



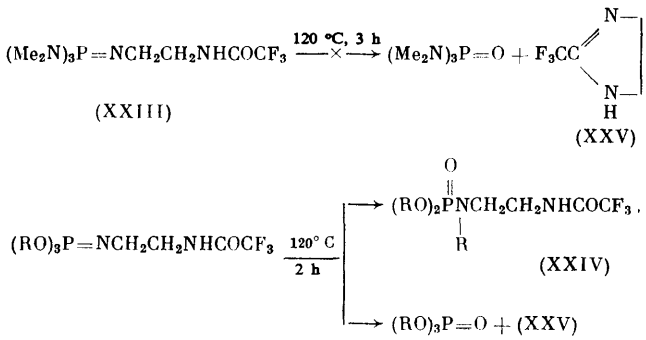
(XXI) (XXII)

3. Cyclisation of phosphazoamides

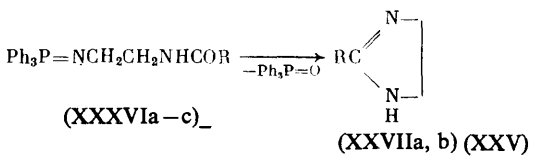
As the electrophilicity of the amide carbonyl group is lower than that of the ester group, phosphazo compounds generally do not react with carboxylic acid amides unless the amide group is activated by an additional acceptor group (see, for example, Ref. 33).

In those instances where intramolecular aza-Wittig reaction does take place with amides, the readiness to cyclise depends largely on the nature of the substituents on the phosphorus and amide nitrogen atoms. Thus, it has been found that phosphazo compound (XXIII) with dimethylamino groups on the phosphorous atom do not react,[34] while the analogues *N*-(trialkoxyphosphazoethyl) amides, based on trifluoroacetic acid, are converted to trialkyl phosphate and 2-trifluoromethyl-2-imidazoline (XXV), in addition to amide (XXIV) derived via imine-amide rearrangement. The more facile the

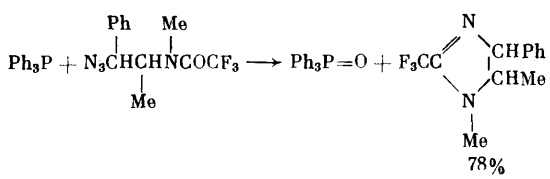
rearrangement into amide (XXIV), the lower the yield of imidazoline (XXV), being 1–1.5% for R = Et, and 27% for R = Bu.[35]



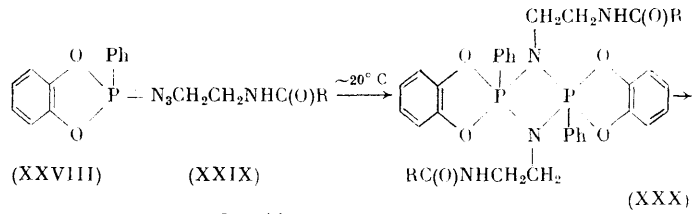
The tendency of phosphazoamides to cyclise is greater for compounds with a phenyl group on the phosphorus atom. Heating such compounds affords a high yield of imidazolines substituted in the 2-position by alkyl or aryl groups. Thus, triphenylphosphazo compounds (XXVI) based on acetamide and benzamide are converted into triphenylphosphine oxide and the corresponding 2-imidazoline (XXVIIa, b) at 180 °C; similarly, the trifluoroacetamide derivative (XXVIc) provides the imidazoline (XXV) at 120 °C, the yield of the three products being 72%, 91% and 80%, respectively.



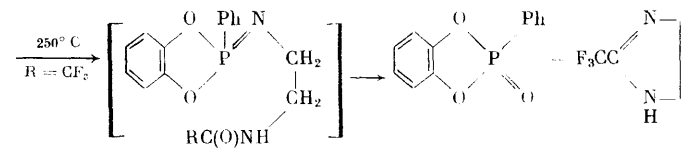
Substituted imidazolines are formed more readily by using phosphazo compounds derived from azidoamides with substituents on the chain linking the two reactive functions. Thus, in the reaction of triphenylphosphine with the azide obtained from racemic pseudoephedrine cyclisation to 4,5-disubstituted 2-imidazolines can be effected, even at room temperature, with associated cleavage of triphenylphosphine oxide. The intermediate phosphazo compound cannot be isolated.[26]



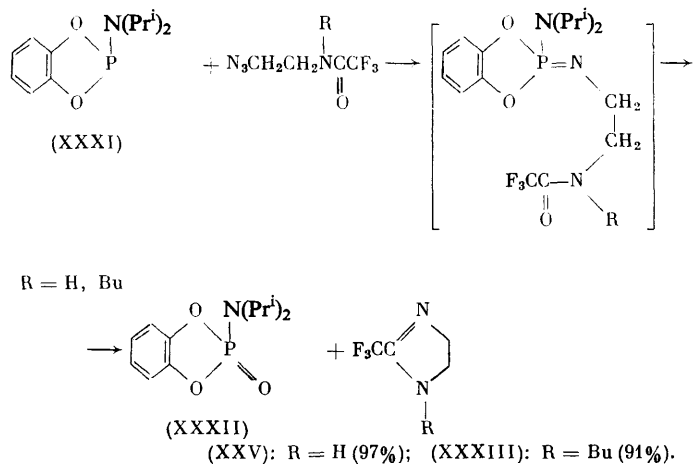
Phosphazo compounds derived from cyclic phosphorus(III) acid esters exhibit a noticeably different mode of cyclisation. Thus, interaction of the cyclic phosphonite (XXVIII) with azides (XXIX) affords exclusively the corresponding dimeric phosphazo compound (XXX), which may be converted to 2-imidazolines on heating to 250 °C, as exemplified below with (XXXc). It is possible that reaction is facilitated via initial thermal cleavage to a monomeric phosphazo compound.[26]



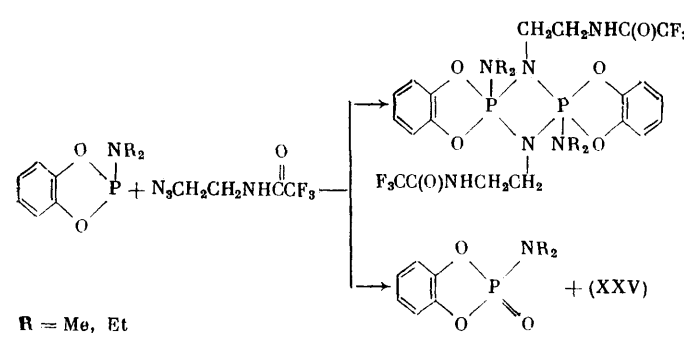
R = Me (a), Ph (b), CF_3 (c)



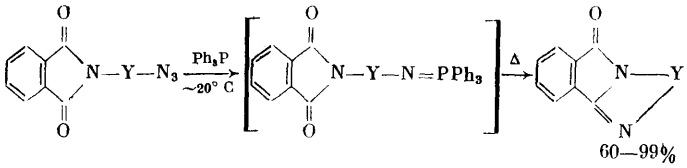
On the other hand, treatment of the pyrocatechol amidophosphite (XXXI) with azide (XXIXc) and its *N*-butyl derivative, even at 80 °C, affords the P-oxide (XXXII) and imidazolines (XXV) and (XXXIII), respectively. An intermediate situation obtains with the dimethylamino- and diethylamino-analogues of (XXXI). In each case, the interaction with azidoamide (XXIXc) proceeds with the simultaneous formation of a phosphazo compound and a mixture of imidazoline (XXV) and the corresponding catechol dialkylamidophosphate.[34,35]



(XXV): R = H (97%); (XXXIII): R = Bu (91%).



One of the carbonyl groups of cyclic imides (phthalimides, succinimides, glutarimides) participates in the aza-Wittig reaction by heating the appropriate phosphazo compounds in toluene or xylene. Five-, six- and seven-membered 1,3-diazaheterocyclics are thereby obtained.[36]



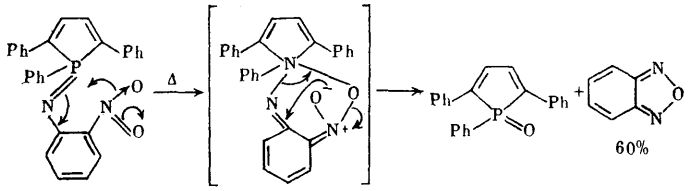
Y = $(CH_2)_n$ (n = 2—4), o-$CH_2C_6H_4$, o-$CH_2C_6H_4CH_2$



n = 2,3 92%

4. Cyclisation of nitrophosphazo compounds

On heating the *o*-nitrophosphazobenzene (XXXIV), derived from 1,2,5-triphenylphosphole, in mesitylene, aza-Wittig ring closure takes place with participation of the nitro group to give benzofurazan in 60% yield. The nature of the substituent on the phosphorus atom has a marked effect on the course of this reaction. Thus, the analogous phosphazo compound derived from triphenylphosphine and triethyl phosphite do not undergo ring closure, while the trichlorophosphazo analogue affords benzofurazan in the same way.[37]

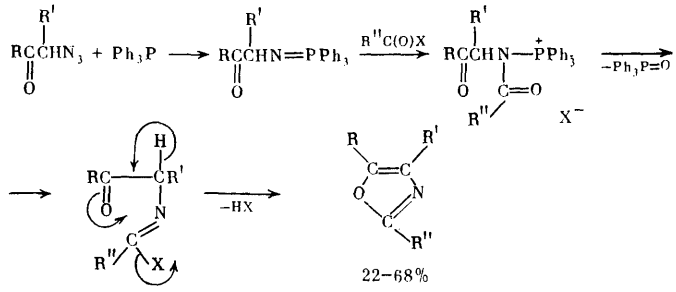


(XXXIV)

III. Syntheses where the aza-Wittig reaction is included in a multi-step route

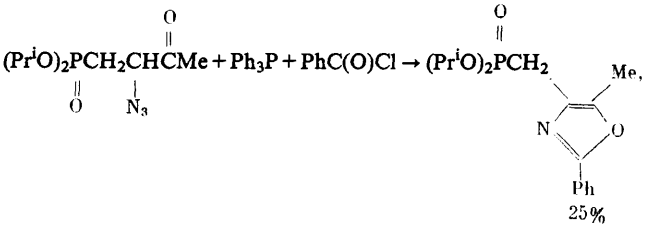
1. Acylation and aza-Wittig reaction

Oxazoles with a wide variety of substituents may be obtained by three-component reaction of triphenylphosphine, acyl halides, and α-azidoketones possessing an α-hydrogen atom. The synthesis, which takes place at room temperature, involves an initial Staudinger reaction, followed by acylation of the *in situ*-formed phosphazo compound, and aza-Wittig cyclisation of the resulting β-ketoimidoyl halide with liberation of triphenylphosphine oxide.[38]

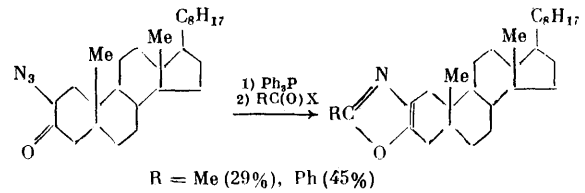


Although hydrogen halide is formed in the last step of the reaction, no additional base is required to trap it. This is possibly why 1.5—2 equivalents of triphenylphosphine are required, and may explain the moderate yield of oxazole.

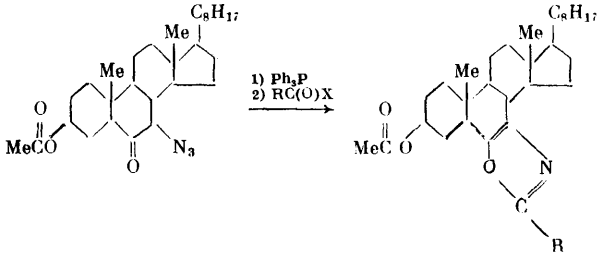
The same reaction has been applied for the preparation of phosphorylated oxazoles.[39]



It has also been adapted for annelation of the oxazole ring to the steroid skeleton for the synthesis of cholest-2-eno[2,3-*d*]oxazoles and cholest-6-eno[7,6-*d*]oxazoles.[40]



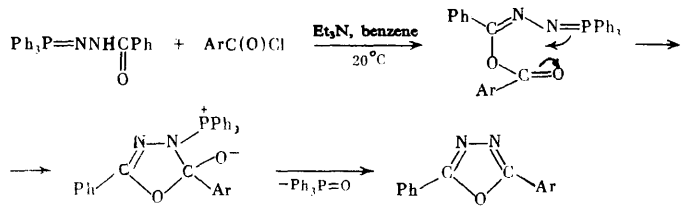
R = Me (29%), Ph (45%)



R = Me (29%), Ph (21%), $PhCH_2$ (36%), EtOOC (42%).

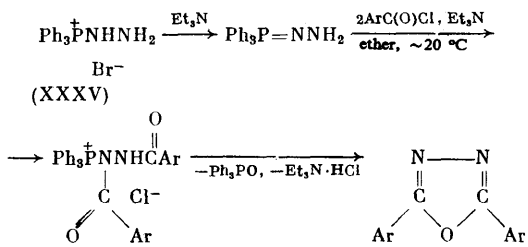
Extension of this reaction to phosphazo compounds having an acylamino group on the imine nitrogen leads to an effective mixture of preparing 1,3,4-oxadiazoles. In this case, reaction is carried out in

the presence of base (butyllithium[3] or triethylamine[19]), and the yield exceeds 90% in certain cases.

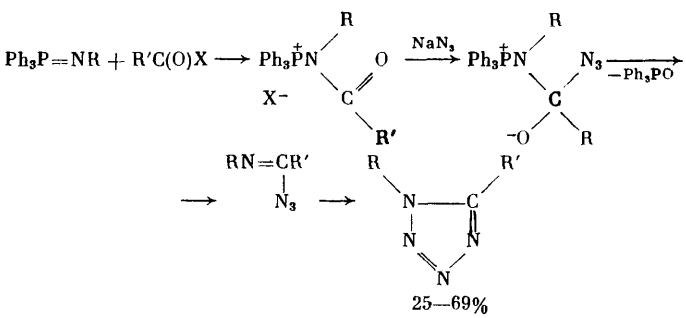


Ar = Ph, $4\text{-}O_2NC_6H_4$, $3,5\text{-}(O_2N)_2C_6H_3$, $4\text{-}BrC_6H_4$.

In a similar way, symmetrically substituted 1,3,4-oxadiazoles are obtained by treatment of phosphonium salts (XXXV) with an excess of triethylamine and two equivalents of aroyl halide.[19]



Tetrazoles may be obtained by interaction of phosphazo compounds with acyl halides and sodium azide under mild conditions (in benzene at room temperature). In certain cases, acyl azides may be used efficiently in place of the acyl halide and NaN_3.

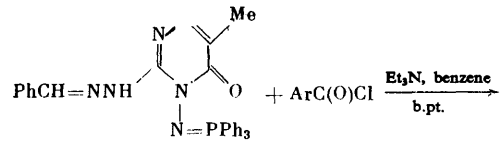


25—69%

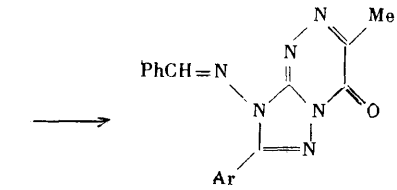
R = Ar, 2-pyridyl, R′ = Alk, alkenyl, alkadienyl.

Under these conditions, trifluoroacetic acid derivatives are converted to acylic imidoyl azides which exist in equilibrium with the corresponding tetrazole. Phosphazo compounds with trimethylsilyl, *tert*-butyl and methoxymethyl groups do not form tetrazoles as reaction proceeds by another pathway.[41]

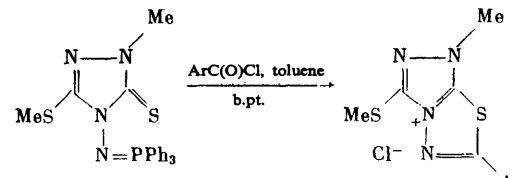
N-Phosphazohetaryls with adjacent benzylidenehydrazino, thione or aldimine groups undergo ring closure with acyl chlorides to give bicyclic systems. Thus, heating triazine (XXXVI) with aromatic aroyl chlorides and triethylamine in benzene affords 1,2,4-triazolo-[5,1-c][1,2,4]triazines,[42] while heating triazole (XXXVII) with acyl chlorides in toluene gives 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazolium salts;[43] the interaction of pyrazoles (XXXVIII) with aroyl chlorides yields pyrazolo[5,4-*d*]pyrimidinium fluoroborates at room temperature.[44]



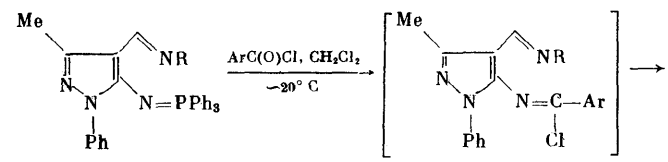
(XXXVI)



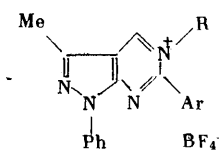
68—80%



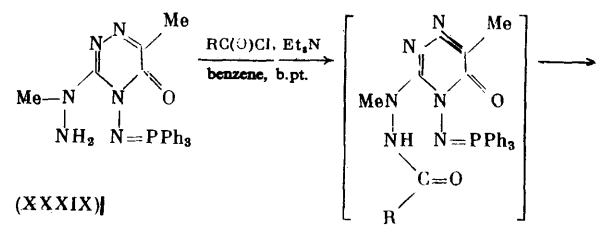
(XXXVII) 48—67%



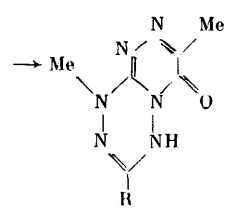
(XXXVIII)



In a similar way, the 4-triphenylphosphazo-3-(1-methylhydrazino)-1,2,4-triazine (XXXIX) with acyl chlorides yields the corresponding *N*-condensed 1,2,4,5-tetrazine derivatives on heating in benzene containing triethylamine.



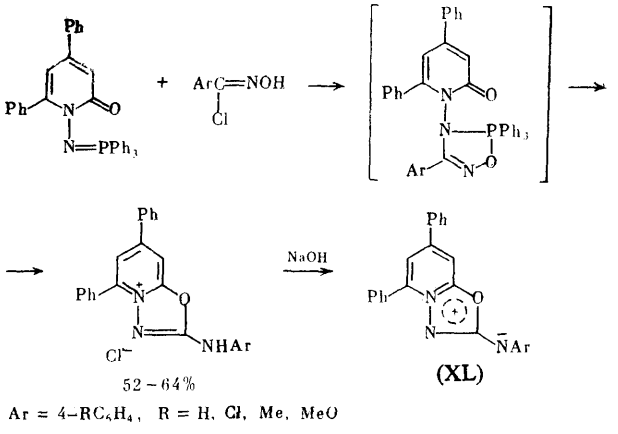
(XXXIX)



37—64%

An intermediate acylhydrazine has been isolated by acylation of the triazine (XXXIX) at room temperature.[45]

The interaction of 1-triphenylphosphazo-4,6-diphenyl-2-pyridone with 1,1-oximinochlorides on heating in benzene is accompanied by C→N-aryl migration to give 1,3,4-oxadiazolo[3,2-*a*]pyridinium chlorides in moderate yield. The structure of the product has been confirmed by its dehydrochlorination to the mesoionic heterocycle (XL) which has been prepared by an independent route.[46]

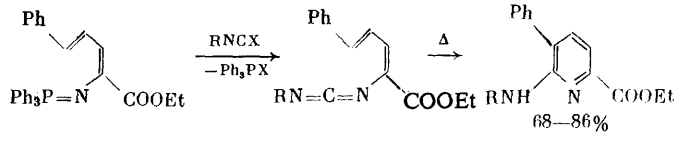


Ar = 4-RC$_6$H$_4$, R = H, Cl, Me, MeO

2. Aza-Wittig reaction and cyclisation

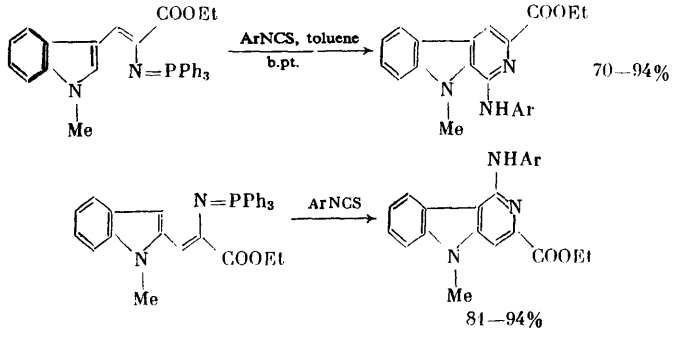
The commonest sequence of this type comprises the interaction of phosphazo compounds with heterocumulenes, such as isocyanates and isothiocyanates. Reaction proceeds via ring closure of an intermediate carbodiimide which, in most cases, is not isolated.

Pyridine derivatives were the first to be prepared by this route, involving ring closure of unsaturated carbodiimides. The preparation of 6-arylaminopicolinic acid esters illustrates the methodology. Here, the phosphazo compound interacts with alkyl or aryl isocyanates or isothiocyanates in toluene at room temperature to give the corresponding carbodiimide which cyclises on heating in the same solvent. The intermediate carbodiimides can be isolated as oils following column chromatography.[47,48]

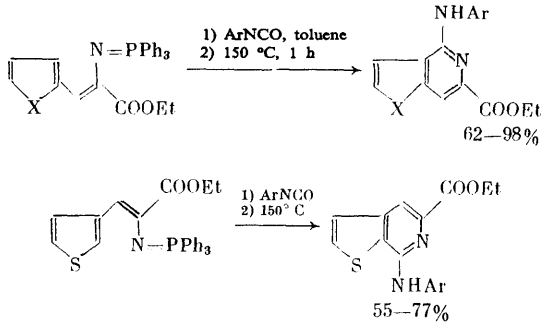


R = Et, Bu^t, Ph, Ar; X = O, S.

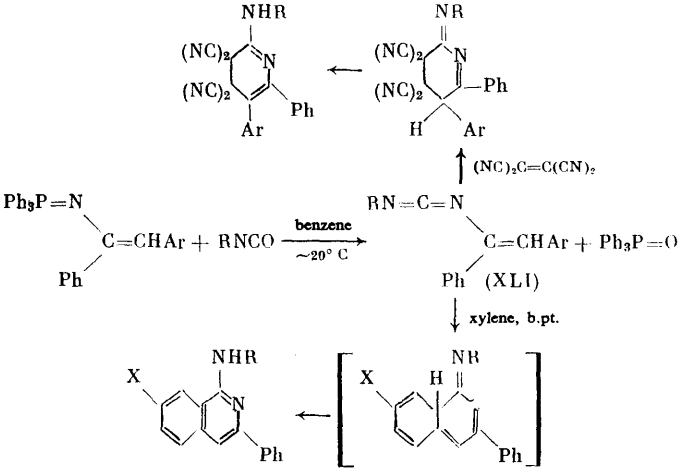
Derivatives of β- and γ-carbolines have been prepared similarly:[49]



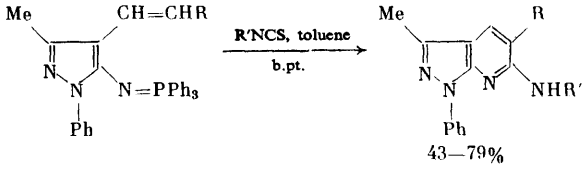
The method has also been applied to the synthesis of thieno- and furo-[3,2-*c*]pyridines as well as thieno[2,3-*c*]pyridines.[50,51]



1-Arylaminoisoquinolines have been synthesised by high-temperature ring closure of unsaturated carbodiimides (XLI), obtainable from the corresponding phosphazo compound and isocyanate. [4+2]-Cycloaddition of this enecarbodiimide to tetracyanoethylene leads to tetrahydro- or dihydro-pyridines, depending on the nature of the substituent.[52]

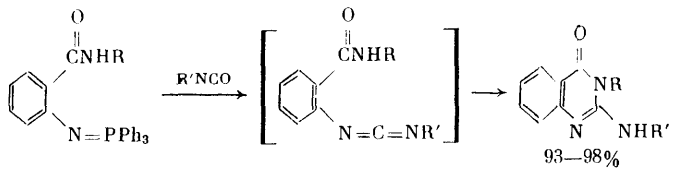


The carbodiimide group can also interact with a neighbouring carbon-carbon double bond activated by a strong electron-accepting group. This is exemplified by the synthesis of 6-aminopyrazolo-[3,4-*b*]pyridines, formed by annelation of the pyridine ring onto a pyrazole derivative.[53]

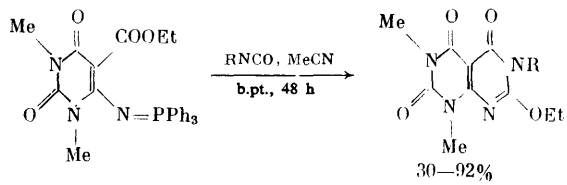


R = MeCO, NO_2; R' = Me, allyl, Ar.

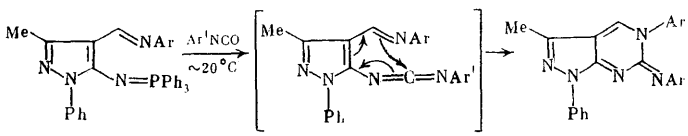
Quinazoline derivatives have been prepared in almost quantitative yield by reaction of *o*-phosphazobenzamides with isocyanates. This is the first example of an intramolecular addition of an amide group to a carbodiimide. The intermediate formation of a carbodiimide is confirmed both by its isolation in the case of *N,N*-disubstituted amides and by the formation of *o*-ureidobenzonitriles by reaction of *N,N*-unsubstituted benzamides.[54]

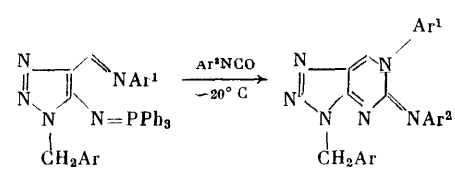


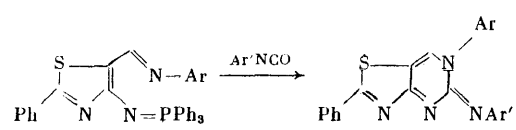
Annelation of the pyrimidine ring can be achieved by cyclisation of a carbodiimidoheterocycle having an *o*-substituted carbethoxy group. Reaction proceeds in refluxing acetonitrile without isolation of the carbodiimide. The resulting pyrimido[4,5-*d*]pyrimidines display a variety of physiological activities.[51]



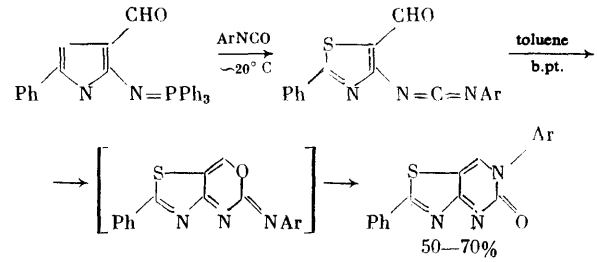
Similarly, annelation of the pyrimidine ring to pyrazole, triazole and thiazole derivatives can be achieved, even at room temperature, by ring closure of carbodiimides with neighbouring aldimine groups. In this way, pyrazolo[5,4-*d*]pyrimidines, 1,2,3-triazolo[5,4-*d*]pyrimidines and thiazolo[4,5-*d*]pyrimidines, having an arylimino group in the 2-position of the pyrimidine ring, have been prepared in high yield,[44,55]



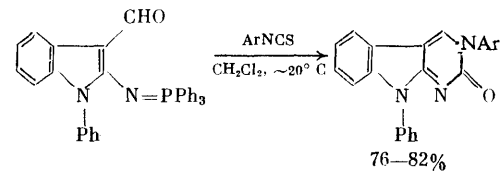




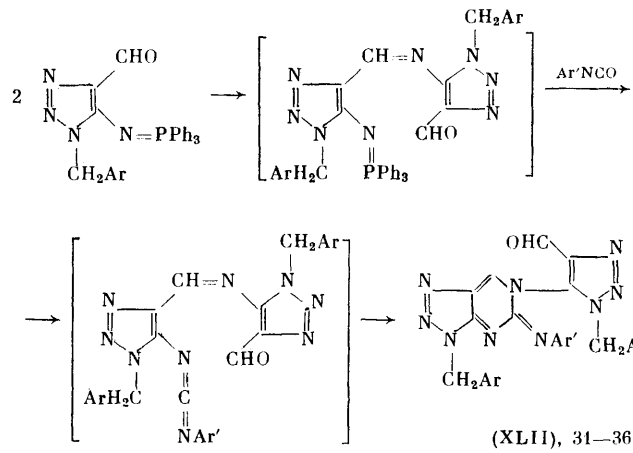
Carbodiimides have also been prepared by interaction of 2-phenyl-4-triphenylphosphazothiazole-5-carboxaldehyde with aryl isocyanates at room temperature. However, the subsequent ring closure to thiazolo[4,5-*d*]pyrimidin-5-ones requires heating in toluene, and is evidently associated with Dimroth rearrangement of the intermediate thiazolo[4,5-*d*]-1,3-oxazines.[44]



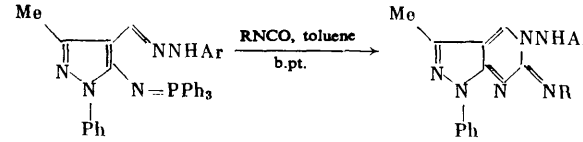
Dimroth rearrangement is also evident in the reaction of a 2-phosphazoindole-3-carboxaldehyde with aryl isothiocyanates, providing pyrimido[4,5-*b*]indoles in methylene chloride at room temperature.[49]



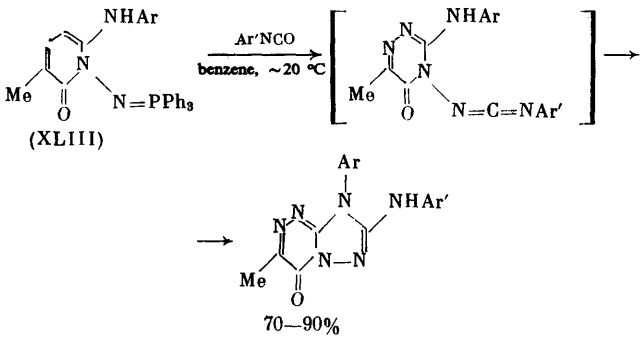
There is no reaction between 5-triphenylphosphazo-1,2,3-triazole-4-carboxaldehydes and aryl isocyanates at room temperature, while heating in toluene affords a more complex product (XLII). Formation of the latter can be explained by an initial aza-Wittig reaction involving the phosphazo group of one molecule with the aldehyde group of a second molecule; the aryl isocyanate then condenses with the remaining phosphazo group, and the intermediate carbodiimide cyclises as before.



Aryl isocyanates react readily on heating with 4-hydrazono-5-phosphazopyrazoles in toluene to give pyrazolo[5,4-*d*]pyrimidines having an arylamino group on a nitrogen atom of the pyrimidine ring.[44]

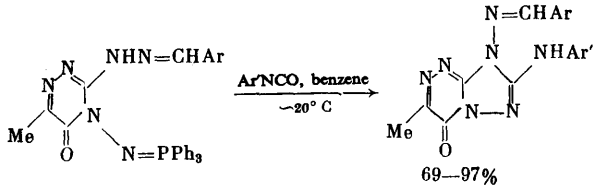


Annelation of the 1,2,4-triazole ring can be achieved by interaction of aryl isocyanates with hetaryls having a phosphazo group on an endocyclic nitrogen atom and an adjacent *o*-arylamino functionality. Thus, 1,2,4-triazolo[5,1-*c*]-1,2,4-triazines are obtainable in high yield by reaction of aryl isocyanates with phosphazotriazines (XLIII), even at room temeprature.[56]

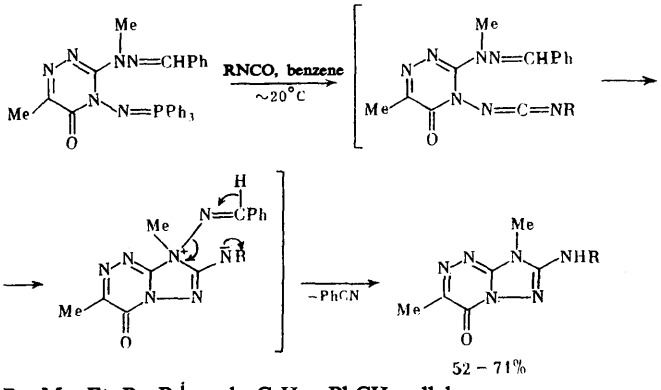


(XLIII)

The reaction also proceeds smoothly on replacing the arylamino group in the starting phosphazo compound by a benzylidenehydrazino group. In this case, the method provides 1,2,4-triazolo-[5,1-*c*][1,2,4]triazines having a benzylideneamino group on the triazole ring.

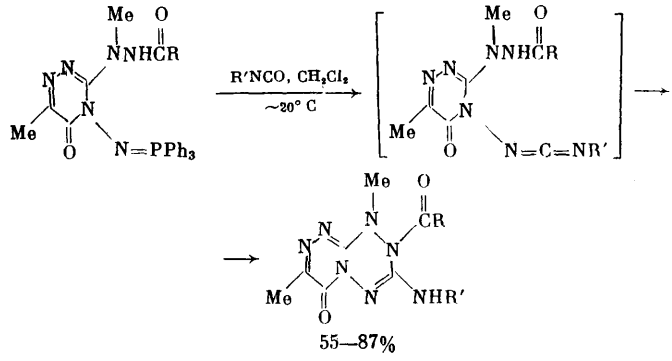


Reaction with the *N*-methylbenzylidenehydrazino analogue of the above phosphazo compound also proceeds under mild conditions, but in this case the benzylideneamino group is eliminated as benzonitrile.[57]

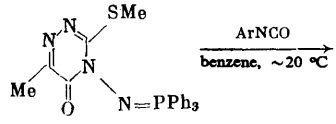


R = Me, Et, Pr, Pr^i, cyclo-C_6H_{11}, $PhCH_2$, allyl.

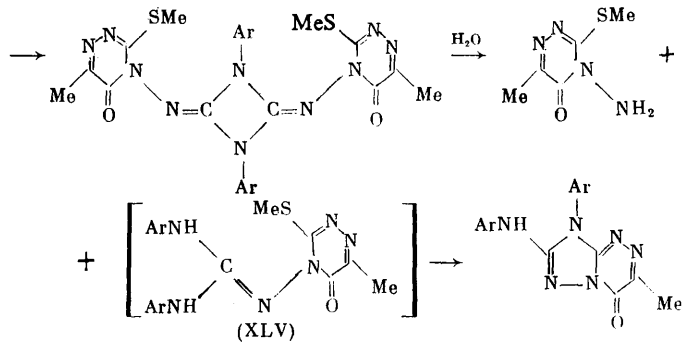
Molina et al. have reported what in their view is the first example of ring closure of a carbodiimide with a hydrazide group. Thus, 1,2,4-triazino[4,3-*b*]-1,2,4,5-tetrazines have been obtained by reaction of aryl isocyanates with 1,2,4-triazines having a phosphazo group at the 4-position and an acylhydrazino group at the 3-position.[57]



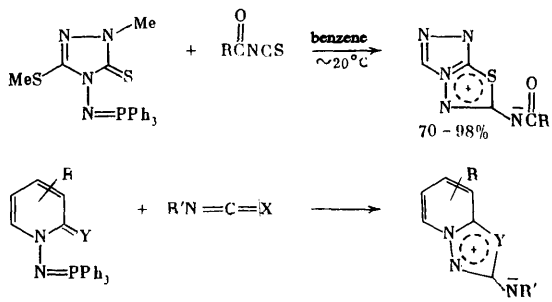
On the other hand, the 2-methylthio analogue (XLIV) reacts quite differently. Treatment with aryl isocyanates at room temperature affords a stable carbodiimide dimer, which can be converted to 1,2,4-triazole[5,1-*c*][1,2,4]triazines by prolonged heating in 85% aq. ethanol. It is likely that reaction proceeds via a guanidine intermediate (XLV).[42]



(XLIV)

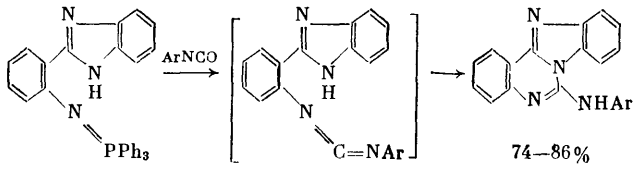


Fusion of a ring onto an *N*-phosphazohetaryl is also possible by reaction of the intermediate carbodiimide with a neighbouring oxo or thioxo group. However, in such cases mesoionic bicyclic systems are formed. Thus, 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazolium-6-aminides[43] are obtained by interaction of 4-triphenylphosphazo-1,2,4-triazoline-3-thiones with acyl isothiocyanates at room temperature, while salts (XLVI) are formed by reaction of 1-phosphazo-2-pyridones and -2-pyridinethiones with isocynates and isothiocyanates under the same conditions.[46,58,59]



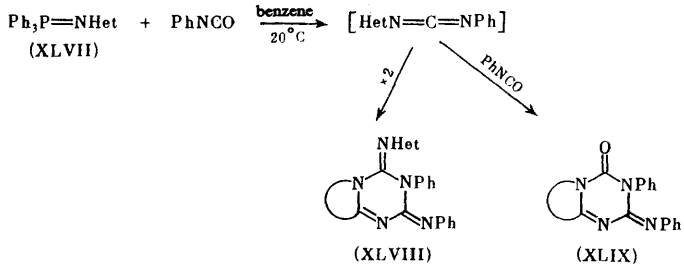
X, Y = O or S.

Ring closure of the carbodiimide function with an imino group can also take place, as in the synthesis of benzimidazo[1,2-*c*]-quinazolines from 2-(*o*-phosphazophenyl)benzimidazoles.[54]



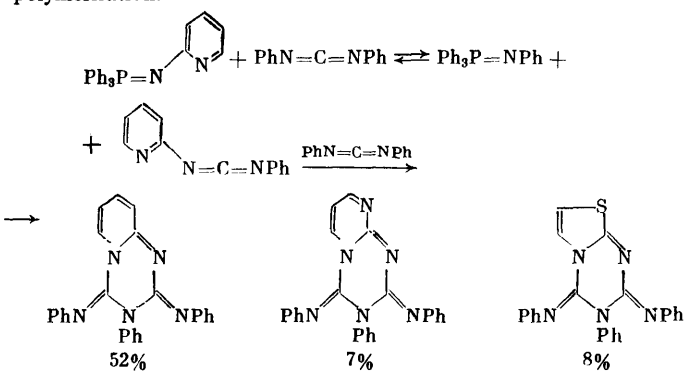
2-Triphenylphosphazohetaryls (XLVII) without an associated functionality react with phenyl isocyanate via intermediate carbodiimides to give either the corresponding carbodiimide dimers (XLVIII) or the bicyclic compound (XLIX), formed by cycloaddition of the carbodiimide with a second isocyanate molecule. In each case, reaction provides an *N*-condensed 1,3,5-triazine system. The proportion of the two products depends on the order of addition of the reactants: by addition of the phosphazo compound (XLVII) to phenyl isocyanate only compound (XLIX) is formed, whereas gradual addition of the isocyanate to the phosphazo compound normally affords a mixture of both products; the phosphazo-quinoline derivative is an exception in that only the product of type (XLIX) is obtained under the latter conditions.

The interaction of phosphazo compound (XLVII) with phenyl isothiocyanate requires a higher temperature than the corresponding reaction with phenyl isocyanate, and the reaction time is much longer. It leads primarily to the product of type (XLVIII).[60]

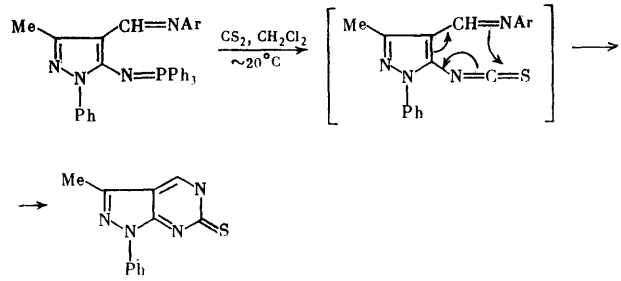


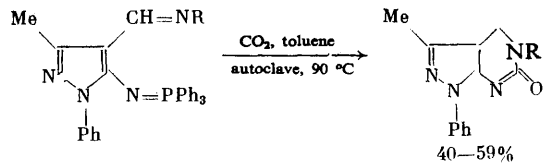
Het = 2-pyridyl, 2-quinolyl, 2-pyrimidyl, 2-thiazolyl

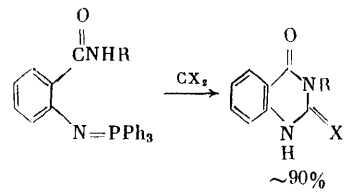
Phosphazohetaryls react with diphenylcarbodiimide on heating in benzene. As with phenyl isocyanate, the reactants condense in 1 : 2 proportion, affording again a condensed 1,3,5-triazine system with two phenylimino groups. The yield of the pyrido[1,2-*a*]-[1,3,5]triazine analogue, from 2-(triphenylphosphazo)pyridine and diphenylcarbodiimide, is respectable (52%), but normally the yield is poor, as in the case of the pyrimidino- and thiazolo-analogues (7–8%), because of the susceptibility of the carbodiimide to polymerisation.[61]



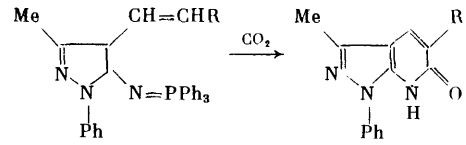
A variety of condensed ring systems have been secured by reaction of carbon dioxide or carbon disulphide with phosphazo compounds via intramolecular condensation of the resulting isocyanates or isothiocyanates with neighbouring aldimine,[44,45] amide or imine groups,[54] as well as with electron-deficient carbon-carbon double bonds.[53] Bicyclic α-oxo- or α-thioxo-*N*-heterocyclics are thereby obtained, for example:



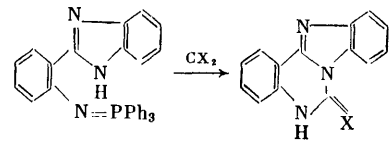




X = O, S,

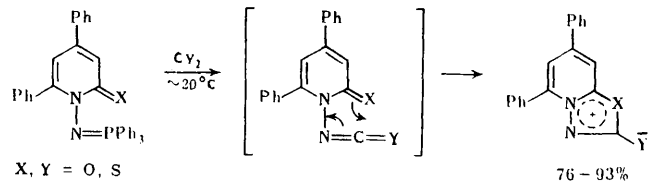


R = MeC(O), NO_2

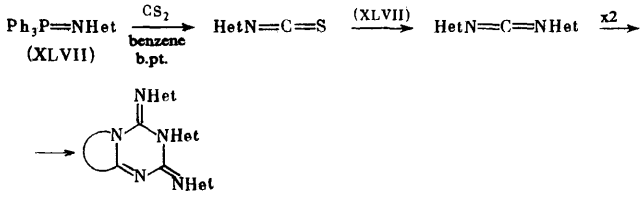


X = O, S.

Mesoionic bicycles are formed by interaction of *N*-phosphazo-α-oxo- or *N*-phosphazo-α-thioxo-*N*-heterocyclics with carbon dioxide or carbon disulphide.[58,59]

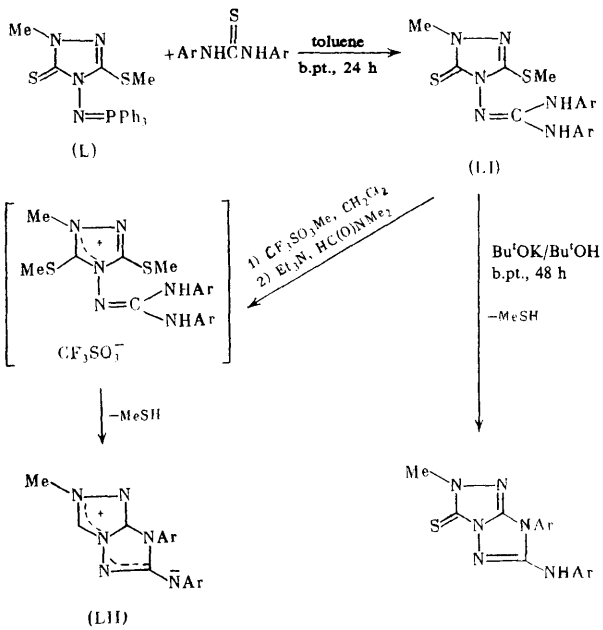


In the absence of a neighbouring functionality, the isothiocynates, obtained as intermediates by reaction of 2-triphenylphosphazohetaryls with carbon disulphide, condense with a second molecule of the phosphazo compound to give the corresponding *N,N'-bis*(hetaryl)carbodiimides which cyclodimerise as shown below.[60]

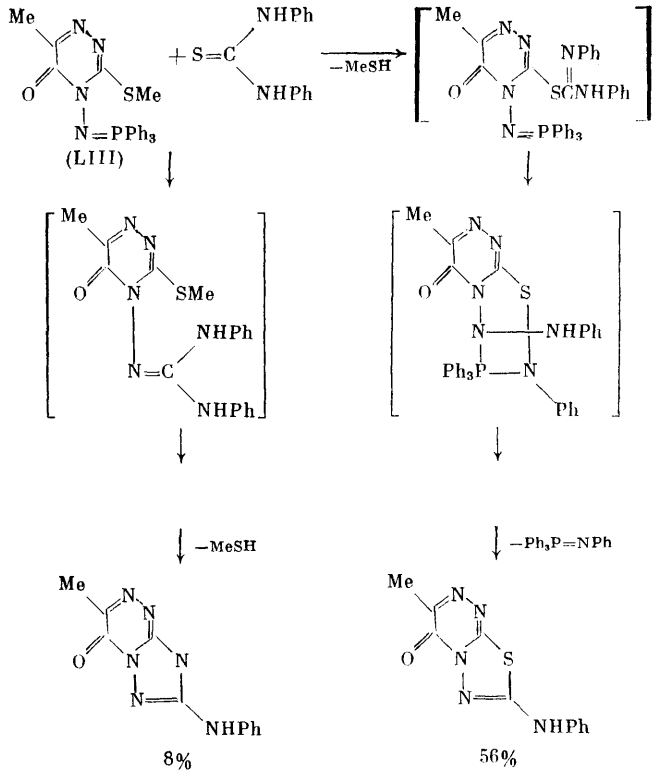


Het = 2-pyridyl, 2-thiazolyl, 2-quinolyl, 2-benzothiazolyl

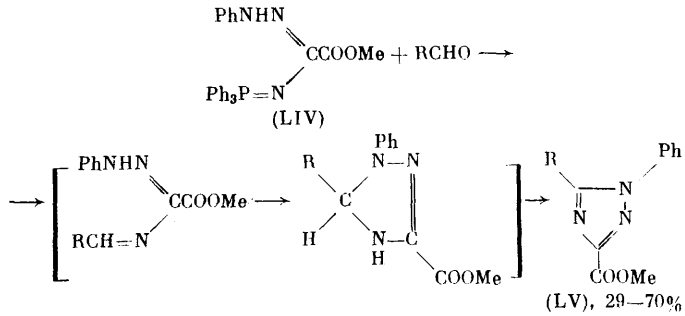
Ring closure to bicyclics can also be achieved by aza-Wittig reaction of phosphazohetaryls with *N,N'*-diarylthioureas. Thus, heating the latter with methylthio-substituted phosphazo compound (L) in toluene affords the guanidine derivative (LI) which cyclises to 1,2,4-triazolo[4,3-*b*]-1,2,4-triazoles in strongly basic media. However, treatment of the guanidine (LI) with methyl triflate followed by triethylamine in dimethylformamide provides the bicyclic betaine (LII).[62]



Two reactions take place in parallel on heating the related 4-phosphazo-1,2,4-triazine (LIII) with *N,N'*-diphenylthiourea in benzene: a small amount of 1,2,4-triazolo[5,1-*c*]-1,2,4-triazine is formed by the same route as shown above for the reaction with (L); however, the principal product is a fused thiadiazole—a 1,3,4-thiadiazolo[2,3-*c*]-1,2,4-triazine derivative—formed by condensation of the thiourea with the methylthio group of (LIII) followed by intramolecular condensation of the intermediate isothiourea with the phosphazo group.[42]



5-Substituted monocyclic 1,2,4-triazoles (LV), including derivatives with heterocyclic residues, may be prepared from phosphazohydrazones (LIV) and the appropriate aldehyde in benzene or toluene. Such products have potential pharmacological activity. It is suggested that the intermediate triazolines are oxidised in the last step of the reaction by atmospheric oxygen.[63]

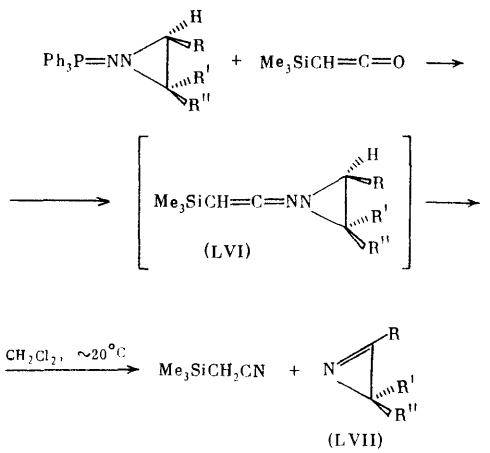


R = H, Me, Pr^i, 4-O2NC6H4, 4-pyridyl, 2-furyl, 2-pyrrolyl.

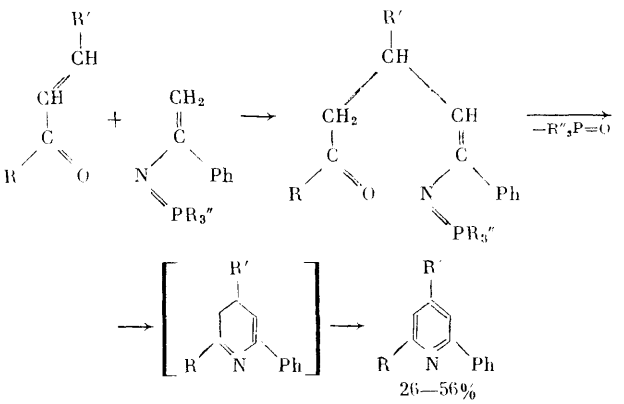
3. Other syntheses incorporating an aza-Wittig reaction

N-(1-Aziridinyl)trimethylsilylketenimines (LVI), obtained by aza-Wittig reaction from *N*-(triphenylphosphazo)aziridines and trimethylsilylketene, may be converted to 2*H*-azirines (LVII) by

elimination of trimethylsilylacetonitrile. The facility of this process depends on the nature of the substituents on the ring and their relative stereochemistry: the *cis*-2,3-diphenyl derivative (LVI, R = R″ = Ph, R′ = H) decomposes at room temperature to give azirine (LVII, R = R′ = Ph; R″ = H) in 70% yield (half-life 15 min), while the *trans*-isomer affords only 25% of this product with a half-life of 24 h.[64]

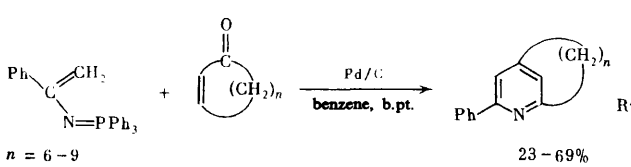


It is considered that the formation of 2-phenylpyridines from α-phosphazostyrenes and α,β-unsaturated ketones involves an initial Michael addition followed by an intramolecular aza-Wittig reaction. Evidently, reaction proceeds via oxidation of the intermediate dihydropyridines.[65,66]

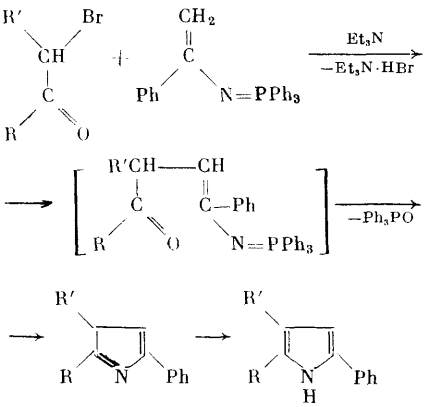


R = Me, Ph; R′ = H, Me, Ph; R″ = Ph, Bu.

[*n*](2,4)Pyridinophanes have been prepared similarly from cyclic α,β-unsaturated ketones with 9 – 12 carbon atoms.[67]

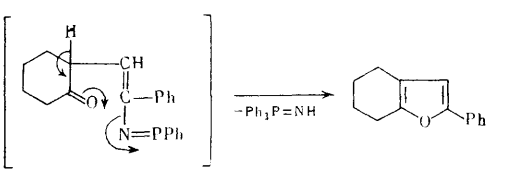


The synthesis of 2-phenylpyrroles from α-phosphazostyrenes and α-bromoketones in the presence of triethylamine is also thought to involve an initial carbon-carbon bond formation, followed thereafter by intramolecular aza-Wittig reaction.[65,68]

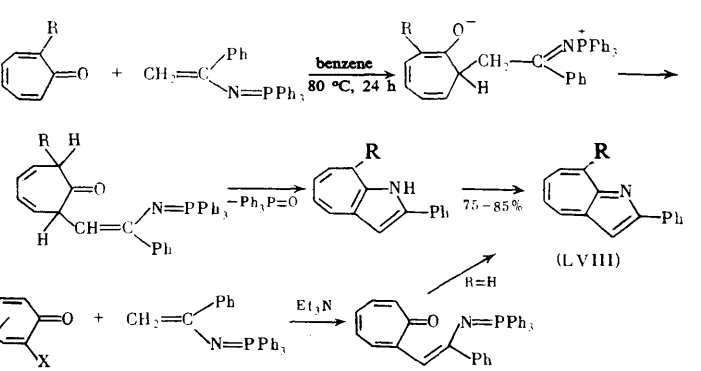


R = Ar, Me; R′ = H, Me, Ph or R + R′ = $(CH_2)_n$ (*n* = 4,5).

The same reaction with 2-bromocyclohexanone proceeds similarly to give the anticipated 2-phenyltetrahydroindole in 20% yield, together with 12% of 2-phenyl-4,5-tetramethylenefuran. The latter arises by ring closure of the intermediate γ-phosphazoketone with elimination of triphenylphosphine imine.[68]

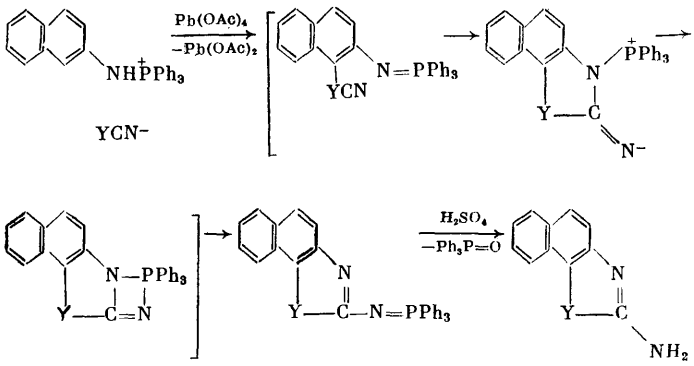


Two methods of preparing 2-phenyl-1-azaazulenes from α-phosphazostryenes have been reported. In a two-step procedure, 2-substituted tropones condense with an α-phosphazostyrene on heating in benzene to give 2-phenyl-8*H*-cycloheptanopyrroles, which are oxidised with nickel peroxide or manganese dioxide to give (LVIII). However, treatment of 2-halogenotropones with an α-phosphazostyrene in the presence of triethylamine leads to the 2-phenyl-1-azaazulenes (LVIII) in one step.[69,70]



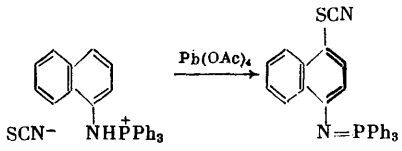
2,7-Diobromo-, 2,4,7-tribromo- and 2,3,5,7-tetrachloro-tropones react similarly to give the corresponding 1-azaazulenes in low yield.[70]

It is likely that oxidation of (2-naphthylamino)triphenylphosphonium thiocyanate and selenocyanate with lead tetraacetate also proceeds through an intermediate phosphazo compound. The interaction involves incorporation of the pseudohalide ion in the 1-position of the naphthalene ring, followed by a rather unusual cyclisation, which can be considered as an aza-Wittig reaction with participation of the cyano group; this is accompanied by an *N*-triphenylphosphino group migration. 2-Triphenylphosphazonaphtho[2,1-*d*]-thiazole and -selenazole are thereby obtained in 60–70% yield, and may be converted to the corresponding 2-aminoderivatives in 70–80% yield on hydrolytic cleavage.[71]

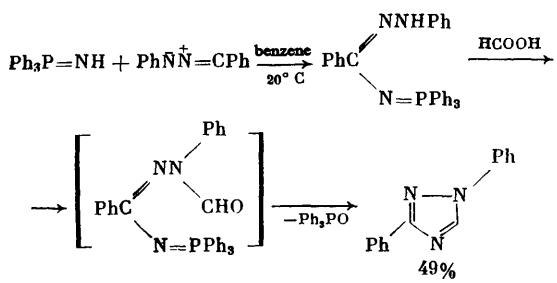


Y = S, Se

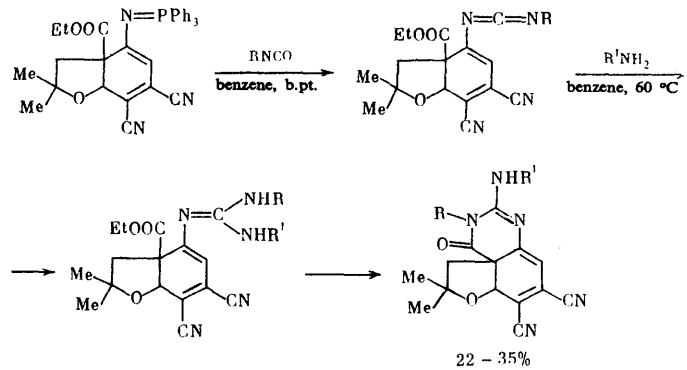
The suggested formation of a 1-thiocyano-2-phosphazonaphthalene in the first stage of the reaction was confirmed by the fact that similar oxidation of 1-naphthylaminotriphenylphosphonium thiocyanate, in which the 1-position is occupied, results in incorporation of the thiocyano group at the *para*-position to give 4-thiocyanato-1-triphenylphosphazonaphthalene in 65% yield.[71]



1,3-Diphenyl-1,2,4-triazole may be prepared via addition of triphenylphosphine imine to the 1,3-dipole, diphenylnitrilimine, followed by cyclisation of the resulting phosphazohydrazone on treatment with formic acid. It is most likely that ring closure proceeds by intramolecular aza-Wittig reaction after *N*-formylation of the intermediate hydrazone.[72]



The pyrimidine ring can be obtained via ring closure of an intermediate carbodiimide having a neighbouring carbalkoxy group, as shown below.



In the presence of an amine, reaction is complicated by formation of an intermediate guanidine, which condenses with the carbalkoxy group to give a low yield of furo[3,2-*e*]quinazolines.[73]

As is apparent from the data which has been collected, many types of N-heterocycle can be synthesised by the aza-Wittig reaction. These range from simple monocyclic compounds to complex polycyclic systems. The phosphazo groups—one of the components of this reaction—is readily prepared, notably from azides, and is resistant to a wide range of reagents. It can thus be retained while adjacent functionalities are manipulated, and then undergo intramolecular condensation as required to give heterocyclic compounds with a variety of different substituents.

In many cases, the resulting compounds are physiologically active or are of potential value as intermediates in the synthesis of physiologically active compounds including analogues of natural products.

A whole range of polycyclic compounds is available for the first time, and for many syntheses the aza-Wittig route is clearly more advantageous than alternative methods. The structures of the new heterocyclic compounds have been established, in most cases, by spectral data, by independent syntheses, and/or by studying their chemical properties.

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Translated from *Uspekhi Khimii* **60** 317–338 (1991) U.D.C. 547.79

Compounds of dicoordinate arsenic: chemical properties

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ABSTRACT. The present review presents the known types of compounds of dicoordinate arsenic ($\lambda^3\sigma^2$As) with the exception of compounds with a formally charged dicoordinate arsenic atom. Data on the reactivity of the $\lambda^3\sigma^2$As systems are surveyed and described systematically. It is shown that the most characteristic and the most thoroughly investigated property is addition to a multiple or diene bond involving an arsenic atom. Certain cyclic $\lambda^3\sigma^2$As derivatives are known to exhibit the properties of aromatic compounds. The ability of derivatives of dicoordinate arsenic to behave as ligands in complex formation reactions involving the As atom, the As–X bonds (X = C, As, P), or the entire π-bond system is reported.

The bibliography includes 109 references.

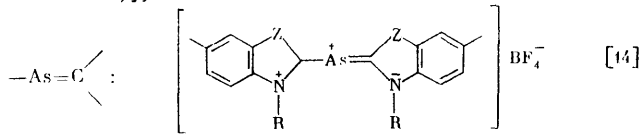
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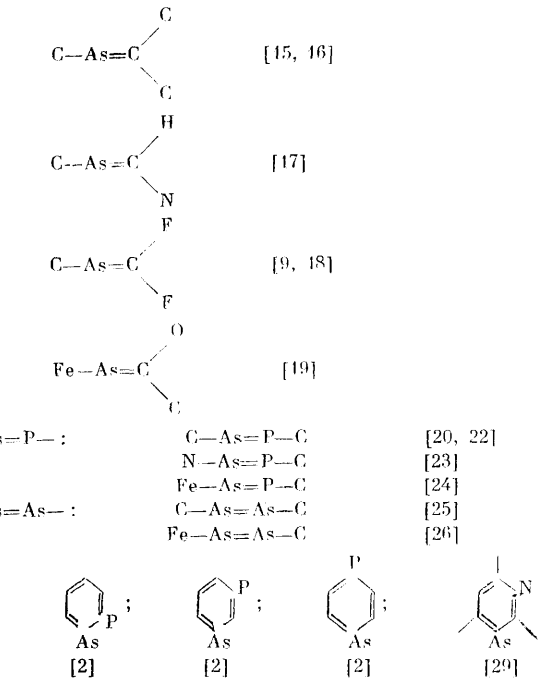
I. Introduction

As a consequence of the unusual coordination and the unusual reactivity, compounds of phosphorus and arsenic atoms involved in a low coordination have continually attracted the attention of chemists. Studies in the field of monocoordinate and dicoordinate phosphorus have appreciably overtaken the development of the chemistry of analogous organoarsenic derivatives. A whole series of review articles have been devoted to compounds of dicoordinate phosphorus ($\lambda^3\sigma^2$P).[1–12] There are virtually no reviews on $\lambda^3\sigma^2$As systems. As regards compounds of monocoordinate arsenic, the existence of a single representative is known: 2,4,6-t-$Bu_3C_6H_2$–C≡As.[13] This review surveys the results of the authors' own studies and the literature data on the reactivity of $\lambda^3\sigma^2$As compounds.

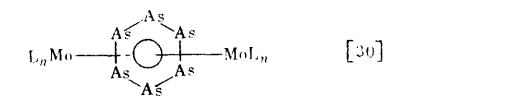
The known types of $\lambda^3\sigma^2$As derivatives are presented below {the literature references are given for the first representatives of the series [the numerals in square brackets denote references (Ed. of Translation)]}.



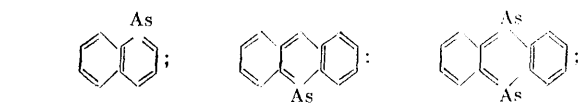
[14]



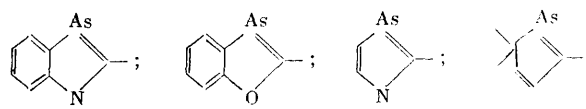
[15, 16] [17] [9, 18] [19] [20, 22] [23] [24] [25] [26] [27, 28] [2] [2] [2] [29]



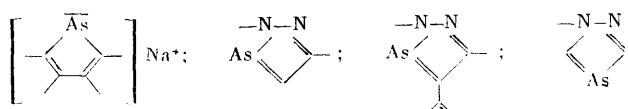
[30]



[31] [32, 33] [32]*



[34] [35] [36] [37]

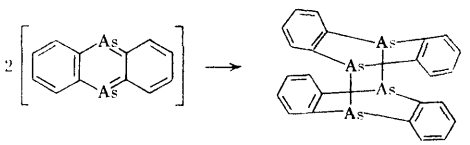


[38] [39] [40] [41]

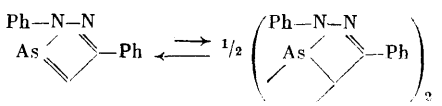
* Detected in the form of primary unstable products.

II. Dimerisation and 1,2-addition

The first data on the chemical properties of derivatives of dicoordinate arsenic concern their instability and tendency to dimerise. Thus, when an attempt was made to synthesise 9,10-diarsaanthracene,[32] its dimer was obtained:

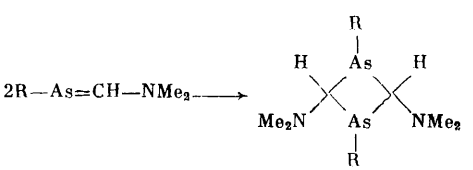


In the synthesis and on prolonged storage of 2,5-diphenyl-1,2,3-diazaarsole, we observed[42] its partial dimerisation. It was noted that there is a mobile equilibrium between the monomer and the dimer, the displacement of which in one direction or another depends on the nature of the solvent. Thus, in ether, benzene, and CH_2Cl_2, diazaarsole dimerises, while in solution in isooctane the dimer associates into the monomer, which was established with the aid of UV spectra:

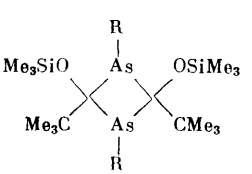


2,5-Diphenyl-1,2,3-diazarsole dimerises faster than it interacts with trichloroacetyl isocyanate or diphenyldiazomethane at room temperature.

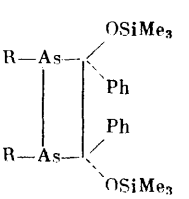
Dimerisation also takes place in the case of acyclic $\lambda^3\sigma^2$As compounds. Thus the ready dimerisation of compounds with the $\lambda^3\sigma^2$As=C bond has been noted:[17]



Two types of dimerisation with formation of 1,2- or 1,3-diarsaethanes have been observed:[43]



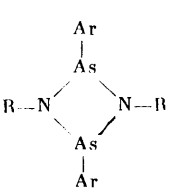
R = Me, Et, $PhCH_2$



R = iso-Pr

In the case of perfluoroheteroalkenes[9] $F_3C-E=CF_2$ (E = P, As), a much greater tendency towards the dimerisation of arsaalkenes than of phosphaalkenes was noted.[9]

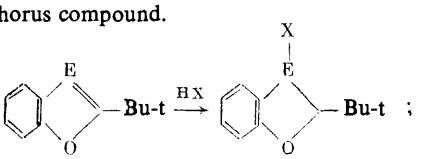
The attempts to obtain derivatives with the $\lambda^3\sigma^2$As=N bond[44,45] led to a negative result. The authors isolated diazadiarsetidines.



The structure of the compound with R = *p*-BrC_6H_4 was demonstrated by X-ray diffraction.

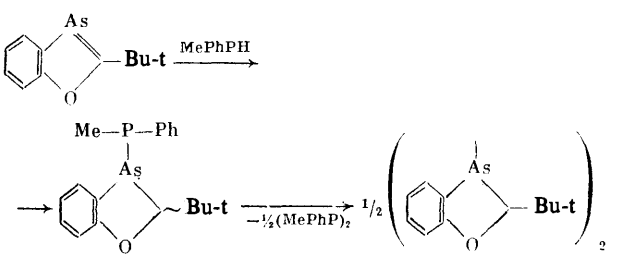
1,3-Benzoxa- and benzaza-arsoles can be classified as unsaturated compounds in terms of their tendency to undergo 1,2-addition reactions.[46]

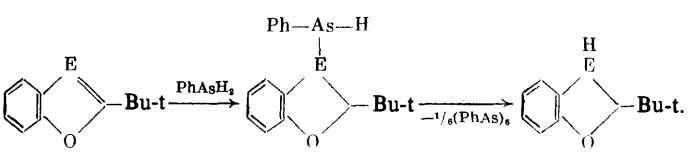
2-t-Butyl-1,3-benzoxazarsoles and the corresponding phosphole combine with "soft" bases at the E=C bond (E = As, P). The arsenic-containing compound is more reactive than the analogous phosphorus compound.



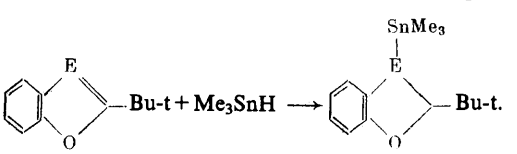
X = I, LL, SPh.

The higher reactivity of the compound with the As=C bond has been observed also in the reactions with methylphenylphosphine and phenylarsine. The reactions proceed in accordance with the following mechanism:

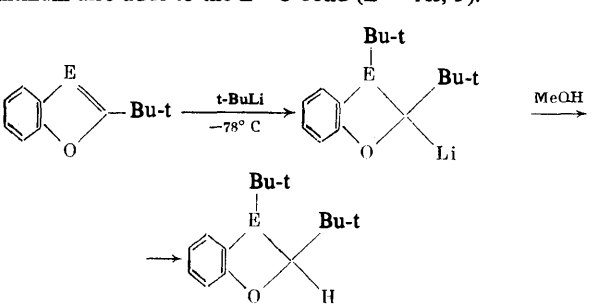




The addition of trimethyltin hydride takes place at the As=C and P=C bonds in 1,3-benzoxaarsole and 1,3-benzoxaphosphole:

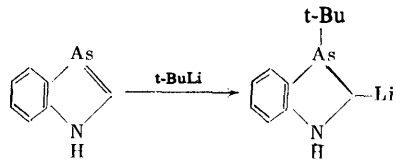


t-Butyllithium also adds to the E=C bond (E = As, P):



In contrast to 1,3-benzoxaarsoles, 1,3-benzazaarsoles show a greater tendency to undergo alkylation or metallation reactions (see Section V) than 1,2-addition reactions with participation of the As=C bond. Thus, among the known 1,3-benzazaarsoles, only the

unsubstituted 1,3-benzazaarsole reacts with t-butyllithium via the 1,2-addition mechanism:[47]



In the case of substituted 1,3-benzazaarsoles or other organolithium reagents, metallation in the 1- or 2-position in the ring takes place.

The above difference in the chemical behaviour of 1,3-benzazaarsoles and 1,3-benzoxaarsoles has been explained[46] by their different aromatic stabilisations. In the case of the oxygen-containing heterocycles, the latter is lower owing to the greater amount of double bond character in the E=C bond.

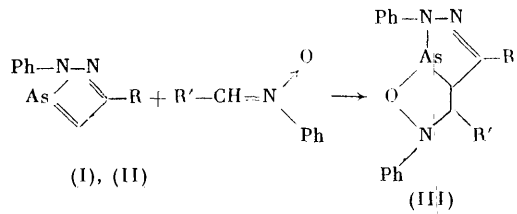
III. [2 + 3]Cycloaddition

Until recently, the first and only objects of the study [2 + 3]cycloaddition were 2*H*=1,2,3-diazaarsoles. In 1986, examples of [2 + 3]cycloaddition to 1*H*=1,2,4-diazaarsoles appeared.

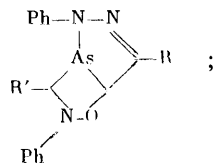
1. 2*H*-1,2,3-diazaarsoles

(a) Reactions with nitrones, nitrile oxides, and nitrile ylides

Cycloaddition to the $\lambda^3\sigma^2$As=C bond was achieved for the first time in the reaction of 2*H*=1,2,3-diazaarsoles (I) and (II) with nitrones:[48–50]



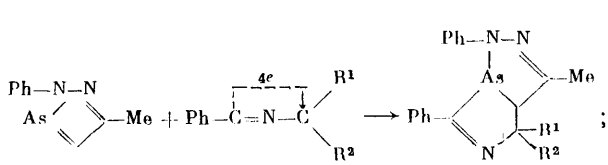
(I), (II) (III)



R=Me (I), R=Ph (II), R′=Ph, *p*-$NO_2C_6H_4$.

It has been established by X-ray diffraction[48] that, of the two possible isomers, 2,7-diphenyl-4-R-6-R′-1-arsa-2,3,7-triaza-8-oxabicyclo[3.3.0]oct-3-ene (III) is formed. Similar compounds based on 2*H*-1,2,3-diazaphosphole could not be obtained.

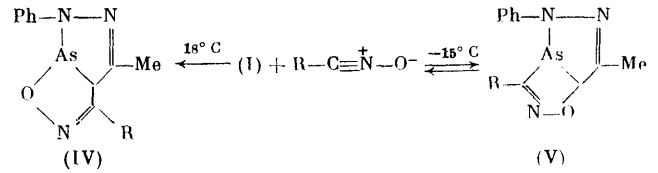
Carrie and co-workers showed that 2*H*-1,2,3-diazaarsoles as well as diazaphospholes react with nitrile oxides[51,62] and nitrile ylides[53] via the $\lambda^3\sigma^2$E=C bond. 2*H*-1,2,3-Diazaarsole (I) reacts with nitrile ylides to form one regioisomer:



(I)

R^1 = Ph, R^2 = H; R^1 = R^2 = H; R^1 = R^2 = Me.

Depending on the conditions, one or other regioisomer is formed in the case of nitrile oxides:



(IV) (V)

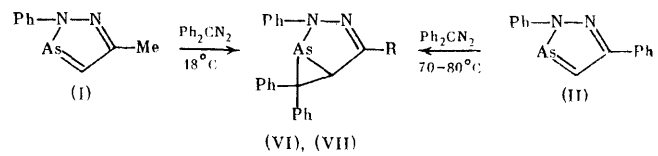
R=*p*-ClC_6H_4, t-Bu, Me, Ph.

The stable isomer (IV) was obtained at room temperature, while at −15 °C the product was the regioisomer (V). At room temperature in solution in toluene, the product (V) is converted quantitatively into compound (IV) via retrocycloaddition.

It may be that in the reaction of 2*H*-1,2,3-diazaarsoles with nitrones described above[48–50] the product (III) is also a thermodynamically controlled stable isomer, while its regioisomer could not be detected.

(b) Reactions with diphenyldiazomethane

The reaction of 2*H*-1,2,3-diazaarsoles (I) and (II) with diphenyldiazomethane leads to the bicyclic arsines (VI)[49] and (VII).[42,54] The formation of the arsirans (VI) and (VII) can be represented by the intial formation of the [2 + 3]cyclic adduct with the subsequent liberation of nitrogen. It has been demonstrated by a special experiment that diphenylcarbene does not afford the arsirans (VI) and (VII) on its reactions with diazaarsoles:

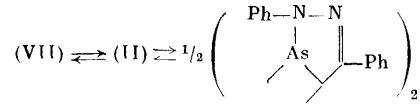


(I) (VI), (VII) (II)

R = Me(VI); R = Ph(VII).

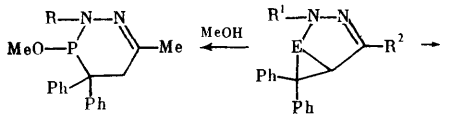
The diazaarsole (I) is more reactive in this reaction than the diazaarsole (II). Compounds (VI) and (VII) obtained are the first representatives of bicyclic arsirans. The structure of the product (VII) was established by X-ray diffraction.[55] Comparison of the X-ray diffraction data for the bicyclic compound (VI) and the analogous phosphorus-containing system[56] revealed a greater strain in the arsiran ring, which explains its lower stability.

The bicyclic arsiran (VII) is stable only when stored in the dark in the absence of solvents. In solutions at room temperature, it exists for 24 h. It then decomposes to diazaarsole (II), which dimerises:

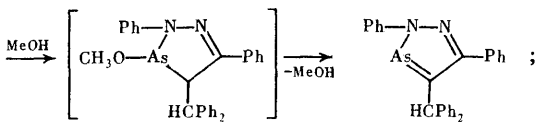


The difference between the strains in the arsiran and phosphiran rings is reflected in their different behaviour in relation to methanol. The addition of the alcohol to the phosphorus derivative (VIII) is accompanied by the dissociation of the inner P–C bond.[57] The addition of the alcohol to the bicyclic arsiran (VII) is apparently accompanied by the dissociation of the outer As–C bond with the subsequent liberation of the alcohol and the formation of 2,5-diphenyl-4-diphenyl-1,2,3-diaza-arsole. A new 2,4,5-trisubstituted 1,2,3-diazaarsole, whose structure was demonstrated by X-ray diffraction, has been obtained.[58] This is the first example of the $\lambda^3\sigma^3$As→$\lambda^3\sigma^2$As isomerisation in the series of diazaarsoles. In the

known [see, for example, Märkl[2] and Section (V) of the present review]:



(VII), (VIII)

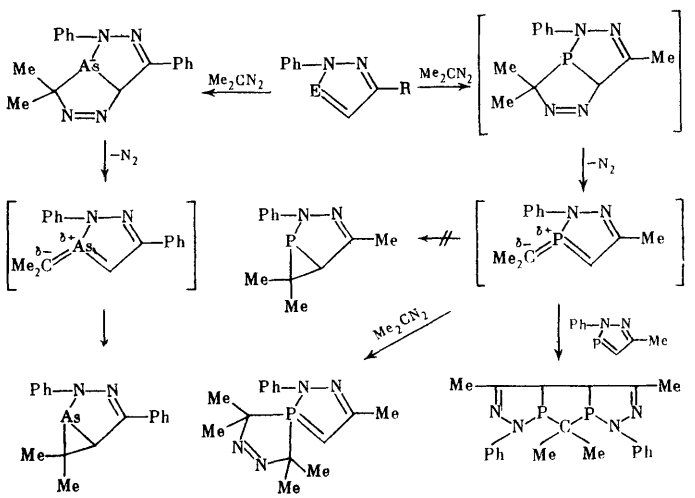


E = As(VII), P(VIII).

(c) Reactions with 2-diazopropane

Whereas 2*H*-1,2,3-diazaarsoles and 2*H*-1,2,3-diazaphospholes react with diphenyldiazomethane similarly to form stable bicyclic arsirans and phosphirans,[55,59] 2-diazopropane[60–66] introduced its characteristic features into these reactions. When 5-methyl-2-phenyl-1,2,3-diazaphosphole reacts with 2-diazopropane,[60–65] the closure to the phosphiran ring does not occur and the intermediate diazaphosphole ylide behaves both as a dipole and as a dipolarophile in the subsequent [2 + 3]cycloaddition reactions with both initial reactants: diazaphosphole and 2-diazopropane. As a result, reactions which led to previously unknown types of organophosphorus compounds were discovered.

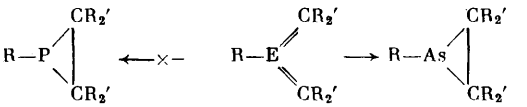
In the reaction with 2*H*-1,2,3-diazaarsole, 2-diazopropane[66] behaves similarly to diphenyldiazomethane. The final product is 2,4-diphenyl-6,6-dimethyl-1-arsa-2,3-diazabicyclo[3.1.0]hex-3-ene (IX). The bicyclic arsiran (IX) is formed via a crystalline cyclic adduct, detected at −70 °C. On further increase in temperature, the adduct evolves nitrogen and is probably converted into the product (IX) via a diylide:



(IX)

The results reported[67] for acyclic phosphorus and arsenic diylides are similar to those obtained in the reaction with 2-diazopropane.

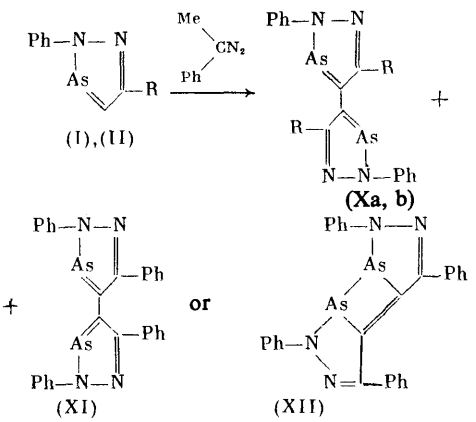
The arsenic diylide undergoes closure to the arsiran ring:



E = As, P; R = Ph, t-Bu; R′ = $SiMe_3$.

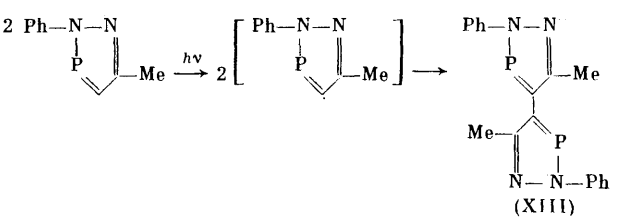
(d) Reactions with methylphenyldiazomethane

The reaction of 2*H*-1,2,3-diazaphospholes with methylphenyldiazomethane afforded in earlier studies[68,69] bicyclic phosphirans as two geometrical isomers. Similar isomers of bicyclic arsirans were not isolated in the reactions of 2*H*-1,2,3-diazaarsoles with the given diazo-compound. 1,4-Diarsabuta-1,3,-dienes (Xa, b) were obtained for the first time:[40]



R = Me (a), Ph (b).

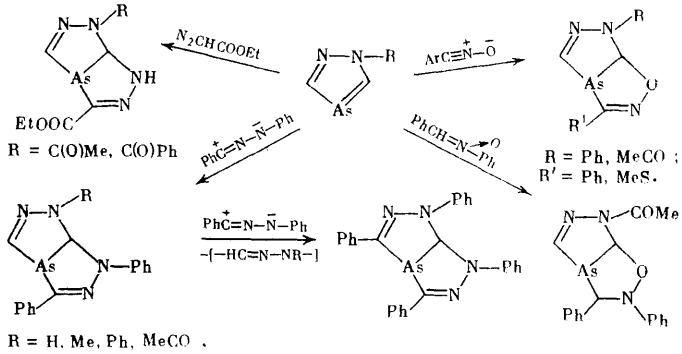
In addition, in the case of 2,5-diphenyl-1,2,3-diazaarsole (II) a second isomer, (XI) or (XII), was isolated. It could not be studied by X-ray diffraction owing to the insufficiently high quality of the crystals. *trans*-4,4′-Didehydrobis(5-methyl-2-phenyl-1,2,3-diazaarsole) (Xb) proved to be a full analogue (on the basis of X-ray diffraction data) of *trans*-4,4′-didehydrobis(5-methyl-2-phenyl-1,2,3-diazaphosphole) (XIII).[40,70,71] The data for the reactivity of diazaarsoles available at the present time, permit inferences about the mechanism of the formation of 1,4-diarsabuta-1,3-dienes (Xa, b). The phosphorus-containing product (XIII) was obtained under other conditions—on UV irradiation of 5-methyl-2-phenyl-1,2,3-diazaphosphole:



2. 1*H*-1,2,4-diazaarsoles

1*H*-1,2,4-Diazaarsoles enter under mild conditions into [2 + 3]-cycloaddition reactions with diazoacetic ester, nitrile imines, nitrile oxides, and nitrones.[41] It has been noted that the reactivity of *N*-acyl- and *N*-benzoyl-1,2,4-diazaarsoles is higher than that of the *N*-alkyl- and *N*-aryl-derivatives, which the authors explain by the reduced stabilisation of the aromatic system of the diazaarsole ring

in the acyl- and benzoyl-substituted compounds:



R = C(O)Me, C(O)Ph

R = Ph, MeCO ; R' = Ph, MeS.

R = H, Me, Ph, MeCO .

The [2 + 3]cycloaddition of nitrile oxides to 1*H*-1,2,4-diazaarsoles leads to a single regioisomer. In contrast to the reactions of 2*H*-1,2,3-diazaarsole (I) with nitrile oxides described previously,[51] the inversion of regioselectivity is not observed in this instance.

The reaction with diphenylnitrile imine results in the formation of cyclic adducts even at room temperature. At a higher temperature, they decompose to 1,3-diphenyl-1,2,4-diazaarsole. The latter enters again into the cycloaddition reaction with diphenylnitrile imine.

1-Acetyl-1,2,4-diazaarsole reacts with diphenyl nitrone to form a bicyclic adduct. It is of interest to note that the reactions of 2-phenyl-1,2,3-diazaarsoles (I) and (II) with diphenyl nitrone afforded in earlier studies[48–51] the product (III) with the opposite orientation of the nitrone relative to the $\lambda^3\sigma^2$As=C bond.

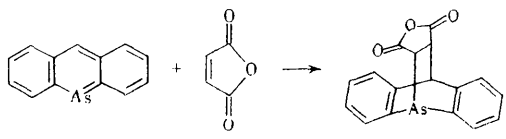
We did not encounter any data in the literature on the polarity of the $\lambda^3\sigma^2$As=C bond. Nevertheless, the formation of different regioisomers from 2*H*-1,2,3- and 1*H*-1,2,4-diazaarsoles and diphenyl nitrone shows that the regioselectivity of the addition to the As=C bond is determined not only by the charges on the atoms but also by the polarisability of the bond and the molecular-orbital characteristics of the reactants.

IV [2 + 4]cycloaddition

Depending on their structure, the $\lambda^3\sigma^2$As derivatives are capable of entering into the diene synthesis reaction as dienes and dienophiles.

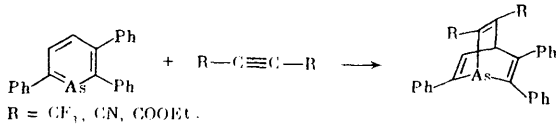
1. 9-Arsaanthracene

The unsubstituted 9-arsaanthracene exists only in solutions. After the addition of maleic anhydride, it gives rise to the [4 + 2]cyclic adduct.[33] This reaction was the first example of diene synthesis with participation of a $\lambda^3\sigma^2$As derivative:



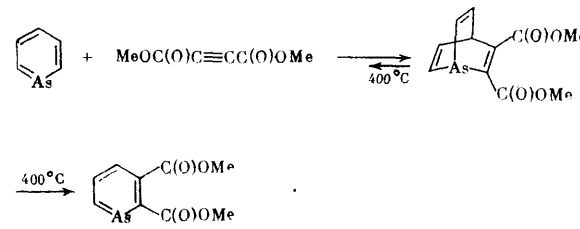
2. λ^3-Arsenins

The reactivity of arsenins as dienes was first reported by Märkl:[72]

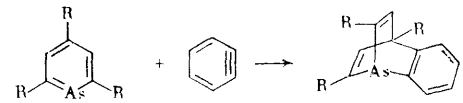


R = CF_3, CN, COOEt .

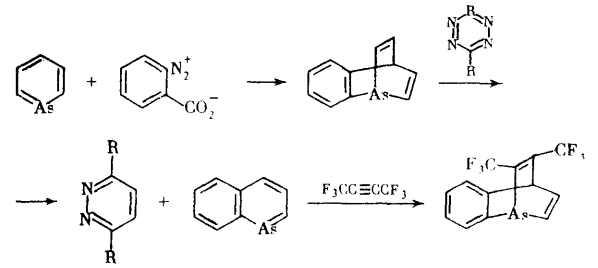
Arsenins exhibit a higher diene reactivity than phosphorins. In contrast to phosphorins, the [2 + 4]cycloaddition of dimethyl acetylenediacarboxylate to arsenins was achieved.[72–76] The thermal reversibility of the formation of arsabarrelenes was demonstrated in relation to the unsubstituted arsenin:[76]



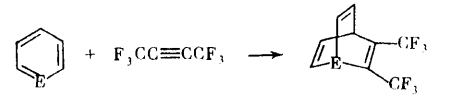
The 2,3-dimethoxycarbonylarsenin obtained at 400 °C enters into the diene synthesis reaction with arynes, which leads to benzarsabarrelenes:[72]



Ashe et al.[31] achieved a series of reactions during which [2 + 4]cycloaddition with participation of the $\lambda^3\sigma^2$As derivatives takes place: (1) reaction of arsenin with benzenediazonium-2-carboxylate and (2) reaction of 1-arsanaphthalene with hexafluorodimethylacetylene:



Comparison of the diene reactivities of benzene, pyridine, phosphorin, arsenin, antimonin, and bismin in relation to hexafluorobutyne showed[76] that the less electronegative the heteroatom in the ring the easier the Diels–Alder reaction:



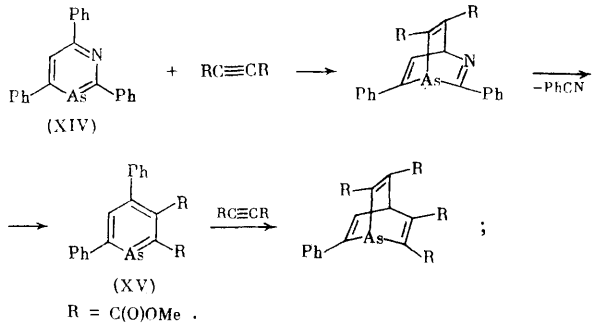
E = CH, N, P, As, Sb, Bi.

3. 1,3-Azaarsenines

The 1,3-azaarsenines synthesised by Märkl and Dietl[29] proved to be preparatively valuable.

2,4,6-Triphenyl-1,3-azaarsenine (XIV) enters into the Diels–Alder reaction with dimethyl acetylenedicarboxylate to form 1,3-azarsabarrelene, which decomposes during the reaction to the arsenin (XV). The latter is involved in a further diene synthesis reaction

with the initial dimethyl acetylenedicarboxylate:[77]



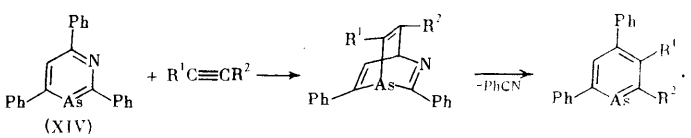
(XIV)

(XV)

R = C(O)OMe .

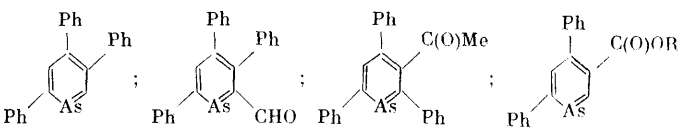
In contrast to the azaarsenine (XIV), the reaction of 2,4,6-triphenyl-1,3-azaphosphorine with acetylenedicarboxylate esters stops at the stage involving the formation of derivatives of $\lambda^3\sigma^2$P-phosphorins analogous to compound (XV). The phosphorins do not react further with acetylenedicarboxylate, which is consistent with the lower diene reactivity of phosphorins compared with arsenins.

1,3-Azaarsenines (XIV) react similarly with less reactive dienophiles. The azaarsabarrelenes obtained are converted into arsenins which do not enter into the Diels–Alder reaction:[77]



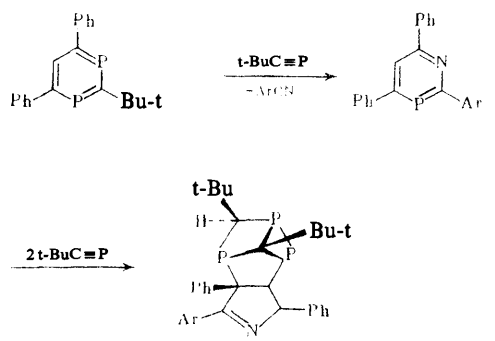
(XIV)

The following arsenins were obtained in this way:

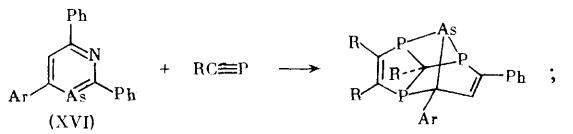


R = Me, H

Interesting data have been secured by Märkl and co-workers in the study of the reaction of 1,3-azaphosphorines[78,79] and 1,3-azaarsenines[80] with t-butyl-1-phosphaacetylene. 1,3-Azaphosphorines give rise to pentatetracyclic compounds in this reaction:



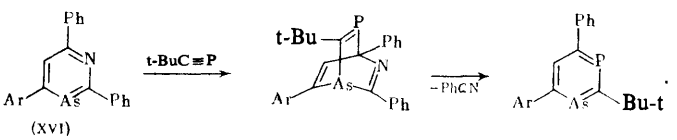
1,3-Azaarsenines (XVI) behave differently in this reaction: a compound with the 1,3-composition is formed. X-Ray diffraction analysis showed that the reaction product consists of a system comprising three five-membered and one four-membered ring:



(XVI)

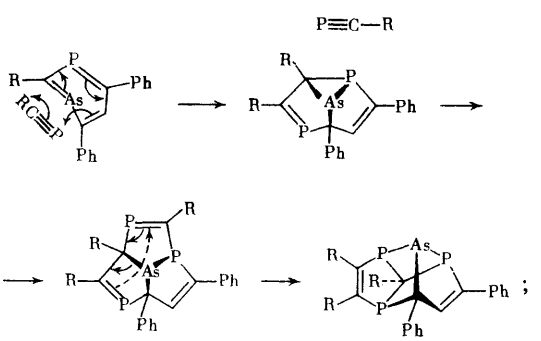
R = t-Bu.

The different behaviour of azaphosphorines and azaarsenines in this reaction has been explained[80] by the lower electrophilicity of the $\lambda^3\sigma^2$As atom in the azaarsenine compared with the electrophilicity of the $\lambda^3\sigma^2$P atom in the azaphosphorine, which leads to different mechanisms of their reactions. Whereas the reaction of the azaphosphorine with t-butylphosphaacetylene is induced by the nucleophilic attack of the acetylene *sp*-carbon atom on the $\lambda^3\sigma^2$P atom of the azaphosphorine in the case of the azaarsenine (XVI) the Diels–Alder reaction takes place initially. A phosphaarsabarrelene is formed. After the introduction of benzonitrile, it is converted into 1,3-phosphaarsenin:



(XVI)

The authors believe that the latter reacts with phosphaacetylene via the following mechanism:



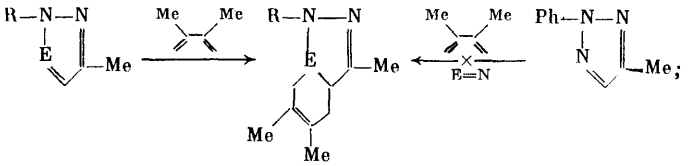
R = t-Bu.

Thus Märkl and co-workers carried out a brilliant series of studies in the field of diene synthesis involving six-membered $\lambda^3\sigma^2$P and $\lambda^3\sigma^2$As derivatives. The investigations led to new substituted λ^3-arsenins and λ^3-phosphorins. In addition the higher reactivity of arsenines compared with phosphorines in the Diels–Alder reaction was demonstrated and justified.

4. 2*H*-1,2,3-Diazaarsoles

We showed earlier[57] that 2*H*-1,2,3-diazaphospholes, which are derivatives of dicoordinated phosphorus, enter into the diene synthesis reaction with hexachlorocyclopentadiene. The ability of 2*H*-1,2,3-diazaarsoles to react with dienes was reported by Carrier and co-workers[81] in relation to the interaction with cyclopentadiene and 2,3-dimethylbutadiene. The reactivity of 5-methyl-2-phenyl-1,2,3-diazaarsole, 2,5-dimethyl-, 5-methyl-2-phenyl, and 2-acetyl-5-methyl-1,2,3-diazaphospholes, and 5-methyl-2-phenyl-1,2,3-triazole

in relation to 2,3-dimethylbutadiene were compared:

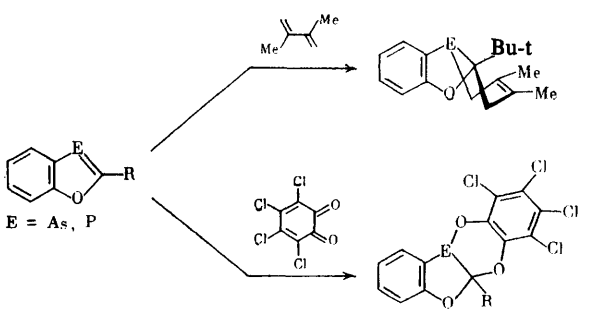


E = P, R = MeCO, Ph; E = As, R = Ph (I).

2-Acetyl-5-methyl-1,2,3-diazaphosphole and 5-methyl-2-phenyl-1,2,3-diazaarsole are the most reactive in this reaction. Cyclic adducts with 2,5-dimethyl-1,2,3-diazaphosphole and the corresponding triazole were not obtained. The absence of the reaction between the triazole and 2,3-dimethylbutadiene clearly demonstrates the greater reactivity of the $\lambda^3\sigma^2P=C$ and $\lambda^3\sigma^2As=C$ bonds compared with the $\lambda^3\sigma^2N=C$ bond in the reactions considered.

5. 1,3-Benzoxaarsoles

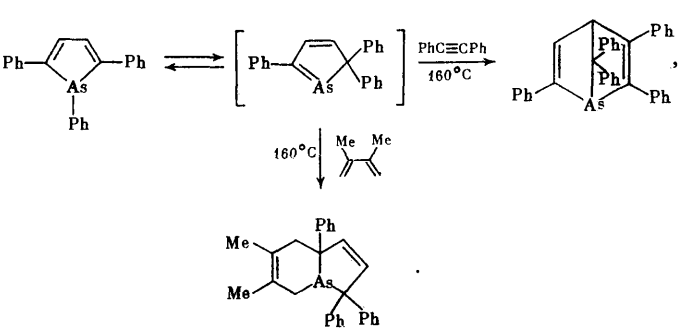
1,3-benzoxaarsoles and 1,3-benzoxaphospholes react [82] with 2,3-dimethylbutadiene and tetrachloro-*o*-benzoquinone to form [2 + 4]-cyclic adducts. The $\lambda^3\sigma^2As$ derivative is more reactive in these processes than the $\lambda^3\sigma^2P$ compound.



R = Me, t-Bu.

6. 2,5,5-Triphenylarsole

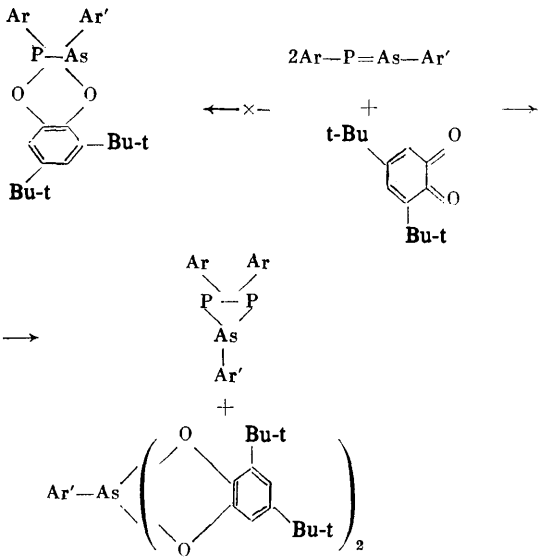
At a high temperature, 1,2,5-triphenylarsole isomerises to 2,5,5-triphenylarsole, which enters into the Diels–Alder reaction both as a diene (in the reaction with tolane) and as a dienophile (in the reaction with 2,3-dimethylbutadiene):[37]



Similar results were obtained for a phosphorus-containing compound — 1-phenylphosphole.[37] The Diels–Alder reaction proceeds more readily with arsoles than with phospholes, because, according to the authors, the lone pair of the arsenic atom is less reactive than that of the phosphorus atom.

7. Phosphaarsaethylenes

Data on reactions involving cycloaddition to acyclic $\lambda^3\sigma^2As$ compounds are almost absent in the literature. There is a communication[83] stating that an attempt to obtain the [2 + 4]cyclic adduct by the reaction of *P*-(2,4,6-tri-t-butylphenyl)-*As*-(2,4,6-tri-isopropylphenyl)phosphaarsaethylene with 3,5-di-t-butyl-*o*-benzoquinone was unsuccessful, diphosphaarsiran and arsine being obtained:

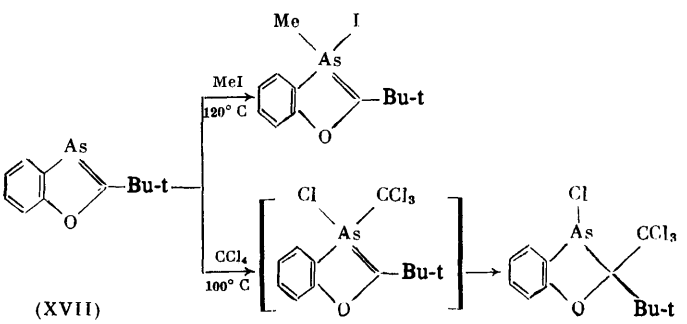


V. Aromaticity

The chemical properties described above (Sections II–IV) characterise $\lambda^3\sigma^2As$ compounds as systems related to unsaturated compounds. However, individual representatives of cyclic derivatives of dicoordinate arsenic exhibit also the properties of aromatic systems.

1,3-Benzaza- and 1,3-benzoxa-arsoles and 1,3-benzaza- and 1,3-benzoxaphospholes can be classified as aromatic compounds in terms of the nature of the delocalisation of the π-electrons (according to UV-spectroscopic and X-ray diffraction data).[84,85] X-Ray diffraction data for unsubstituted benzazaarsole[84] (bond lengths, bond angles, and planarity of the molecule) indicate the aromaticity of the latter. Comparison of the structural parameters of benzimidazole, benzazaphosphole, and benzazaarsole demonstrated their electronic and structural similarly.[85]

2-t-Butyl-1,3-benzoxaarsole (XVII) exhibits a low reactivity in relation to electrophiles. However, under severe conditions it reacts with MeI to form λ^5-1,3-benzoxaarsole:[46]

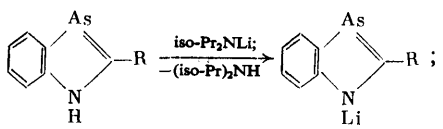


(XVII)

The reaction with CCl_4 proceeds differently. The primary 1,1-adduct rearranges under these conditions to λ^3-dihydrobenzoxaarsole.

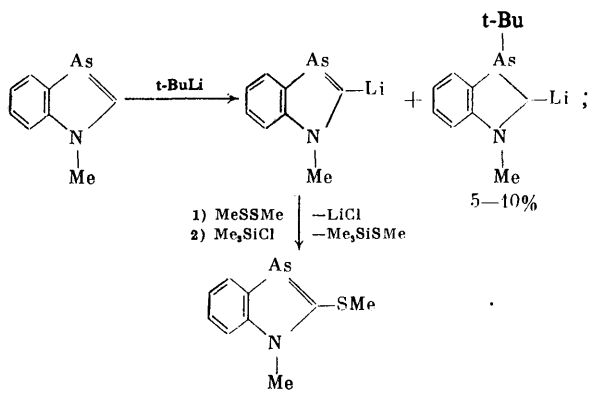
1,3-Benzoxaarsole and 2-t-butyl-1,3-benzoxaphosphole do not react with "hard" bases,[46] which also indicates their aromaticity.

The metallation of 2R-1,3-benzazaarsoles[47] takes place in the 1-position in the azaarsole ring:

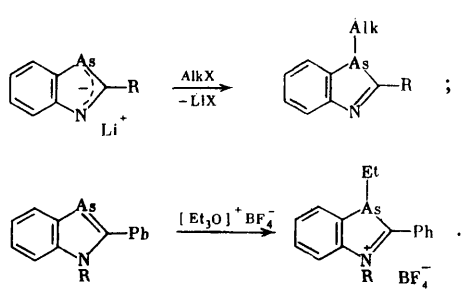


R = H, Me, t-Bu, iso-Pr.

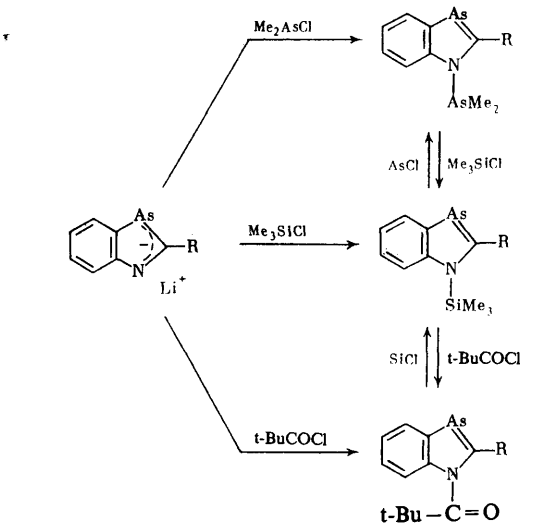
In contrast to unsubstituted 1,3-benzazaarsole, which reacts with t-butyllithium via the 1,2-addition mechanism, 1-methyl-1,3-benzazaarsole is metallated by t-butyllithium in the 2-position. The metallation product reacts with dimethyl disulphide, forming 1-methyl-2-methylthio-1,3-benzazaarsole:



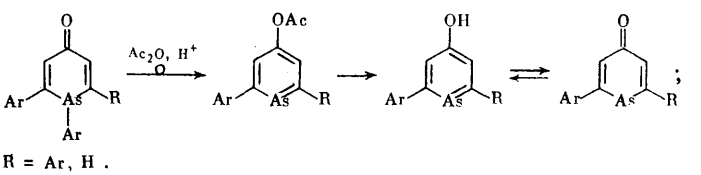
Whereas unsubstituted 1,3-benzaazaarsole does not react with MeI,[86] substituted 1,3-benzazaarsoles are alkylated[47] at the arsenic atom:



An interesting chain of substitutions has been achieved by Heinicke et al.:[47]

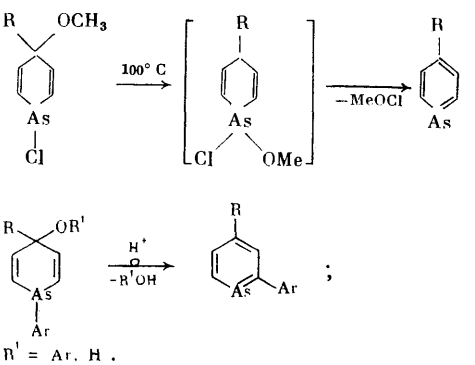


The properties of aromatic systems are also shown by representatives of another class of $\lambda^3\sigma^2$As compounds—arsenins. Thus 1-aryl- and 1,2-diaryl-arsacyclodienones[87,88] in acetic anhydride undergo, in the presence of a catalytic amount of H_2SO_4, the arsacyclohexadienone-arsaphenol rearrangement, corresponding to the rearrangement in the aromatic series, forming 2-aryl-6R-4-hydroxyarsenin. Alkaline hydrolysis of the latter gives rise to 2,6-diarylarsacyclodien-4-ones, which exist in solution in equilibrium with their enolic forms. In contrast to the 2,6-disubstituted 4-hydroxyarsabenzenes unsubstituted 4-hydroxyarsabenzene[89] exists exclusively in the enolic form and there is no tautomeric conversion into the cyclodienone.



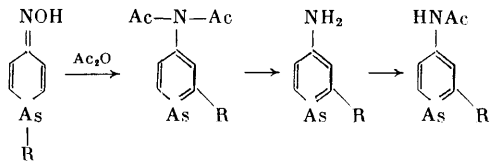
R = Ar, H .

The conversion of $\lambda^3\sigma^3$As derivatives into $\lambda^3\sigma^2$As compounds, which are more conjugated systems,[2,88,90,91] is known to occur in a number of instances:

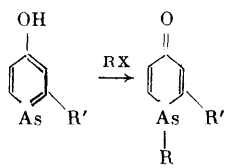


R' = Ar, H .

An interesting series of transformations was achieved by Märkl and Rampal[92] in the oxime–aminoarsenin series:

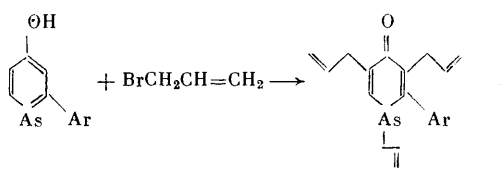


4-Hydroxyarsenins[87] are alkylated preferentially in the hydroxy-group with the subsequent migration of the alkyl substituent to the arsenic atom:



$R' = Ar, H;\ X = I, Br$.

In the reaction of 2-aryl-4-hydroxyarsenin with 3-bromopropene, substitution in the arsabenzene ring also takes place:

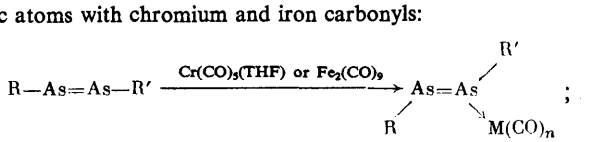


Among the chemical properties of arsinines considered (Sections IV and V), one may note their dual reactivity. On the one hand, they enter into the diene synthesis reaction as dienes and on the other they undergo reactions characteristic of aromatic compounds. Admittedly, both types of reactions characterise arsinines as conjugated systems. The ability of arsinines to enter into complex formation reactions (see the next Section) involving the $\lambda^3\sigma^2$As atom as well as the entire π-system also indicates the wide variety of their properties.

VI. Complex formation

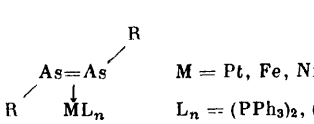
There are some data on the complex formation reactions of derivatives of dicoordinate arsenic. They are partly included in a review article.[7] So far η^1-, η^2-, and η^6-complexes of $\lambda^3\sigma^2$As compounds are known.

Diarsenes[93,94] are capable of forming η^1-complexes via one of the arsenic atoms with chromium and iron carbonyls:

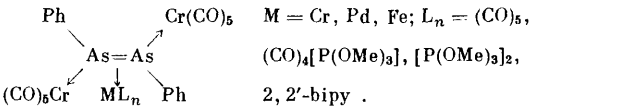


$R = 2, 4, 6\text{-}(t\text{-}Bu)_3C_6H_2$, $R' = (Me_3Si)_2CH$.

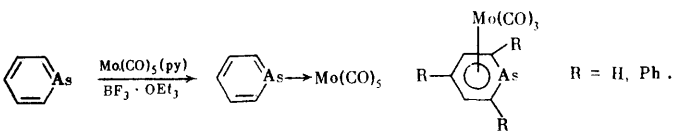
The η^2-complexes of diarsenes have been obtained:[94–97]



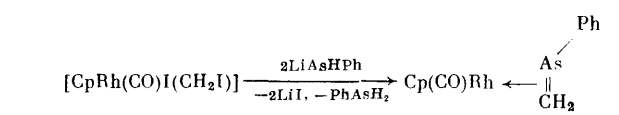
Diphenyldiarsene can enter into the complex formation reaction involving both the double bond and the arsenic atoms,[98–100] forming the following compounds:



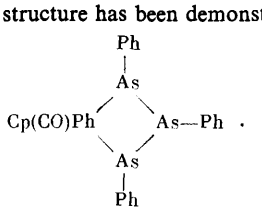
In the case of λ^3-arsenin, the η^1-complexes[101] and the η^6-complexes[101,102] are known:



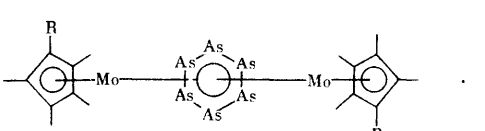
It has been noted that complex formation promotes the stabilisation of $\lambda^3\sigma^2$As atoms. Thus phenylarsene Ph–As=CH_2 does not exist in a free state but its η^2-complex has been obtained:[103,104]



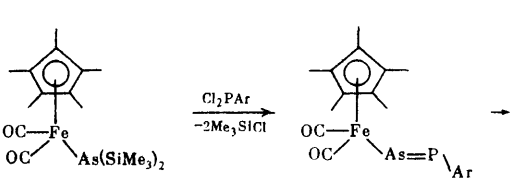
On recrystallisation, the latter is partly converted into a compound whose structure has been demonstrated by X-ray diffraction:



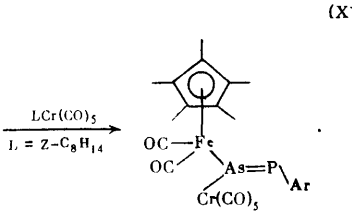
Hexaarsabenzene is known[30] at the present time only in the form of η^6-complexes:



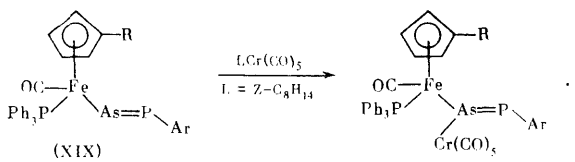
The formation of the phosphaarsene (XVIII) has been detected spectroscopically in the reaction mixture and its complex has been isolated.[105,106] The structure of the latter has been demonstrated by X-ray diffraction:



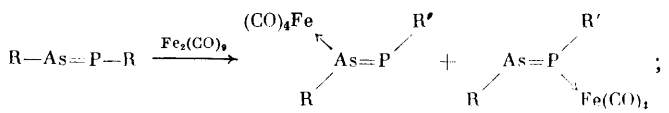
(XVIII)



In contrast to compound (XVIII), the phosphazaarsene (XIX) is stable. Its reaction with $Cr(CO)_3$ afforded[107] an η^1-complex:

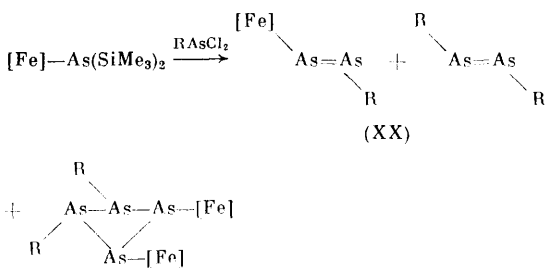


Phosphaarsenes are capable of forming complexes not only via the $\lambda^3\sigma^2$As atom but also via the $\lambda^3\sigma^2$P atom. A mixture of such complexes has been obtained.[108,109] They could not be separated, but they were identified spectroscopically by $^{31}P\{^1H\}$ NMR:



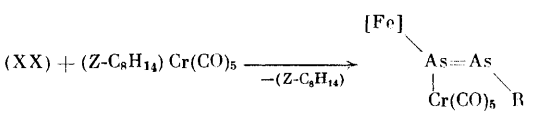
$R = 2,4,6\text{-}(t\text{-}Bu)_3C_6H_2$, $R' = (Me_3Si)_2CH$.

The synthesis of the diarsene (XX) [26] is not ambiguous, in contast to the analogous synthesis of the phosphaarsene (XVIII):



$[Fe] \equiv (\eta^5\text{-}C_5Me_5)(CO)_2Fe$; $R = 2,4,6\text{-}(t\text{-}Bu)_3C_6H_2$.

Compound (XX) is unstable, but its $Cr(CO)_5$ derivative proved to be stable:



- - - o 0 o - - -

The experimental data examined in this review indicate the high reactivity of $\lambda^3\sigma^2$As derivatives. The wide variety of the properties shown by these compounds opens a route to various chemical reactions, new types of reactions, and the synthesis of new organoarsenic compounds. Further study of the chemical properties of dicoordinate arsenic is therefore of current interest.

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Translated from *Uspekhi Khimii* **60** 339–373 (1991) U.D.C. 547.7+547.8+547.25

Functionalisation of heterocycles by Ni- and Pd-catalysed reactions

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ABSTRACT. The review covers carbon–carbon bond formation at heterocyclic ring positions by Ni- and Pd-catalysed cross-coupling, alkenylation and alkynylation. The influence of the catalyst and the metal of the organometallic component on the facility of cross-coupling has been analysed, and the limitations emphasised.

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I. Introduction

The substitution of heterocyclics is a key step in the synthesis of many physiologically active compounds. A carbon–carbon bond can be formed conveniently by reacting lithiated heterocyclics with sufficiently reactive electrophiles, such as alkyl halides.[1] However, the method cannot be used for coupling aryl, alkenyl and heterocyclic halides where the halogen is at an sp^2-hybridised carbon atom, since here the halogen is not reactive enough.

Cross-coupling is defined as a process where a simple carbon–carbon bond is formed between two carbon radicals. The reaction of organometallic compounds with organic halides or other electrophiles falls in this category:[2]

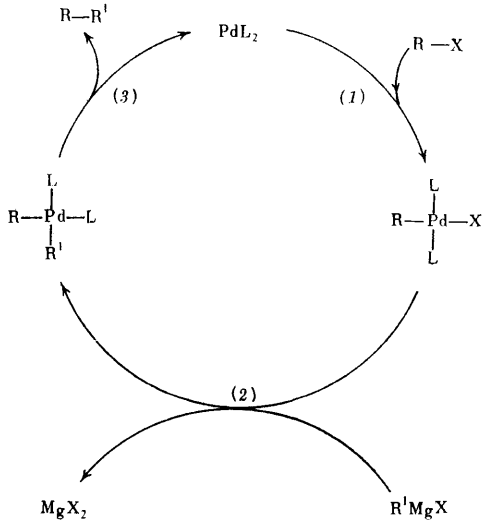
$$R^1M + R^2X \rightarrow R^1{-}R^2 + MX.$$

Although the above scheme appears simple, this type of cross-coupling is complicated by side-reactions. The classical Wurtz synthesis is a variation on this theme, where a halogen-metal exchange is followed by homo-coupling. If the halide has a branched alkyl group, α- and β-elimination takes place. Uncatalysed cross-coupling does not take place with unsaturated halides where the halogen is bonded to an sp^2- or *sp*-carbon atom.

In 1972 Corriu and Masse[3], and Kumada et al.,[4] introduced nickel-catalysed cross-coupling between reactive Grignard compounds and organic halides. Later, palladium and other Group VIII complexes were found to catalyse this reaction. The main advantages of using Ni and Pd complexes for such catalysed cross-coupling are the higher selectivity of the reaction, the mild conditions, and the possibility of using unsaturated halides. As a result, synthetic organic chemistry has benefited significantly.

Organolithium compounds have rarely been used in catalysed cross-coupling. The use of Grignard reagents in this capacity has been limited to some extent by their reducing properties towards transition metal salts. Organo-zinc, -boron and -aluminium compounds are more compatible with complex metal catalysis and are highly reactive towards organic halides. The same is true of organotin compounds in view of their high stability and the potential of introducing functionalised residues. The following catalysts are usually used for cross-coupling: $Ni(acac)_2$, $M(PPh_3)_4$, $MCl_2(PPh_3)_2$, MCl_2(dppe), MCL_2(dppp), MCl_2(dppb), MCl_2(dppf)† (where M = Ni or Pd), $Pd(OAc)_2[P(o\text{-}Tol)_3]_2$ and others. Usually the zero-valent complexes, M(0), are generated from the corresponding M(II) complexes *in situ*. Palladium catalysts are the more widespread. The catalytic cycle is based on the redox couple, Pd(0) ⇄ Pd(II), and comprises the following three stages: (*1*) oxidative addition, (*2*) transmetallation, and (*3*) reductive elimination, as shown below.[5]

Scheme 1



Cross-coupling is complicated if the transferred alkyl group has a β-hydrogen atom since here transfer of β-hydrogen in the Pd-intermediate is dominant with the formation of a Pd–H complex on elimination of olefin. Catalysed cross-coupling is most effective with alkenyl, aryl and heterocyclic halides.

General aspects of catalysed cross-coupling have already been reviewed[6–9] or covered in monographs.[5,10–13] However, cross-coupling with heterocyclic compounds has not been adequately surveyed. Negishi's review[14] is based on literature published up to 1982.

† dppe = $Ph_2PCH_2CH_2PPh_2$, dppp = $Ph_2PCH_2CH_2CH_2PPh_2$, dppb = $Ph_2P(CH_2)_4PPh_2$, dppf = $(\pi\text{-}Ph_2PC_5H_4)_2Fe$.

The present review covers cross-coupling with heterocyclic systems in the presence of Ni and Pd complexes. It focusses on cross-coupling with heterocyclic organometallic derivatives and heterocyclic halides. There is also a section on the reactions of heterocyclic halides with alkenes and terminal acetylenes which lead to vinyl- and alkenyl-heterocyclics under metal complex catalysis. Homo-coupling of heterocyclic halides is considered separately.

In discussing the data, the accent is placed on synthetic aspects of cross-coupling and preparative applications.

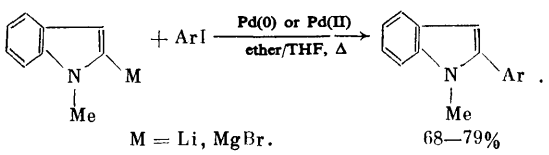
II. Cross-coupling between heterocyclic halides and heterocyclic organometallic derivatives

For the synthesis of substituted heterocyclic compounds by catalysed cross-coupling, one can consider three possible routes: a) cross-coupling of heterocyclic organometallic compounds with organic halides, b) cross-coupling of organometallic compounds with heterocyclic halides, and c) cross-coupling of heterocyclic organometallic compounds with heterocyclic halides.

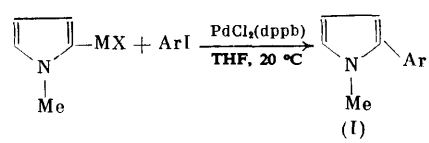
1. Organo-lithium, -magnesium and -zinc compounds

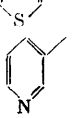
Organolithium compounds are not normally used in cross-coupling. As a rule, they are used as precursors of other organometallic compounds, e. g. organo-zinc, -boron and -tin compounds, etc.

1-Methylindol-2-yl-lithium and -magnesium bromide readily react with aryl iodides in the presence of Pd(0) or Pd(II) complexes to give 2-arylindoles.[15,16]

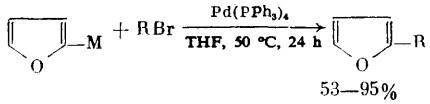


1-Methyl-2-pyrrolyl-magnesium bromide and -zinc chloride react with aromatic or heterocyclic halides in the presence of palladium phosphine complexes to give the corresponding 2-substituted pyrroles:[15]



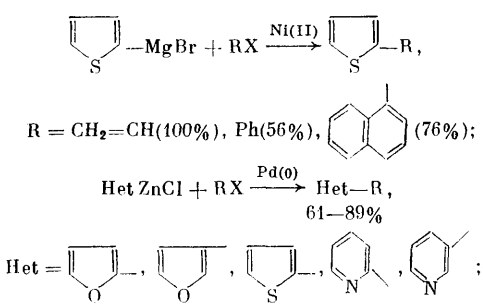
MX	Ar	Yield (I), %
MgBr		87
		71
MX	Ar	Yield (I), %
ZnCl		73
		66

2-Furyl-lithium and -zinc chloride readily interact with aryl, benzyl and cinnamyl bromide in the presence of Pd(0).[17]

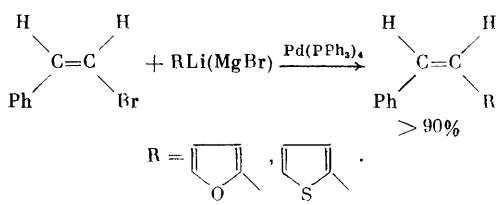


R = Ph, 4-MeC_6H_4, 3-MeC_6H_4, 4-$MeOC_6H_4$, 3-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 4-$O_2NC_6H_4$, $PhCH_2$, $PhCH{=}CHCH_2$.

Unsaturated groups may be introduced at heterocyclic ring positions by cross-coupling of the corresponding heterocyclic organomagnesium[18] or -zinc[19] compounds with vinyl chloride or bromide, bromo- or iodo-benzene, bromonaphthalene, and with 1-bromooct-1-yne in the presence of a Ni or Pd catalyst.

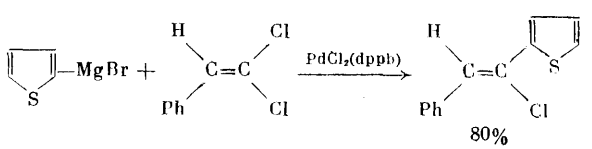


β-Styrylheteroarenes can conveniently be prepared by interaction of β-styryl bromide with 2-furyllithium, 2-thienyllithium and 2-furylmagnesium bromide in the presence of a Pd(0) catalyst.[20]

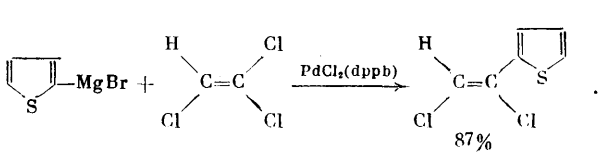


Reaction proceeds with complete retention of configuration, *trans*-β-styryl bromide affording the corresponding *trans*-β-styryl-heteroarene.

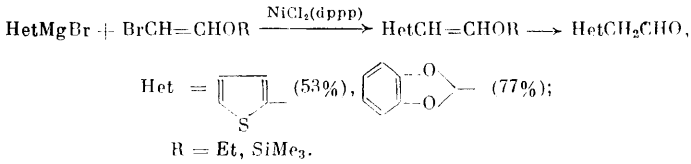
The reaction between 1,1-dichloroalkenes with 2-thienylmagnesium bromide also proceeds with high stereoselectivity.[21]



The corresponding *cis*-dichloroalkenes are obtained with trichloroethylene:

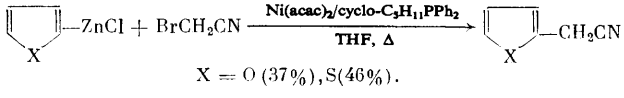


A one-pot bishomologisation of heterocyclic Grignard compounds can be achieved by cross-coupling with β-bromovinyl ethers.[22,23]

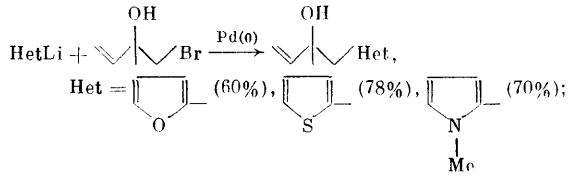


As the resulting vinyl ethers are readily hydrolysed to aldehydes, the above cross-coupling may be viewed as a formylmethylation of Grignard compounds.

2-Furyl- and 2-thienyl-zinc chloride react with bromoacetonitrile to give the corresponding cyanomethyl derivatives in the presence of a Ni catalyst:[24]

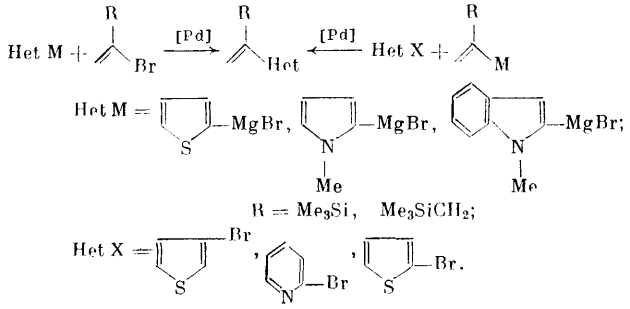


Characteristically, lithiated heterocyclics react with ispropene bromhydrin in the presence of a Pd catalyst to give the corresponding unrearranged allyl alcohol with complete regioselectivity.[25]

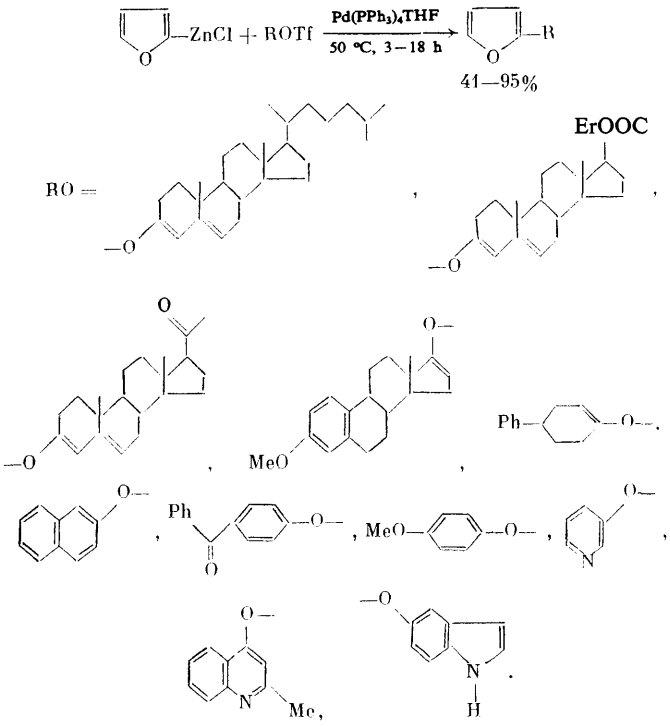


In contrast, alkyl and aryl Grignard compounds react with allyl rearrangement.[26]

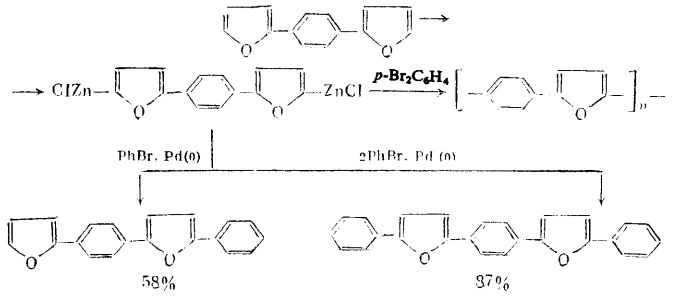
Palladium-catalysed cross-coupling of 1-halogenovinyl- or 2-halogenoallyl-silanes with heterocyclic organo-magnesium or -zinc compounds affords the corresponding heterocyclic vinyl- or allyl-silanes in high yield. Alternatively, these products can be obtained by cross-coupling of heterocyclic halides with the corresponding silylated organometallic compounds:[27]



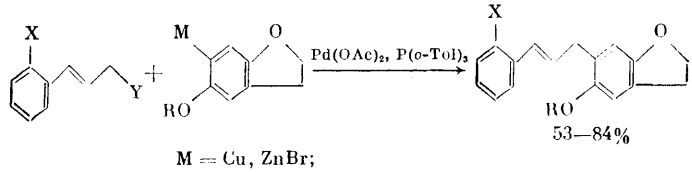
Triflates (ROTf) may be used in place of halides for cross-coupling. Thus 2-substituted furans are readily formed by coupling 2-furylzinc chloride with various vinyl and aryl triflates:[28]



The bis(2-furylzinc chloride) obtained from 1,4-bis(2-furyl)benzene reacts with bromobenzene or 1,4-dibromobenzene to give oligomers or polymers:[29]

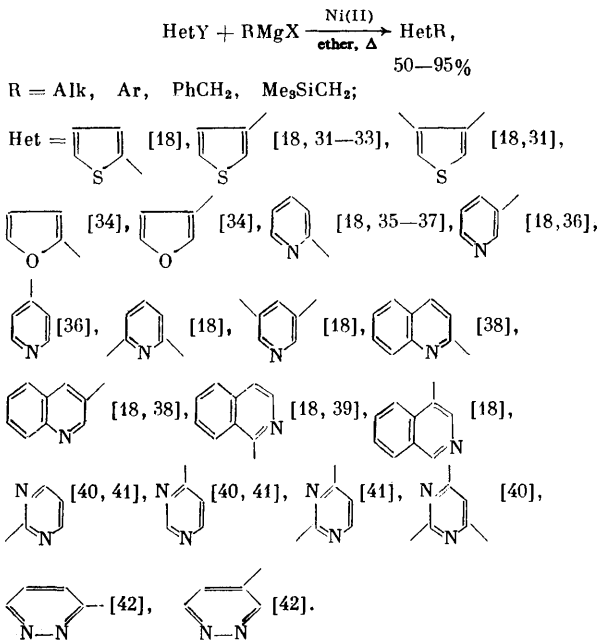


Palladium-catalysed allylic alkylation of organometallic derivatives of dihydrobenzofuran with cinnamyl bromides or acetates leads to the corresponding cinnamyl derivatives which are of interest as antipyretic agents.[30]



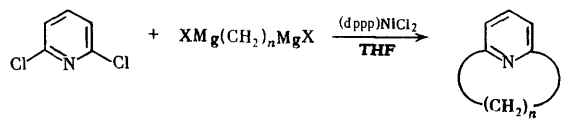
Various types of heterocyclic halides couple with Grignard compounds in the presence of nickel catalysts to give the

corresponding substituted heterocyclics in high yield:



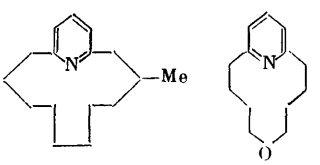
Extension of cross-coupling to heterocyclic dihalides and trihalides leads to the corresponding di- and tri-alkyl or di- and tri-aryl derivatives. Best results have been obtained with catalysts having a bidentate phosphine ligand—dppe, dppp, dppb and dppf.

Interestingly, cycloalkylation takes place on coupling 2,6-dichloropyridine with bis(Grignard compounds) to give 2,6-pyridophanes:[43]



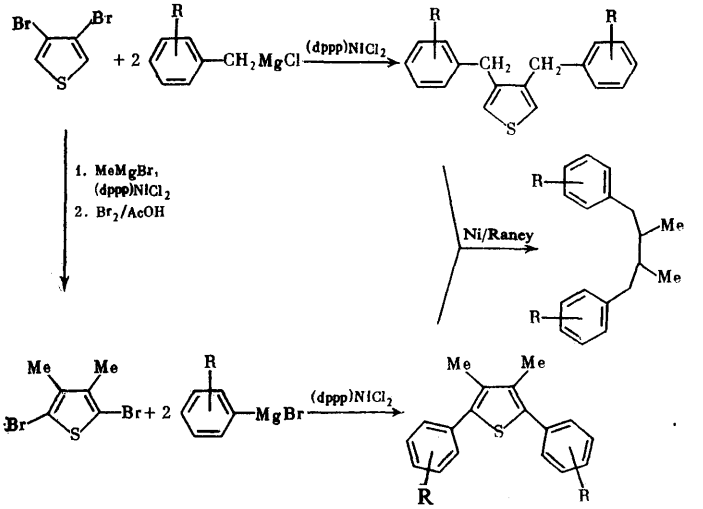
p=6 (11%), 7 (10%), 8 (16%), 9 (15%), 10 (33%), 12 (26%).

Racemic muscopyridine (II) and the oxapyridophane (III) have also been prepared by this route:

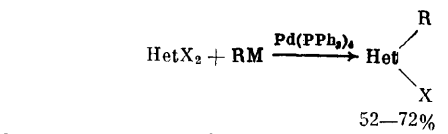


(II), 20% (III), 20%

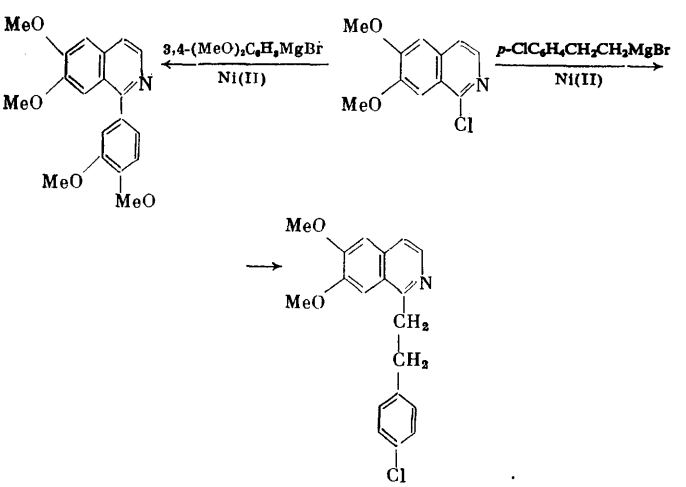
The thiophene molecule has been used as a four-carbon synthon in the synthesis of 2,3-disubstituted butanes, the basic structure of certain ligands. The key step is the cross-coupling of the appropriate dihalogenothiophene with Grignard or organozinc compounds in the presence of a nickel or palladium catalyst:[44]



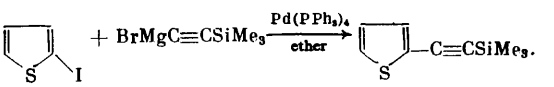
It is also possible to prepared unsymmetrically substituted heterocyclics by Pd-catalysed mono-benzylation or -arylation of the corresponding heterocyclic polyhalides:[45]



The reaction of 1-chloro-6,7-dimethoxyisoquinoline with 3,4-di-methoxyphenylmagnesium bromide and *p*-chlorophenylethyl-magnesium bromide leads to intermediates *en route* to pharmacologically active isoquinoline alkaloids.[18]

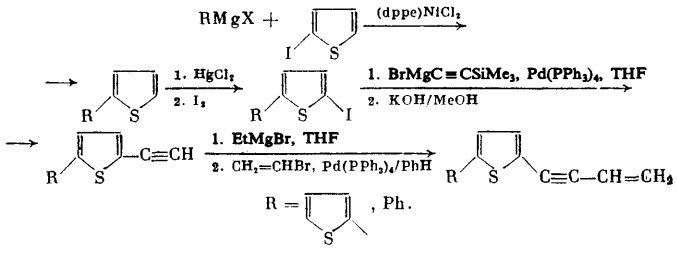


2-Iodothiophene cross-couples with trimethylsilylethynyl-magnesium bromide:[46]

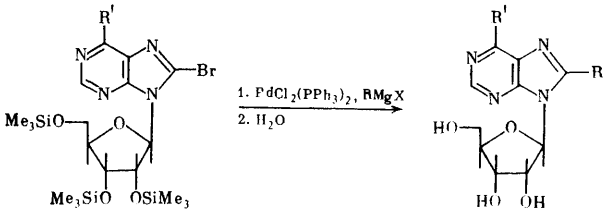


98%

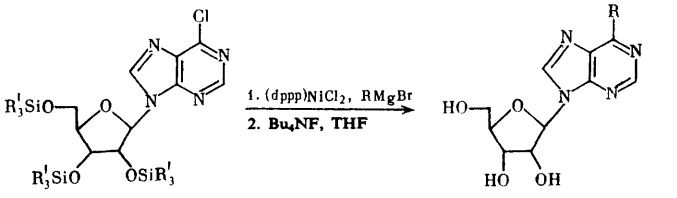
This reaction has been used for the synthesis of natural products containing a thiophene residue, which possess nematocidal activity.[47] One such route is based on a sequential cross-coupling using both nickel and palladium catalysts:



Silyalated 8-bromopurine nucleosides and 8-bromoadenosine-3′,5′-cyclic monophosphate cross-coupling with Grignard compounds in the presence of a Pd catalyst to give the corresponding 8-substituted derivatives;[48]

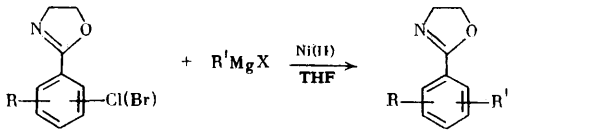


Biologically active 6-substituted purine nucleosides may be obtained similarly by nickel-catalysed cross-coupling of the corresponding 6-chloropurine nucleoside with Grignard compounds:[49]



R = Et, cyclo-C_6H_{11}, Ph, $PhCH_2CH_2$, $PhCH_2CH_2CH_2$, $Me_2C{=}CHCH_2CH_2$.

It has been shown that a halogen atom at the 2-, 3- or 4-position of (Δ^2-oxazolin-2-yl)arenes is readily replaced by an alkyl or aryl group in high yield:[50]



With (Δ^2-oxazolin-2-yl)dichlorobenzenes there is the possibility of regioselective introduction of one or two substituents into the benzene ring, depending on the relative proportion of Grignard compound and substrate.

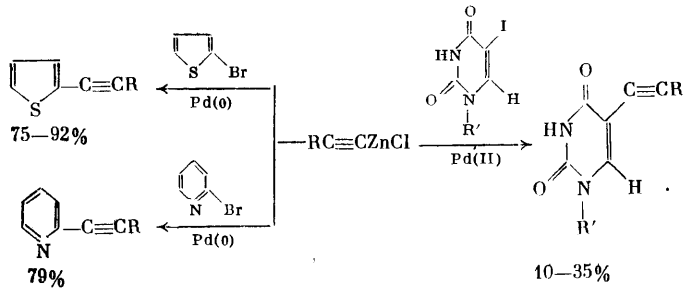
Both simple and functionalised organozinc compounds participate in Pd-catalysed cross-coupling with heterocyclic halides. Thus, 2-, 3- and 4-halogenopyridines, 2, 4- and 5-halogenopyrimidines, and 2-halogenoquinolines readily couple with functionalised organozinc compounds, including the Reformatskii reagent:[51,52]

$$HetX + IZn(CH_2)_nX \xrightarrow{Pd} Het(CH_2)_nX, \quad \sim 95\%$$

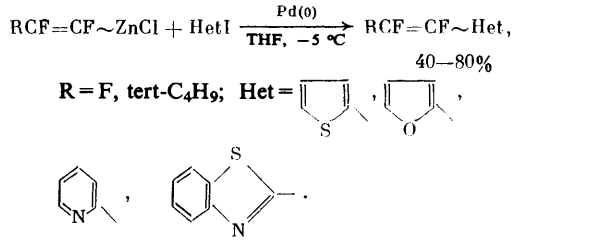
$p = 2, 3, 4$; X = Cl, CO_2Et.

The 2- and 4-halogenopyridines are more active than 3-halogenopyridines in this reaction.

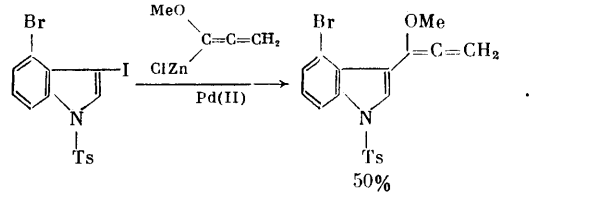
Alkynylzinc chlorides also couple smoothly with 2-bromo- or 2-iodo-thiophene[53] and with 2-bromopyridine[19], and react with 5-iododeoxyuridines to give the corresponding 5-alkenyl derivatives:[54]



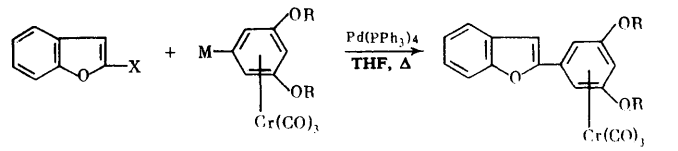
Perfluorovinylzinc compounds cross-couple effectively with a variety of heterocyclic halides:[55,56]



Allenylzinc chlorides have been used to introduce an unsaturated function at the 3-position of the indole ring.[57]



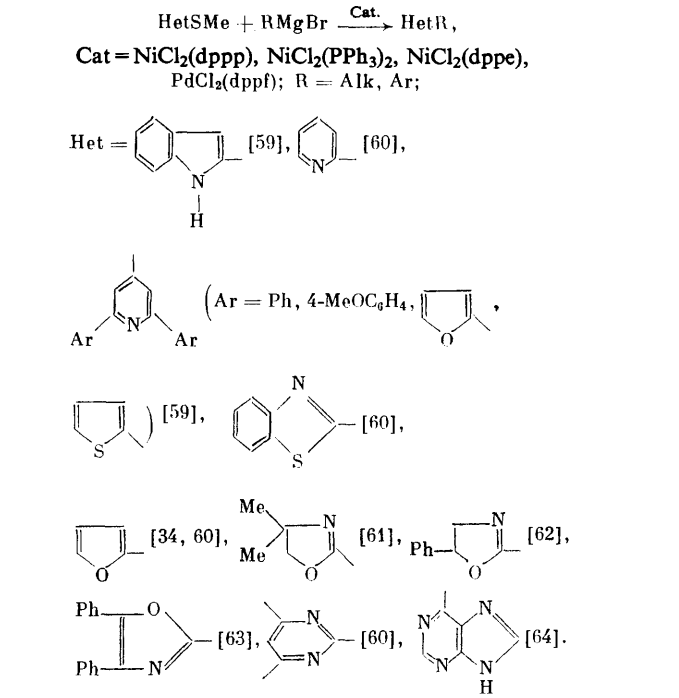
Moracin, a member of a family of biologically active compounds[58], has also been prepared by cross-coupling. The strategy involves Pd-catalysed cross-coupling of two aromatic systems: 2-metallated (or 2-halogenated) benzofurans and 5-halogenated (or-metallated) resorcinols, the latter as their chromium tricarbonyl complexes:



X = I, Br, $ZnBr$, $SnMe_3$,
M = $ZnBr$, I, Cl; R = H, SiR_3', Me.

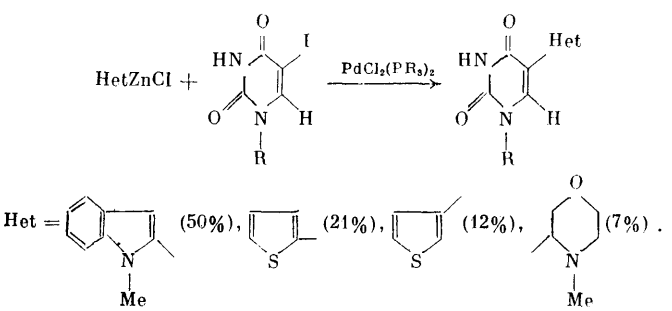
Alkylthio derivatives may be used in place of halides for cross-coupling. Thus, methylthio-substituted *N*-, *O*-, and *S*-heterocyclics undergo Ni- and Pd-catalysed cross-coupling with Grignard

compounds to give the corresponding alkyl- or aryl-heterocyclics.



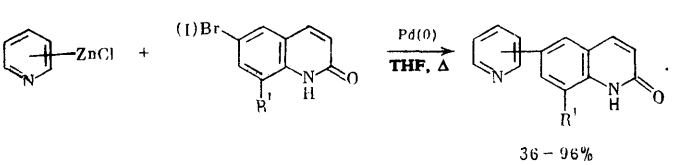
Alkyl- and aryl-derivatives of indole, pyridine, furan, benzothiazole, oxazoline, oxazole, pyrimidine and purine have all been prepared by this route.

Various biheterocyclics are generally available by catalysed cross-coupling of heterocyclic Grignard or organozinc compounds with heterocyclic halides. Thus, interaction of 5-iododeoxyuridines with HetZnCl affords a low yield of the corresponding nucleoside with a heterocyclic substituted in the 5 position:[65]

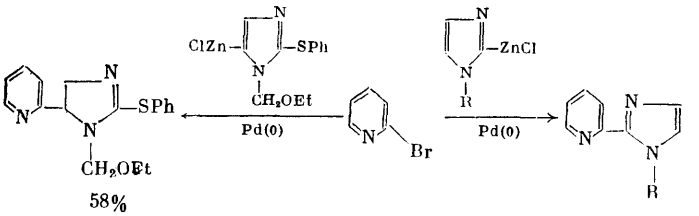


The above reactions proceed in the presence of a Pd catalyst.

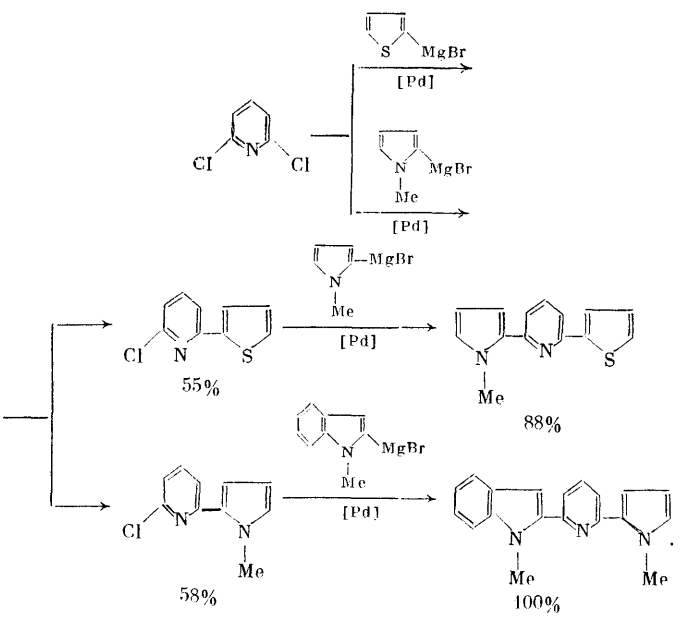
Cross-coupling of pyridylzinc chlorides with 6-halogeno-2(1*H*)-quinolines is a convenient method of preparing 6-pyridyl-2-(1*H*)-quinolines:[66,67]



2-Bromopyridine readily reacts with *N*-substituted 2- and 5-imidazolylzinc chlorides in the presence of a Pd(0) catalyst to give the corresponding imidazolylpyridines:[68]

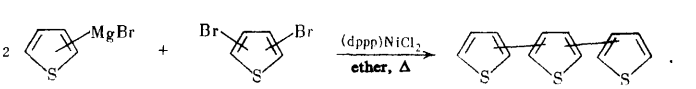


Reactions of dihalogenopyridines with 2-thienyl-, 2-pyyrolyl-, and 2-indolyl-magnesium bromides can be preformed in a variety of sequences to give the corresponding tri-nuclear systems,[69] e. g.



This is the basis of a method of preparing linear polyheterocyclic compounds.

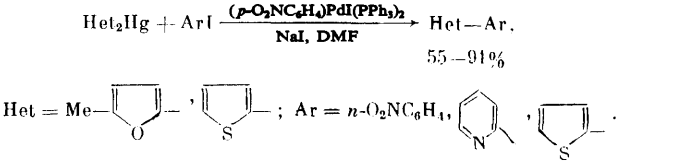
Nickel- or palladium-catalysed cross-coupling of 2- and 3-thienylmagnesium bromides with 2- and 3-bromothiophenes or isomeric dibromothiophenes (in varying proportions) leads to bi-, ter- and oligo-thienyls:[18,70–72]



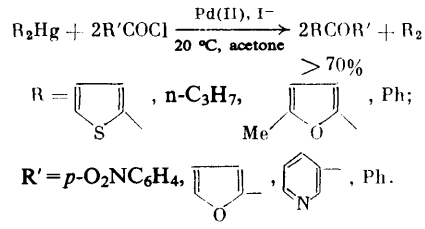
Biheterocyclics of the type furan-thiophene[46] and thiophene-uracil[73] have also been synthesised.

2. Organo-mercury and -copper compounds

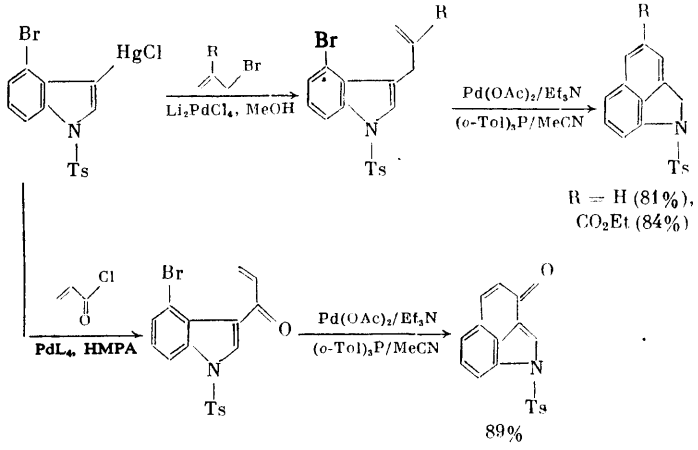
In addition to the organometallic compounds mentioned in section 1, cross-coupling with heterocyclic derivatives can also be achieved with organomercury compounds. Thus, symmetrical diorganomercury compounds react with aryl and heteroaryl iodides in the presence of a Pd-catalyst:[74]



Heterocyclic ketones have been prepared by acyldemetallation of organomercury compounds in the presence of a Pd complex.[75] Thus, the reaction of diorganomercurials, R_2Hg, with acyl chlorides proceeds readily in acetone at 20 °C during 5–30 min in the presence of a Pd(II) salt:

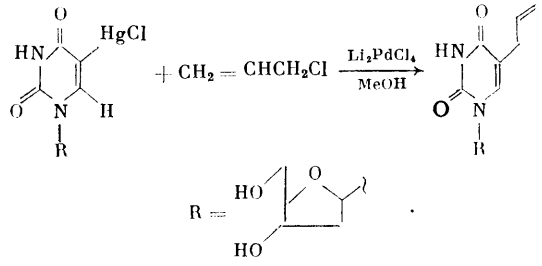


Palladium catalysts have been used in the synthesis of indole derivatives.[76] Thus, 3-substituted indoles are obtained in high yield by treatment of 3-chloromercuri-4-bromoindole derivatives with allyl halides in the presence of Li_2PdCl_4. Feaction proceeds via Hg → Pd transmetallation, followed by insertion of the olefin group into the resulting indolylpalladium complex then elimination of β-halogen. The products readily undergo intramolecular Heck reaction with simultaneous isomerisation of the formed tricyclic indole into the thermodynamically more stable benz[*c*,*d*]indole system.[57]



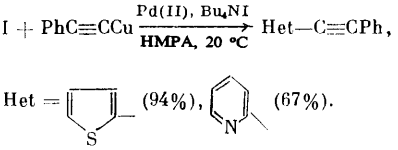
Similarly, 3-chloromercuriindole reacts with acryloyl chloride in the presence of Pd(0) to give the corresponding 3-acylindole which cyclises into a tricyclic ketone in high yield.

5-Chloromercuri-2-deoxyuridine condenses with allyl chloride in the presence of 20 mol% Li_2PdCl_4 to give the corresponding 5-allyl derivative:[77]



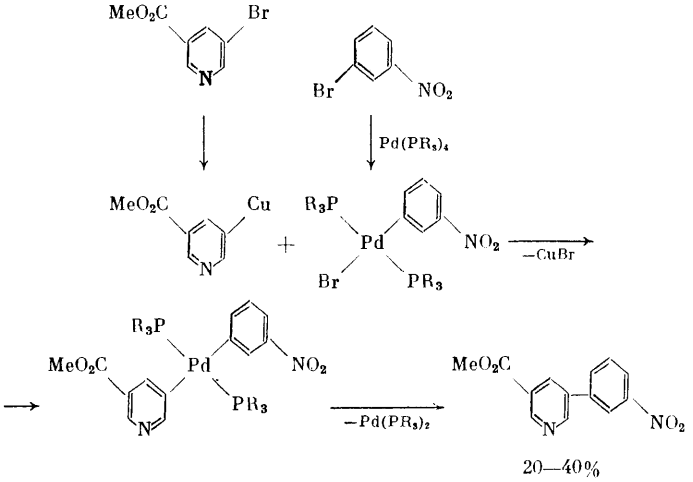
The use of substituted allyl chlorides in this reaction leads to a mixture of regioisomers.[78]

Beletskaya et al.[79] showed that cuprous phenylacetylide reacts quite readily with 2-iodothiophene and 2-iodopyridine to give the corresponding 2-alkynylheterocyclics:



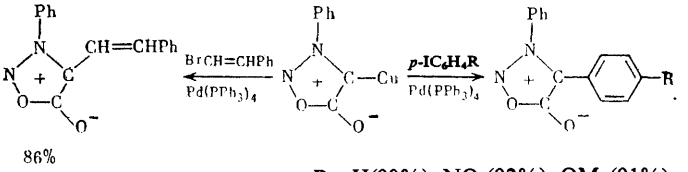
Tetra-π-butylammonium iodide, which increases the solubility of CuI (used for the preparation of the acetylide), has a significant effect on the rate of reaction and the yield of product.

Coupling 5-bromonicotinates with *m*-bromonitrobenzene in the presence of Cu and a Pd(0) catalyst affords the corresponding 5-arylnicotinates which have been used in the synthesis of physiologically active compounds.[80] The mechanism of the reaction is thought to involve formation of a 5-cupronicotinate which couples with the palladium compound formed by oxidative addition of Pd(0) to *m*-bromonitrobenzene; reductive elimination then takes place in the final step:



$Pd(PR_3)_4 = Pd(PPh_3)_4$, $Pd[P(Tol\text{-}o)_3]_4$.

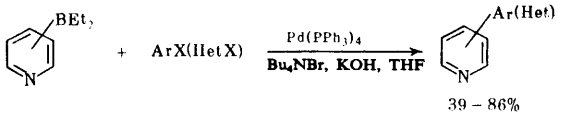
Palladium-catalysed cross-coupling of 4-cuprosydnone with aryl and vinyl halides is the basis of a general method of introducing a 4-substituent into the 3-phenylsydnone ring.[81]



R = H(90%), NO_2(92%), OMe(91%).

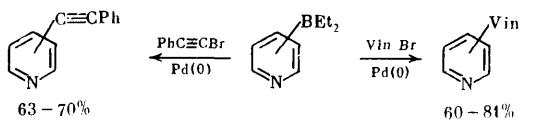
3. Organo-boron, -aluminium and -zirconium compounds

Three-coordinate boron compounds have also been used in cross-coupling. 3-Pyridyl- and 4-pyridyl-boranes react efficiently with various bromo- or iodo-arenes and heterocyclic halides in the presence of a Pd(0) catalyst:[82–84]

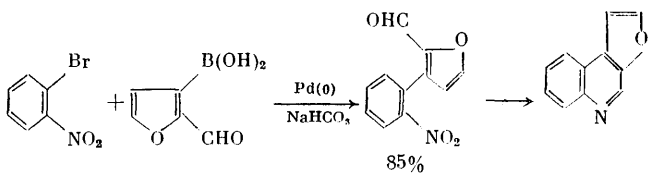


Reaction has been carried out with a wide variety of aryl halides having different functional groups and with a number of heterocyclics, such as substituted pyridines, quinolines, thiophenes, benzoaxoles, pyrimidines and indoles.

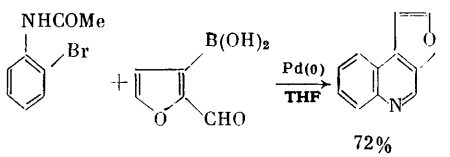
Vinyl and alkynyl bromides couple readily with 3- and 4-pyridyldiethylboranes to give the corresponding vinyl- and alkynylpyridines:[85]



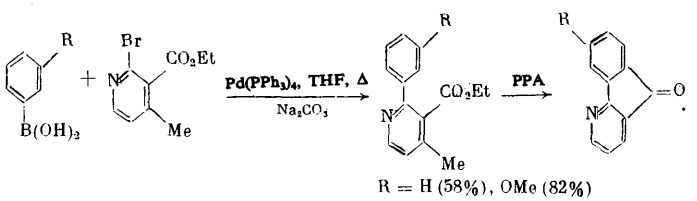
Cross-coupling has been applied in a multi-step route to pharmaceutically interesting furoquinoline alkaloids. Thus, 2-formyl-3-furylboronic acid couples with 2-bromonitrobenzene to produce 2-formyl-3-(2′-nitrophenyl)furan:[86]



A more effective route is based on coupling 2-bromoacetanilides with 2-formyl-3-furylboronic acid, which leads directly to the desired furoquinoline:



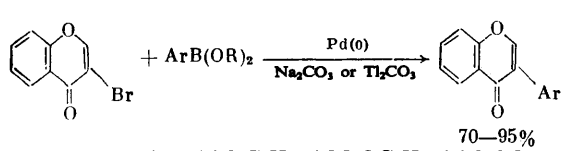
An interesting application of cross-coupling between arylboronic acids and heterocyclic halides has been reported in the synthesis of alkaloids with the azafluorenone skeleton.[87] Palladium-catalysed coupling of arylboronic acids with 2-bromonicotonic acid esters affords dimeric products which subsequently cyclise to give the desired alkaloids.



R = H (58%), OMe (82%)

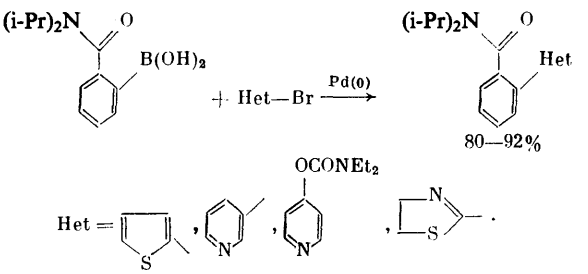
However, in this case, the best results have been achieved with arylstannanes.[87]

Cross-coupling of 3-bromochromones with arylboronic acids or their esters in the presence of a Pd catalyst provides a convenient preparative route to isoflavones:[88]

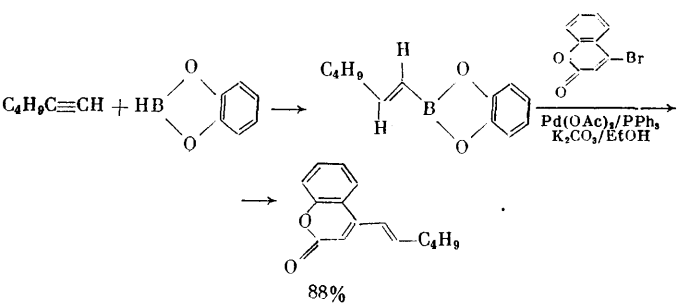


R = H, n-Bu; Ar = 4-MeC$_6$H$_4$, 4-MeOC$_6$H$_4$, 2-MeOC$_6$H$_4$, Ph, 4-FC$_6$H$_4$, 4-O$_2$NC$_6$H$_4$, 1-C$_{10}$H$_7$, 2,4,6-Me$_3$C$_6$H$_2$.

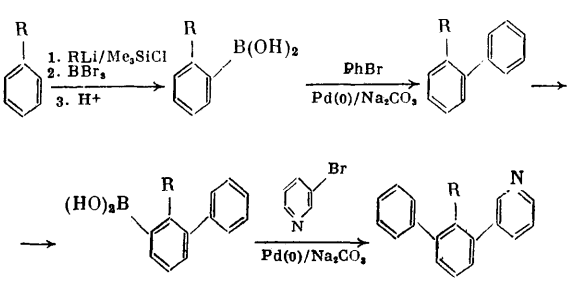
Heterocyclic residues can effectively be incorporated into unsaturated systems by cross-coupling of aryl- and vinyl-boronic acids with heterocyclic halides.[80,89,90] Thus:



2-Alkenyl-1,3,2-benzodioxaboroles, readily formed by hydroboration of acetylenes with catecholborane, are suitable synthons for preparing 2,4-alkadienoates by cross-coupling. The method is applicable to cyclic analogues, such as 4-alkenylcoumarins:[91]

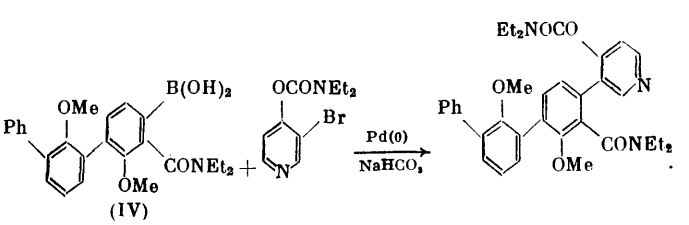


Reference has been given to an original method of preparing *m*-terphenyls containing heteroarene residues.[92] Aromatic compounds with substituents which faciliate *o*-metallation may be used for the preparation of *o*-substituted boronic acids. The latter couple effectively with hererocyclic halides, e. g. 3-bromopyridine:



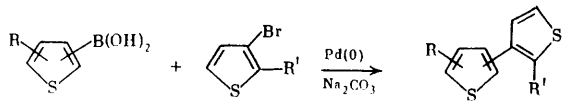
R = $CO_2N(Pr\text{-}i)_2$, $OCONEt_2$, OCH_2OMe, $NHCO_2Bu\text{-}t$.

To illustrate the possibility of preparing polyfunctionalised heteroarenes, we show below the synthesis of pyridotetraphenyl by cross-coupling of (IV) with a 4-pyridyl carbamate:[93]



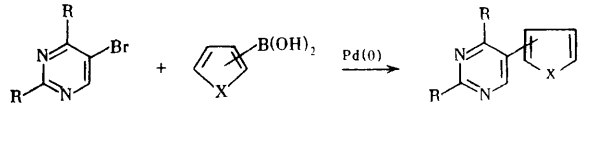
Palladium(0)-catalysed cross-coupling of 2- and 3-thienylboronic acids with mono- and poly-halogenothiophenes provides the basis of a method of preparing bi- and poly-thienyls.[94–96] It has been adapted to the synthesis of compounds with a variety of

substitutents in the thiophene rings, e. g.



R = H, 2-CHO, 4-CHO; R′ = H, 2-CHO, 2-NO_2, 2-SMe.

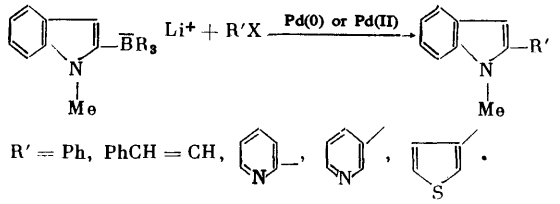
The method has been adapted to the synthesis of other linearly condensed polyheterocycles — thienopyridines,[97,98] thieno- and selenopheno-pyrimidines,[73] benzo- and thieno-condensed quinolines and naphthyridines,[99,100] e. g.



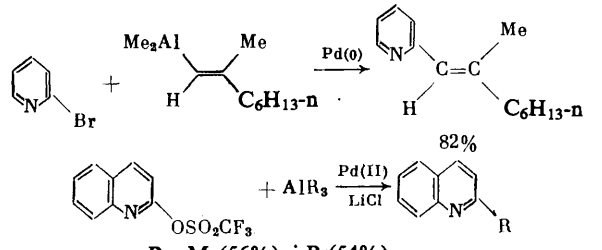
48 – 84%

X = S, Se

Palladium-catalysed coupling of indolylborates with vinyl, aryl and heterocyclic halides has proved of value for the synthesis of 2-substituted indoles:[101]

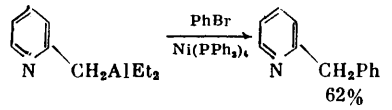


Cross-coupling can also be performed in many instances with organoaluminium compounds. Thus, chloropyrazines,[102] chloropyrazine *N*-oxides,[103] 2-bromopyridine,[19] and 2-quinolinyl triflate[104] react smoothly with organoaluminium compounds in the presence of a palladium catalyst.



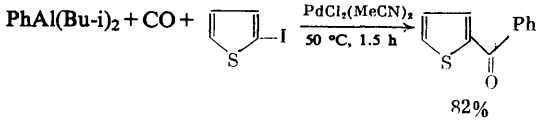
R = Me(56%), i-Pr(54%).

In addition to this, 2- and 4-picolinyl-aluminium and -zinc reagents readily react with aryl and heterocyclic halides in the presence of a Ni(0) catalyst,[105] e. g.



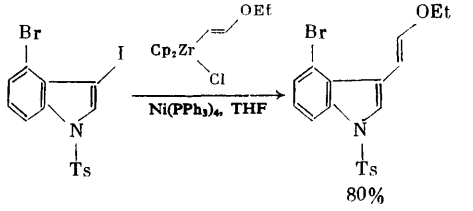
62%

2-Benzoylthiophene is formed smoothly on carbonylation of 2-iodothiophene in the presene of phenyldiisobutylalane:[106]



82%

The 2-ethoxyvinyl group may be effectively transferred from zirconium to the 3-position of indole via Ni(0)-catalysed oxidative addition-transacetalation:[107]

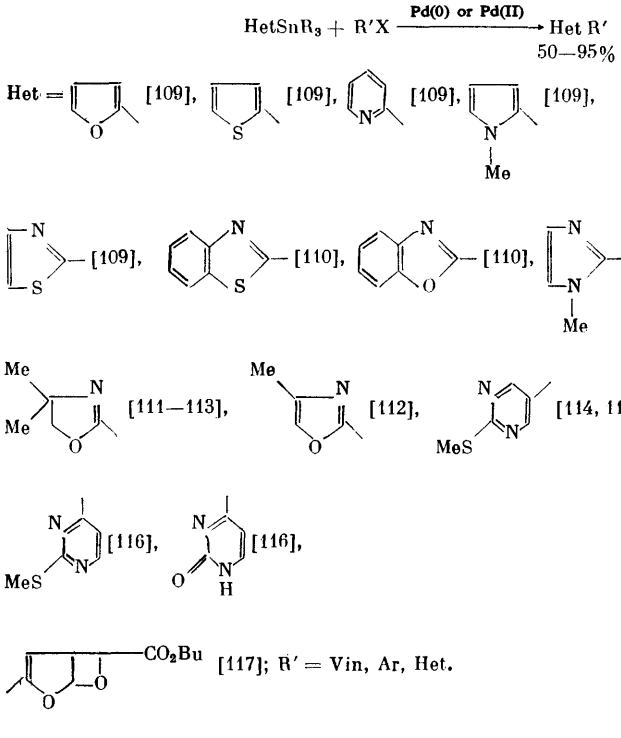


80%

5-Alkenyldeoxyuridines have been prepared by Pd-catalysed coupling of vinylzirconium compounds with deoxyuridine.[108]

4. Organotin compounds

Organotin compounds have been widely used in cross-coupling in view of their chemical stability, the simplicity of their purification, and the possibility of incorporating a variety of functionalised residues. Five- and six-membered heterocyclics with a F_3Sn group have been coupled with aryl, heterocyclic, and vinyl halides:

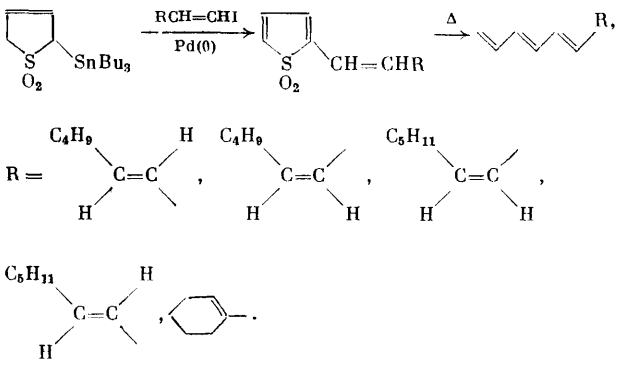


R′ = Vin, Ar, Het.

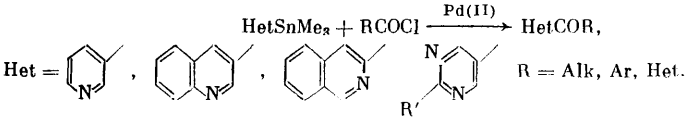
Cross-coupling with oxazolines is particularly interesting since such compounds serve as synthons for preparing carboxylic acids, aldehydes, nitriles and other functionalised derivatives.[118]

The cross-coupling of 2-tributylstannyl-2,5-dihydrothiophene *S,S*-dioxide with vinyl iodides is the key step in the preparation of conjugated trienes, which are generated in desulfonylation of the

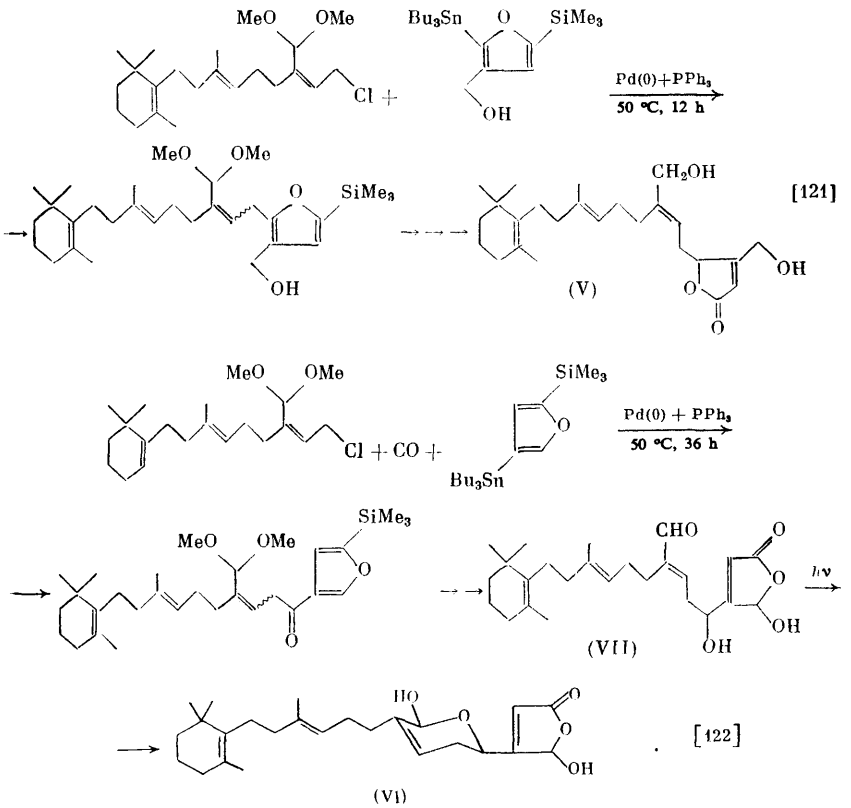
intermediate 2-vinyl derivatives.:[119]



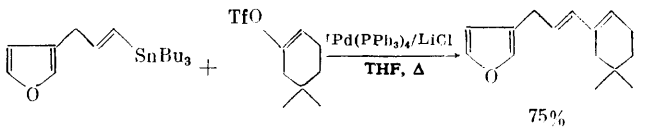
Ketones have been prepared by treatment of trimethylstannyl derivatives of pyridine, quinoline, isoquinoline and pyrimidine with acyl halides in the presence of a Pd catalyst:[114,120]



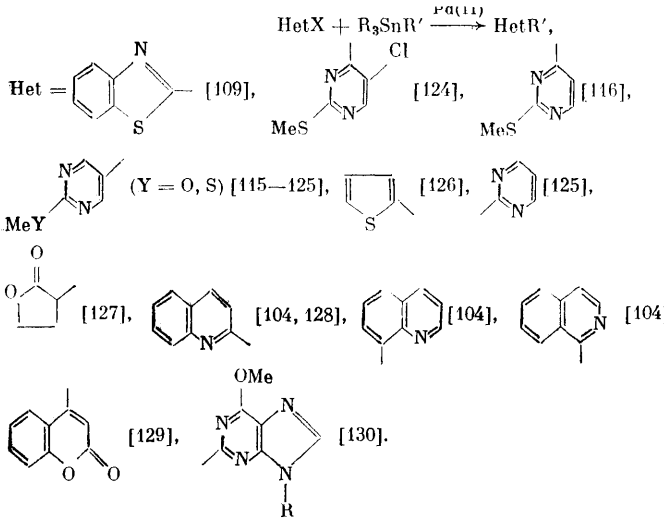
Cross-coupling with stannylfurans has been applied to the synthesis of the biologically active terpenoids, (*E*)-neomanoalide (V), manoalide (VI), and secomanoalide (VII). These compounds possess antiinflammatory and antifungal activity and have an effect on phospholipid metabolism.[121,122]



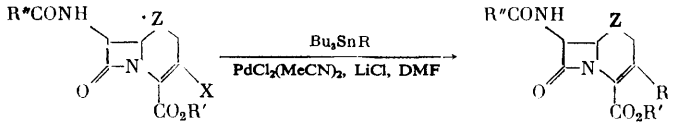
Pd-catalysed coupling of vinyl triflates (TfOR) with organostannanes has been adapted in an elegant synthesis of pleraplysillin:[123]



Various heterocyclic halides and triflates participate in catalysed coupling with organostannanes:

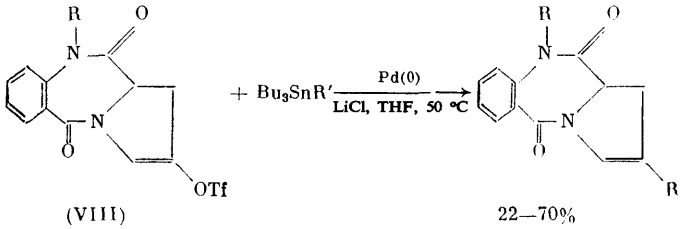


Substituents may be introduced into the 3-position of the caphalosporin and 1-carbacephalosporin nuclei by Pd-catalysed cross-coupling:[131–133]



$Z = CH_2$, S; X = OTf, Br.

Anthramycin analogues have been synthesised by cross-coupling of triflate (VIII) with various unsaturated compounds having a Bu_3Sn residue:[134]

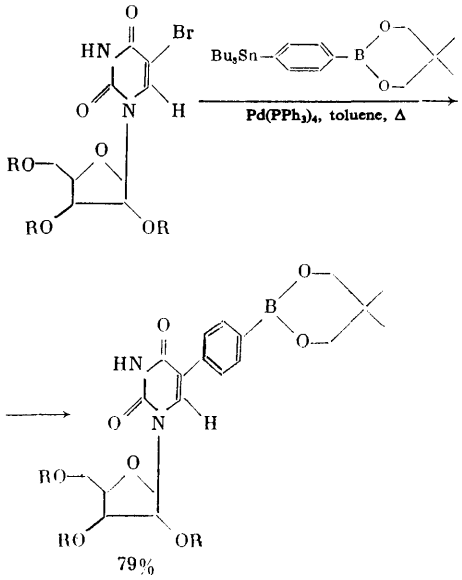


R = Me, CH_2OMe; R′ = CH_2=CH, EtO_2CCH=CH,

MeO_2CCH=CH, H_2NCCH=CH.

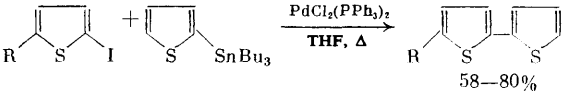
The same products have been obtained independently by interaction of triflate (VIII) with acrylic acid amides and esters in the presence of a Pd catalyst.

Cross-coupling of halogenonucleosides with boron-substituted arylstannanes has been extended to the synthesis of ^{10}B-containing nucleosides which are of value in neutron-capture therapy:[135]



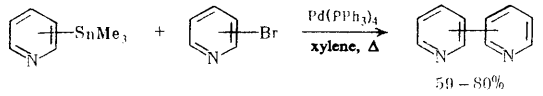
R = $SiMe_2$(Bu-t).

Bi- and poly-nuclear heterocyclics have been synthesised by reaction of heterocyclic halides with trialkylstannylheterocyclics. 2,2′-Bithienyls have thus been prepared in high yield by cross-coupling of 2-iodothiophenes with 2-stannylthiophenes:[136]

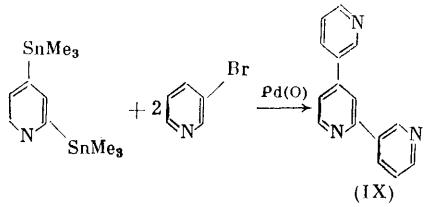


R = H, CH_2OAc, CH_2OH, CHO, CH_2OCOCH_2Pr-i, $C{\equiv}CCH_2CH_2OCOCH_2Pr$-i.

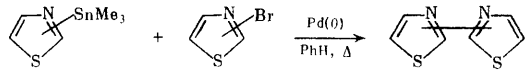
Isomeric bipyridyls are formed by interaction of trimethylstannylpyridines with bromopyridines:[137]



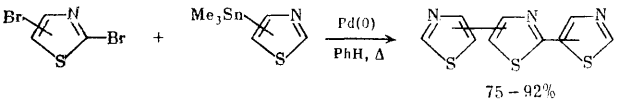
The reaction has been extended to the preparation of substituted quinolines. The synthesis of nicotelline(IX) is of particular interest:



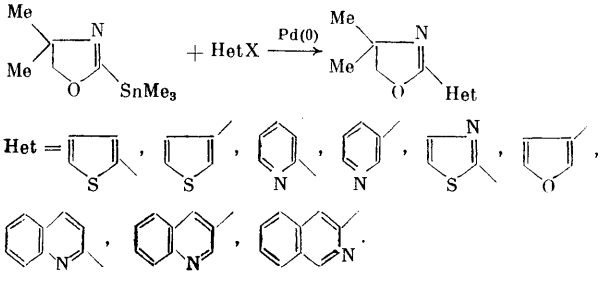
Bi- and ter-thiazolyls have been obtained by cross-coupling of stannyl- and halogeno-thiazoles:[138]



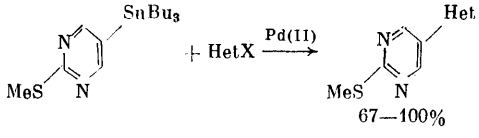
Double cross-coupling takes place readily with dibromothiazoles.

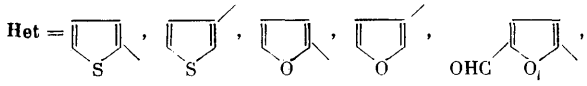


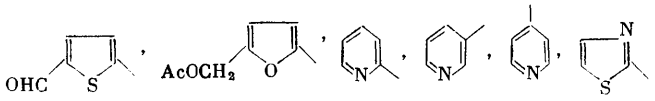
Catalytic cross-coupling of stannyl-oxazoles or -oxazolines with a variety of heterocyclic halides has been applied to the synthesis of oxazol-2-yl- and oxazolin-2-yl-heterocyclics which are intermediates *en route* to carboxylic acid derivatives,[112] e. .g.



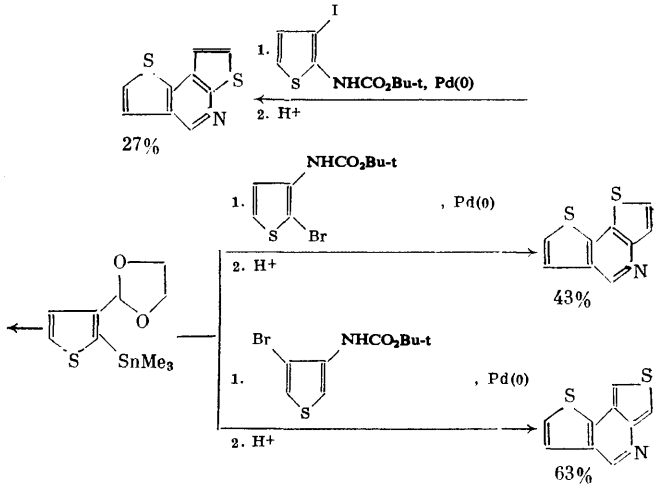
5-(Tributylstannyl)pyrimidines couple effectively with various heterocyclic halides to give the corresponding unsymmetrical biheterocyclics:[139]



Het = 



Isomeric dithienopyridines have been prepared by a novel route involving Pd-catalysed coupling of 2-(2′-trimethylstannyl-3′-thienyl)-1,3-dioxolane with tert-butyl *N*-(*o*-halogenothienyl)carbamates followed by acidic hydrolysis. The ultimate cyclisation takes place instantaneously under the conditions of the hydrolytic step.[140,141]

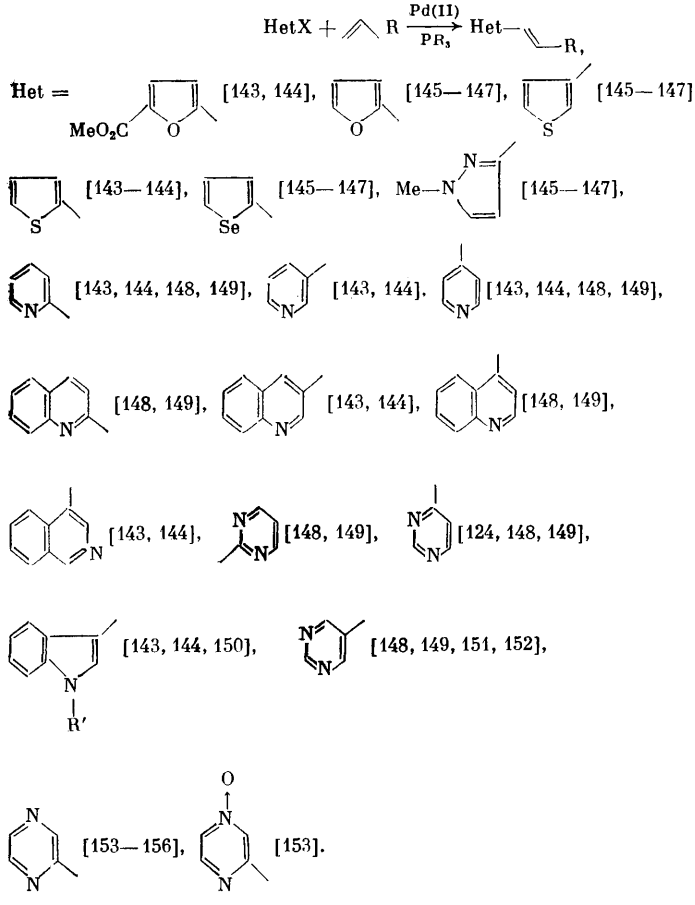


III. Reactions of heterocyclic halides with alkenes and alkynes

1. Reactions of heterocyclic halides with alkenes

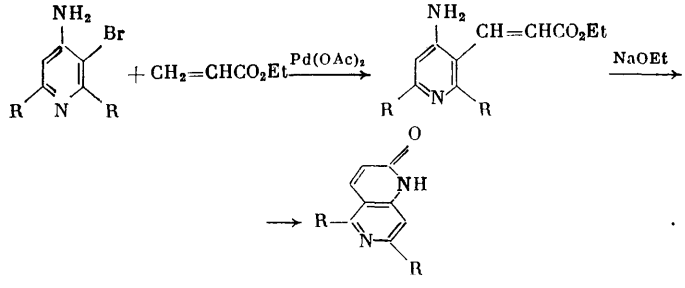
Palladium-catalysed vinylation of organic halides provides a route to substituted heterocyclics by carbon–carbon bond formation.[5,142] This method has been widely used with organic halides which do not possess a β-hydrogen atom, such as aryl, benzyl, vinyl and heterocyclic halides. In the previous sections of this review we have examined cross-coupling of heterocyclic halides with metal alkenyls as a route to vinylheterocyclics. Clearly, palladium-catalysed reaction of heterocyclic halides with alkenes themselves is more preferable. This is the basis of the Heck reaction.

Vinylheterocyclics can thus be prepared by Pd-catalysed condensation with a wide spectrum of alkenes—alkyl acrylates, acrylonitrile, styrene, vinylpyridines, butenylphthalimide, vinyltrimethylsilane, α-acetamidoacrylates, indole, etc.



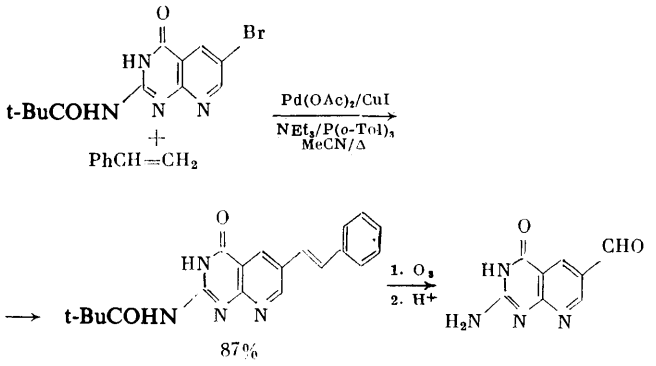
Heterocyclic triflates also participate in the Heck reaction with activated olefins.[104] Palladium catalysis is effective in the functionalisation of the pyrimidine ring of nucleosides.[130]

Isomeric naphthyridines have been prepared by a novel two-step conversion involving Pd-catalysed cross-coupling of *o*-amino-substituted 2-, 3- and 4-halogenopyridines with ethyl acrylate followed by cyclisation,[157–161] e.g.

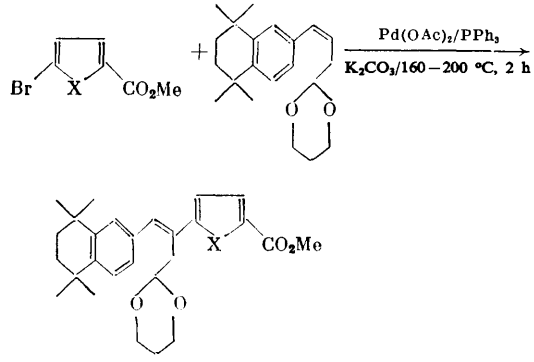


6-Formyl-5-deazapterin, a key intermediate in the synthesis of various 5-deaza-analogues of folic acid, has been readily prepared by Pd-catalysed cross-coupling of 2-pivaloyl-6-bromo-5-deazapterin with

styrene, followed by ozonolysis and hydrolysis

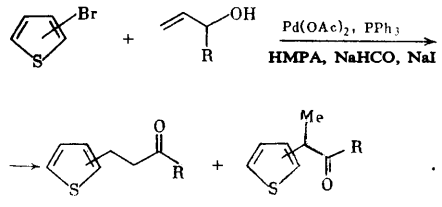


The Heck reaction is particularly useful for the preparation of synthons *en route* to retinoids.[163] Thus, bromo-furans and -thiophenes readily couple with ω-substituted styrenes to give the corresponding (*E*)-stilbenes:



X = O, S.

Treatment of 2- and 3-bromo-thiophenes with allyl alcohols affords aldehydes and ketones with a thienyl residue.[164–166] β-Thienylcarbonyl compounds are formed as the major products:

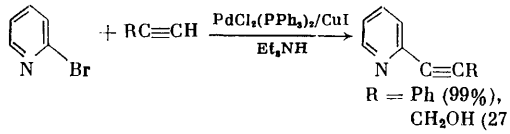


3-Bromopyridine reacts with allyl alcohols similarly.[167]

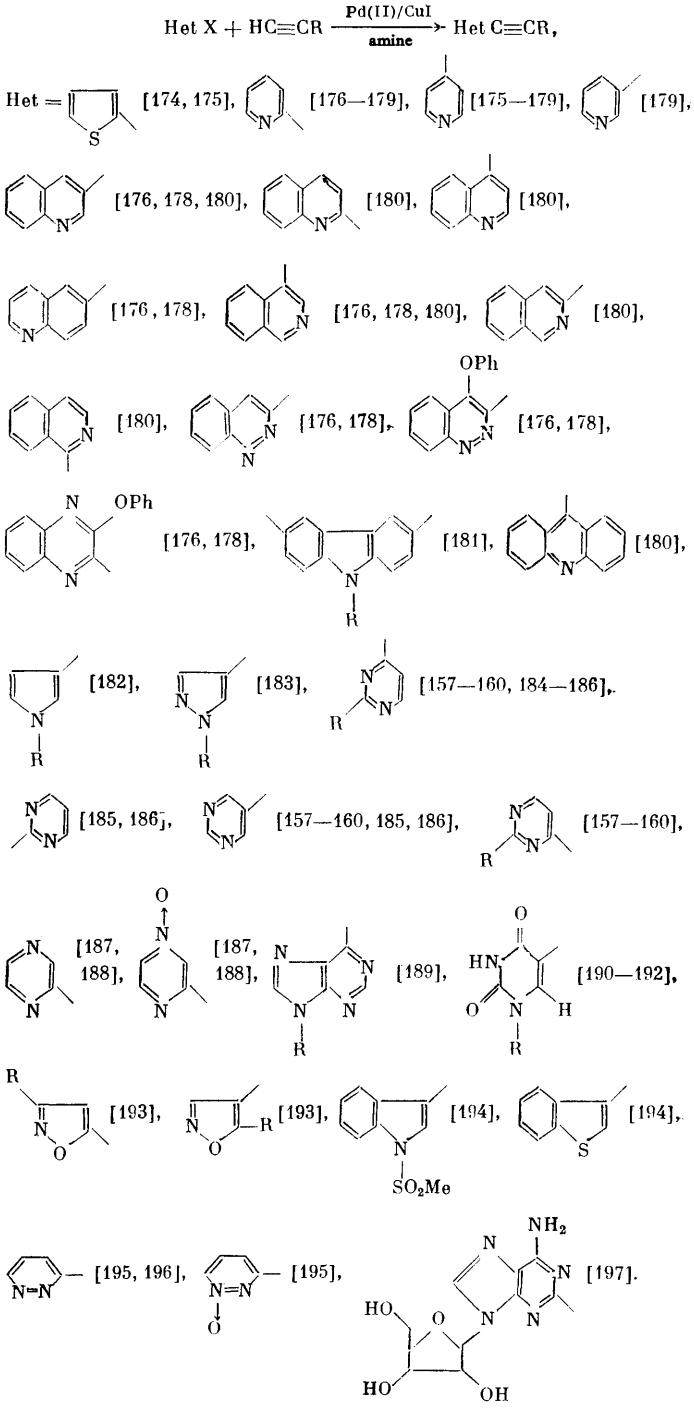
Heterocyclic mercurials react with alkenes in the same way as heterocyclic halides. Thus, 5-alkenyluracil nucleosides and nucleotides have been synthesised by Pd-catalysed cross-coupling of the appropriate mercuriuracil derivatives with a variety of alkenes.[168–170]

2. Reactions of heterocyclic halides with alkynes

The preparation of alkynylarenes by Pd-catalysed reaction of aryl halides with terminal alkynes was pioneered in 1975.[171–173] Sonogashira et al.[171] showed that reaction was most efficient with CuI as co-catalyst. In this way, 2-alkynylpyridines were prepared by reaction of 2-bromopyridine with acetylene derivatives:

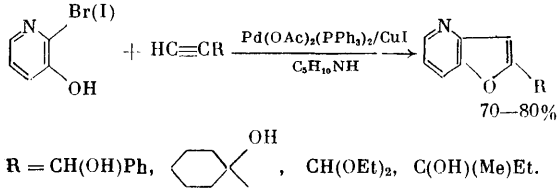


Subsequently, the method was extended to the preparation of a variety of alkynylheterocyclics. As a rule, the yield of the latter is high and the method is preparatively useful.

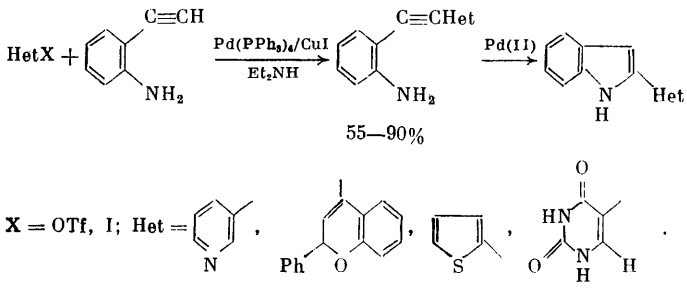


Bis(alkynyl)heterocyclics are formed by reaction of heterocyclic dihalides, e.g. diiodopyrimidines[185,186] and dibromopyridines[198], with terminal acetylenes. Mono-alkynyl derivatives may be isolated by mixing the appropriate proportion of the two reactants. Pyridyl triflates react with terminal acetylenes in the same way as pyridyl bromides.[198]

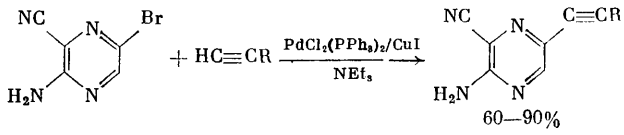
Palladium-catalysed reaction of 3-hydroxy-2-halogenopyridines with terminal acetylenes leads directly to furo[3,2-*b*]pyridines:[199]



2-Substituted indoles have been prepared by coupling heterocyclic triflates or halides with 2-ethynylaniline, followed by Pd(II)-catalysed ring closure of the product:[200]

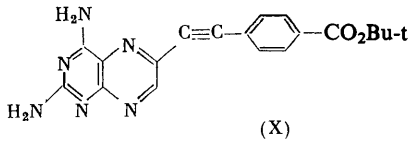


2-Amino-3-cyano-5-bromopyrazine couples with acetylenes as follows:[201,202]



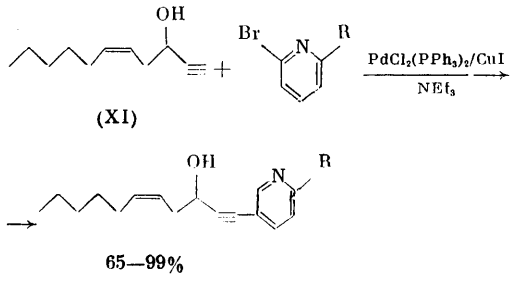
R = Ar, Bu, t-Bu, $MeOCH_2$.

This method is effective for the synthesis of pteridine (X), an intermediate *en route* to the anticancer drug, methotrexate.

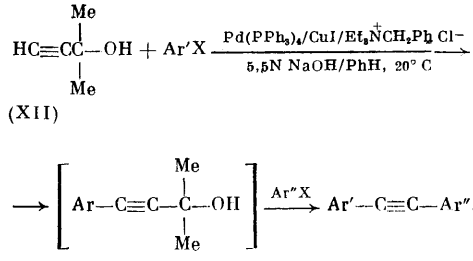


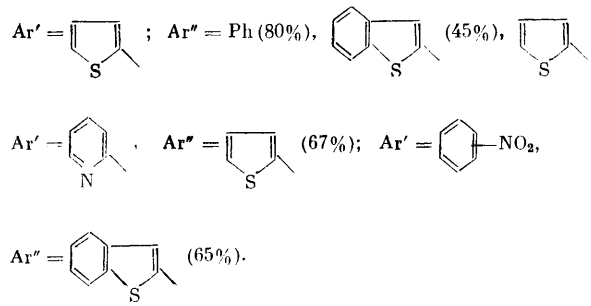
(X)

Synthons for the preparation of leukotriene B_4 antagonists have been synthesised by reaction of 6-substituted 2-bromopyridines with acetylene (XI):[203]

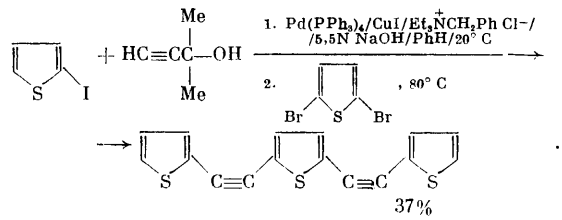


The readily available dimethylethynylcarbinol (XII) couples effectively in the presence of a Pd-catalyst to yield symmetrically and unsymmetrically disubstituted diarylacetylenes in one step.[204] The reaction of (XII) with heterocyclic halides affords the corresponding arylalkynols quantitatively under phase transfer catalysis. The addition of a second molecule of aryl or heterocyclic halide during the reaction leads to the corresponding disubstituted acetylene on raising the temperature to 70—80 °C:

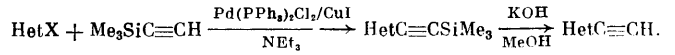




Bisacetylenic compounds, such as 2,5-bis(2'-thienylethynyl)-thiophene, may also be prepared by this route.



Cross-coupling of azinyl and diazinyl halides with trimethylsilylacetylene, followed by desilylation, provides a preparative route to the corresponding ethynylheteroarenes:[205]



IV. Other reactions

Homo-coupling of heterocyclics can be effected by complex metal catalysis. Thus, reductive dimerisation of heterocyclic halides takes place in the presence of both Ni and Pd catalysts. The following systems have been used for homocoupling: $Zn/NiCl_2/PPh_3$ [206—210], $Zn/NiCl_2(PEt_3)_2$ [211], $Ni(COD)_2$ [212],

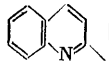
Pd–C/NaOH/HCOONa/H_2O/$Et_3\overset{+}{N}CH_2PhCl^-$ [213], Raney nickel [214], $Ni(OAc)_2$/NaH/PPh_3/*t*-BuOK [215], and $NiBr_2(PPh_3)_2$/Zn/Et_4NI [216]:

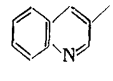
HetX $\xrightarrow{\text{catalyst}}$ Het—Het,

Het =  [206, 210—212],  [211],

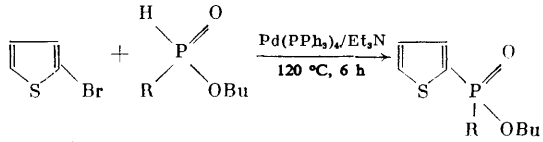
 [207—210, 213—216],

 [200—202, 208, 209],  [200—202, 206, 208],

 [200—202, 209],  [208—210, 216],  [211],

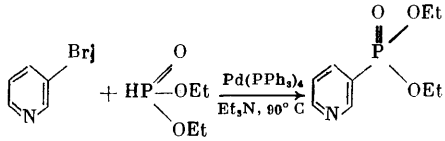
 [211],  [216]  [216],  [216].

Heterocyclic halides also participate in Pd-catalysed cross-coupling with phosphorus compounds possessing a P–H bond. Thus, 2-thienyl bromide reacts with monobutyl alkyl- or aryl-phosphonites in the presence of a Pd(0) catalyst:



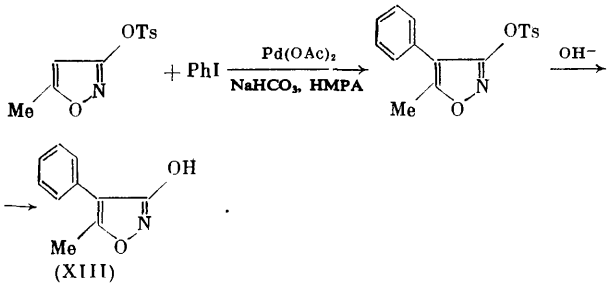
R = Me (70%) [217], Ph (53%) [218].

Diethyl 3-pyridylphosphonate is obtained by coupling of 3-bromopyridine with diethyl phosphite:[219]



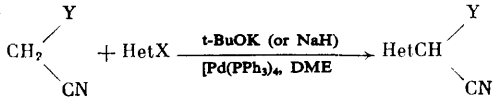
77%

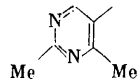
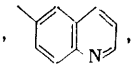
Isoxazole derivatives couple with aryl iodides in the presence of a Pd catalyst to give 4-arylisoxazoles.[220] 4-Phenylmuscimol (XIII), an important neuro-pharmacological drug, has been obtained by this route.

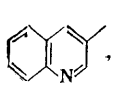
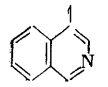


(XIII)

The incorporation of active methylene groups into "unreactive" positions of *N*-heteroarene ring can be conveniently achieved under Pd catalysis. Thus, heterocyclic halides react with the carbanions derived from malononitrile and ethyl cyanoacetate to give the corresponding heteroarylmalonitriles and ethyl α-cyano(heteroaryl)-acetates. Reaction is of a general nature:[221]

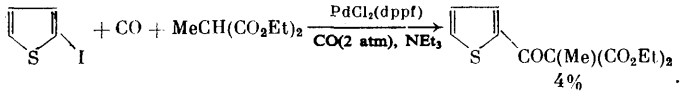


X = Br, I; Y = CO_2Et, CN; Het =  ,  ,  ,

 ,  .

Although $Pd(PPh_3)_2Cl_2$ may be used as catalyst for such coupling with aryl halides[222,223], it is unsuitable for the reactions with heterocyclic halides shown above.

It should be noted that 2-iodiothiophene, like iodobenzene, couples with active methylene groups on carbonylation to give a low yield of the corresponding ketone:[224]



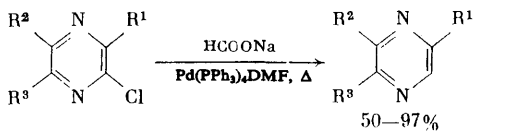
4%

A general synthesis of 2-cyanopyrazines by Pd(0)-catalysed replacement of chlorine by cyano group has been reported:[225]



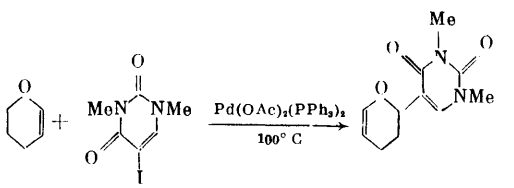
31—98%

Dicyanopyrazines are obtained similarly from the corresponding dichloropyrazines. However, 2-chloropyrazine, as well as its 1- and 4-oxides, are readily dechlorinated on heating with sodium formate in the presence of a Pd(0) catalyst:[226]



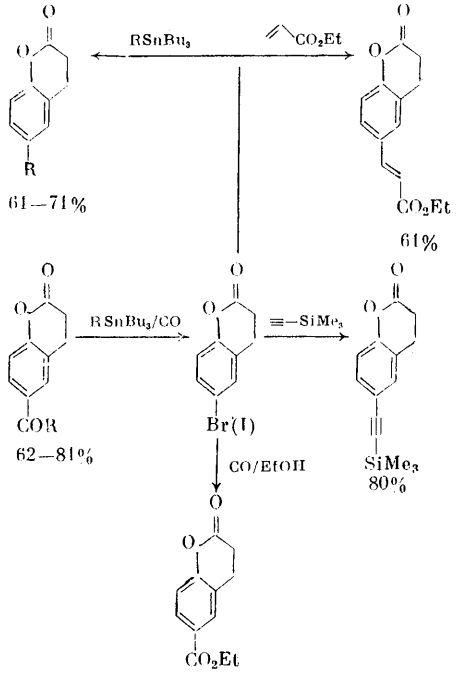
50—97%

Dihydropyran couples with 1,3-dimethyl-5-iodouracil in the presence of a Pd(II) catalyst:[227]



Functional groups may be introduced into the 6-position of the dihydrocoumarin ring by Pd-catalysed coupling (Scheme 2).[228]

Scheme 2



R = Vin, Ph, PhC≡C.

The catalytic formation of a carbon—carbon bond in heterocyclic systems, as described in this review, is potentially very useful in the synthesis of physiologically active compounds and natural products.

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Translated from *Uspekhi Khimii* **60** 374–397 (1991) U.D.C. 541.183:661.183:678.01

Regulation of the adsorption and chromatographic properties of polymeric adsorbents by varying their porous structure

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ABSTRACT. The review surveys the results of studies (using various physicochemical methods) of the geometrical structures of 2,3-epoxypropyl methacrylate–ethylene dimethacrylate and styrene–divinylbenzene copolymers as well as ultracross-linked polystyrenes ("Styrosorbs")—both the initial structures and those modified by amines and aminoalcohols. The influence of the porous structure of the aminated polymers on the adsorption and chromatographic properties was examined mainly in relation to the absorption of carbon and sulphur dioxides. The importance of the optimisation of the structures of the polymeric adsorbents in their practical application is demonstrated.

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I. Introduction

Studies of the chemistry of the surfaces of solids, adsorption, and chromatography have developed appreciably in recent times. This was promoted by the creation of new adsorbents—in particular porous polymers. Polymeric adsorbents are widely used as sorbents in gas, liquid, ion-exchange, and ion chromatography, sieve (exclusion) chromatography of oligomers and polymers, biospecific (affinity) chromatography, and the ligand exchange chromatography of optical isomers and also as catalysts and selective absorbers of substances polluting the atmosphere.[1–3] Furthermore, the creation of polymeric adsorbents promotes the development of the molecular theory of adsorption on inhomogeneous surfaces.

Porous polymers have many important advantages over traditional adsorbents such as silicas, zeolites, and charcoals. They can be obtained not only as spherical grains corresponding to a narrow fraction comprising different sizes but also in the form of fabrics, films, and membranes.[4–7] The selection of monomers in the synthesis of porous polymers makes it possible to regulate their thermal stability and resistance to acids and alkalis. Porous polymers are highly permeable. They actively adsorb substances from both dry and moist atmospheres and from solutions. Finally, porous polymers can be readily regenerated by heating or by washing with acids and alkalis, which is important in their practical application.

In order to employ porous polymers in chromatography and also for the adsorption of gases and vapours, it is essential to be able to regulate their adsorption and selective properties. By varying the conditions in the synthesis of porous polymers, namely by carrying out the copolymerisation reactions of the monomers in inert solvents of different nature and composition and using different amounts of the cross-linking agent, it is possible to regulate the steric structure of the resulting three-dimensional polymer network and to obtain adsorbents with different porosities, i.e. their adsorption properties can be varied. By changing the chemistry of the surfaces of polymers during synthesis (by using monomers with specific functional groups) and by modifying the porous framework already formed (by carrying out polymer-analogue reactions), one can obtain adsorbents with a great variety of narrowly specific functional groups, i.e. one can regulate within wide limits their adsorption capacity and selectivity in relation to a wide variety of compounds.[1,8]

There have been so far no reviews of this problem, although extensive data have accumulated. In this review an attempt is made to survey studies on the geometrical structures of various porous polymers and its influence on the adsorption and chromatography of molecules of different natures. The elucidation of this problem is associated with the development of a specific synthesis of porous polymers with the optimum structure, which is imnportant in their practical application.

II. Classification of polymeric adsorbents in terms of their geometrical structures

Porous polymers are usually obtained by copolymerising mono- and di-vinyl monomers in the presence of inert solvents (pore-forming agents), which effectively dissolve the mixture of monomers and precipitate the polymer formed but do not participate in the copolymerisation reaction.[9–29] In the synthesis of porous polymers, a mixture of a solvent and a precipitant is sometimes used.[30] Low-molecular-weight and high-molecular-weight compounds of the solvating and non-solvating type are used most often as pore-forming agents.[9–29] After the removal of the solvent occupying the interstructural spaces, cavities or pores remain in the copolymer.

Since the porous structures of the majority of organic polymers of the polymerisation type as well as inorganic xerogels are formed on drying the gel, pore structures of the same type are therefore observed for them. Inorganic xerogels—silica gels and alumina gels—have corpuscular and especially globular structures (see the list of references in Kiselev and Yashin's book[31]). Electron microscope

studies on a series of organic porous polymers showed that their structures are also globular.[32–40,54] The suspension copolymerisation process consists in the construction of gel microparticles and their agglomeration into globules. The pores consist of the channels between the globules.

Table 1 presents a classification of the polymeric sorbents in terms of the nature of their geometrical structures on the basis of ideas developed for traditional adsorbents: the structure is believed to be macroporous if the pore diameter (d) is greater than 200 nm, mesoporous if $d = 3-200$ nm, and microporous if d is less than 3 nm.[41] Pore diameters $d > 100$ nm, $d = 4-100$ nm, and $d < 4$ nm respectively have been adopted by Gregg and Sing.[42] Copolymers of the methacrylate type are mesoporous adsorbents, but, under certain conditions of synthesis, macroporous specimens can also be obtained. Styrene–divinylbenzene copolymers have a mesoporous structure, but they contain as a rule a small number of micropores as a result of the parallel divinylbenzene–divinylbenzene copolymerisation.[105] Cross-linked macronetwork isoporous polystyrene copolymers (Styrosorbs) can have mesoporous and microporous structures and the mesoporous specimens can also contain micropores, i.e. can have a biporous structure. The polymers obtained on polycondensation of *m*-aminophenol with formaldehyde have only a macroporous structure, while phenol–formaldehyde resins have a mesoporous structure.[106,107] Thus polymeric adsorbents of different structural types have now been synthesised.

Table 1. Classification of the polymeric adsorbents investigated in terms of the nature of their porosity.

Type	Polymer chain	Designation or brand of the initial and modified polymers	$d>200$ nm (macropores)	$d=3$ to 200 nm (mesopores)	$d<3$ nm (micropores)	Refs.
I	2,3-Epoxypropyl methacrylate (glycidyl methacrylate)–ethylene dimethacrylate	EPMA–EDMA, GMA–EDMA, EPMA–EDMA–modifying agent (60 wt.% EPMA), G-60–modifying agent	+	+	–	[30, 37–40, 43–57]
II	Styrene–divinylbenzene	ST–DVB, CMC (chloromethylated copolymer), anion exchangers: AN-201, AN-211, AN-221, AN-511, AN-521, AN-531, AN-541	–	+	–	[9–24, 26–28, 32 58–74]
III	Polystyrene–xylylene dichloride	PS–XDC, PS–XDC–modifying agent	–	+	+	[75–93]
	Polystyrene–chloromethyl methyl ether	PS–CMME, PS–CMME–modifying agent, Styrosorb, Styrosorb-modifying agent				
IV	Vinylpyridine (vinyl pyridine derivatives)–divinylbenzene	VP–DVB, VP–DVP, anion exchangers: AN-231, AN-251, AN-401, AN-431, AN-441, AN-451	–	+	–	[1–30, 94–104]
	Vinylpyridine–divinylpyridine					

III. The study of the porous structures of polymeric adsorbents of different types

Polymeric adsorbents swell appreciably in many solvents. In gas-chromatographic studies and also in the study of the adsorption of gases and vapours, where the adsorbates have a comparatively low vapour pressure, kinetic measurements have shown that mainly adsorption processes take place. However, in certain cases absorption, the extent of which is determined by the nature of the polymer and of the adsorbed molecule as well as by the nature and regularity of the cross-linking of the polymeric skeleton, may occur. Fairly complete and reliable information about the nature of the porous structure of such "non-rigid" adsorbents can therefore be obtained by employing a set of different techniques.

1. Methods for the measurement of the parameters of the porous structures of polymers

In the analysis of the porous structures of polymers, we shall consider the adsorption method using adsorbates of different nature—nitrogen, cyclohexane (in the vapour of which partial swelling of the polymers takes place), and perfluoro-n-octane (in the vapour of which polymers hardly swell). The use as the adsorbate in the adsorption method of perfluoro-n-octane, which is adsorbed as a result of weak non-specific interactions with the polymer surface, makes it possible to investigate the porous structures of both initial (as a rule non-polar) matrices and the anion-exchange resins obtained from them.[73,108] This review considers also the mercury porometric method[108] whose application to polymers is complicated by the possibility that the skeleton may be compressible.[23]

The isotherms for the adsorption of nitrogen by porous polymers presented in this review were measured by the vacuum volumetric method at –195 °C. The specific surfaces of the specimens S_{N_2} were then calculated from them by the Brunauer–Emmett–Teller (BET) method. The specific surfaces were also measured by the dynamic method involving the thermal desorption of nitrogen or argon (S_{N_2}, S_{Ar})[109] on the Quantosorb apparatus (USA) or on the Sorbtometr apparatus (USSR). The calculation was carried out by the BET method on the basis of three adsorption points or using as the standard a polymer specimen with a known value of S calculated by the BET method from the nitrogen adsorption isotherm at –195 °C. In calculating S for the polymers, use was made of the surface area per nitrogen molecule in a dense monolayer $\omega_m = 0.162$ nm^2. This value is usually employed for adsorbents such as carbon blacks and silica gels.[110] However, one should bear in mind that ω_m for nitrogen depends on the chemical nature of the adsorbent. The influence of the chemical state of the surface on the packing density of the nitrogen adsorption layers has been studied.[111] Loose layers are formed on non-polar and polar organic surfaces with $\omega_m^{N_2} = 0.20$ nm^2. The value $\omega_m = 0.22-0.28$ nm^2 has been obtained by a comparative method[112] for organic polymeric sorbents. The values of S calculated using such values of ω_m are greater, but the observed features are not altered.

This review presents and analyses the adsorption isotherms for nitrogen vapour on polymers measured at –195 °C with the temperature of the specimen raised to 30 °C.[73] One measures initially the degree of adsorption at –195 °C by the generally accepted method and the specific surface S_{N_2} is then calculated from this isotherm by the BET method. Subsequently the experiment is carried out as follows: the adsorption isotherm is measured at –195 °C up to a certain point (for example, up to the equilibrium pressure $p = 8$ mmHg) and the specimen, contained in a small closed volume, is then heated to 30 °C. As a result of desorption, the nitrogen pressure over the specimen increases under these conditions. After this, the adsorbent is again cooled to –195 °C and is maintained at this temperature until the attainment of equilibrium. For certain polymers, the equilibrium pressure does not change under these conditions, while for others the equilibrium pressure

diminishes, the decrease being appreciable in certain cases—for example from 8 to 0.5 mmHg. In the latter case, the degree of adsorption of nitrogen is measured at −195 °C, the heating−cooling operation described above being repeated, and a second isotherm is obtained. It lies above the first. The specific surface S_2 is calculated from this isotherm using the BET equation. Comparison of S_{N_2} and S_2 permits certain conclusions about the structures of the porous polymers.

The adsorption isotherms for the vapours of organic substances quoted in this review were measured at 25 °C with the aid of a McBain−Baker vacuum balance (with quartz springs) on specimens evacuated beforehand to 10^{-4} kPa at 70−80 °C.[109] S was estimated from the degree of sorption of n-C_8F_{18} vapour using the area ω_m = 1.06 nm^2. The specific surface $S'_{C_8F_{18}}$ of the adsorption film formed on the sorbent at the beginning of the capillary condensation was also calculated from the n-C_8F_{18} vapour sorption isotherm.[109,113] For polymers containing mesopores and micropores, S_{meso} was determined by a comparative method,[114,115] using the sorption isotherm for the n-C_8F_{18} vapour on a coarsely porous styrene copolymer with 12% of divinylbenzene as the reference standard.[73]

The volume of the pores was calculated from the degree of sorption of the n-C_8F_{18} ($V_{C_8F_{18}}$) and cyclohexane ($V_{C_6H_{12}}$) vapours at p/p_0 = 1. For polymers containing mesopores and micropores, the volume of the micropores V_{micro} was initially determined by the comparative method and then the volume of the mesopores V_{meso} was calculated. For comparison, the limiting volume of the absorbed liquid sorbate was determined from the degree of swelling of the polymer in the latter (in the case of cyclohexane, this will be designated by $V^L_{C_6H_{12}}$).[116] The pore volume can also be calculated from mercury porograms in terms of the amount of mercury forced into the specimen (designated by V_{Hg}). The overall volume of the cavities in the initial sorbents was calculated from the true and apparent densities of the polymer (the designation V^p is introduced in this case) or was estimated from its bulk density ($V^{b.d}$).[117]

The effective pore diameters at the maxima on the pore volume distribution curves were calculated from the mercury porograms (d_{Hg}) and from the desorption branches of the n-C_8F_{18} isotherms using the Thompson−Kelvin equation ($d_{C_8F_{18}}$).[118] The average pore diameter was calculated from the formula $\bar{d} = 4V/S$.[37]

2. The porous structure of polymers of the methacrylate type

Methacrylate polymers were obtained by the suspension radical copolymerisation of epoxypropyl methacrylate with different amounts of ethylene dimethacrylate as the cross-linking agent and different proportions of solvent (cyclohexanol) and precipitant (dodecanol) in the inert phase.[43–57] Depending on these factors, specimens with different structures can be obtained. Electron microscope studies[38,39,48] showed that the structure of the methacrylate polymers is globular: the porous structure is formed as a result of the formation of gel microparticles and their agglomeration into globules. The porosity of the polymers is determined by the size of the globules and the distance between neighbouring globules, which depends on their packing.[37] The nature of the aggregation of the microparticles on the surface and in the bulk of the globules is significantly different. The microparticles on the surface and in the bulk of the globules have the same sizes, but on the surface they aggregate in a more compact manner. The pore size in the surface layer is smaller than in the bulk phase. It is believed[55,57] that the surface layer of the globules consists of relatively mobile poly(glycidyl methacrylate) chains. In the case of highly cross-linked methacrylate copolymers, the large values of S can be explained by the presence of very fine microspheres—nodules (whose size is about 10 nm), from which the globules are formed. Using gel permeation chromatography (GPC),[54,56] it has been shown that the characteristics of the porous structures of copolymers in the dry and swollen states are different: the average pore diameter, determined by mercury porometry, is greater for the dry copolymers than the value determined for the swollen copolymers by gel permeation chromatography.

In order to be able to distinguish the geometrical modifications of the copolymers, the following notation has been introduced: the fraction of one of the monomers and the solvent/precipitant ratio are quoted. Thus the EPMA-EDMA-40-91/9 (G-40-91/9) copolymer is obtained by the copolymerisation of 2,3-epoxypropyl methacrylate (2,3-EPMA) (40 wt.%) and ethylene dimethacrylate (EDMA) (60 wt.%) with a cyclohexanol/dodecanol ratio of 91/9. Table 2 presents certain characteristics of such copolymers. The study of the porous structure of EPMA−EDMA by mercury porometry and on the basis of the sorption of nitrogen vapour[30,40,51] showed that, for highly cross-linked copolymers, the pores with d = 3−60 nm (which some authors refer to as micropores) make a large contribution to the value of S. In the presence of a small amount of the cross-linking agent, pores with d < 20 nm are absent. The pore volume determined by mercury porometry is much lower than the pore volume determined from the swelling of the polymers in cyclohexane. This is evidently associated with the partial swelling of the specimens.

Table 2. Characteristics of the porous structures of methacrylate copolymers with different degrees of cross-linking.[30,40,51]

Designation	EDMA content, wt.%	S, m^2 g^{-1}	$V^L_{C_6H_{12}}$, cm^3 g^{-1}	$V_{Hg,\ cm^3}$ g^{-1}	d**, nm
G-5-91/9	95	434	–	1.07	30
G-30-91/9	70	197	–	1.00	40
G-40-91/9	60	120	1.51	–	(50)
G-45-91/9	55	130	–	1.01	40
G-60-91/9	40	69	1.47	1.03	60
G-75-91/9	25	44	–	0.99	80
G-80-91/9	20	36	1.20	–	(132)
G-90-91/9	10	22	0.88	–	(134)
G-60-85/15	40	57	1.71	–	(120)
G-60-100/0	40	94	1.43	1.00	–
G-80-100/0	20	20	0.62	–	(126)

*G denotes the EPMA−EDMA copolymer (see Table 1).
**Here and henceforth the average value of $\bar{d}$ is given in brackets, while the figure without brackets denotes the effective value.

The structure of certain aminated EPMA−EDMA specimens has been investigated by various methods (Table 3).[30,40,51,108] The isotherms of the adsorption of cyclohexane vapour, in which the polymers partly swell (for low values of p/p_0 the isotherms are irreversible), were measured on these specimens (Fig. 1). The n-C_8F_{18} adsorption isotherms on the modified specimens are reversible in the initial region of relative pressures and have a distinct and narrow capillary-condensation hysteresis loop of the H1

type, which is characteristic of sorbents with cylindrical pores. The structural parameters of polymers were estimated from such isotherms (Table 3). Table 3 shows that the specific surfaces of the adsorption film $S'_{C_8F_{18}}$ and $S_{C_8F_{18}}$ virtually coincide and the values of S determined from the adsorption of the small nitrogen molecule and the fairly large n-C_8F_{18} molecule are also similar. This indicates the absence of micropores in the test specimens. The values of S_{Hg} exceed in certain cases those of S obtained from adsorption data, sometimes by a factor of two. In all probability, such specimens contain an appreciable number of pores with constrictions (or widened regions), since it is in fact in such cases that $S_{BET} < S_{Hg}$.[118]

Table 3 shows that the parameters of the porous structure of the polymers (S, V, d) hardly change on modification with amines and aminoalcohols. Only on amination with ammonia does S increase for all degrees of cross-linking of the copolymer, possibly owing to the additional cross-linking of the framework. It has been shown[51] that, when copolymers are aminated by amines and aminoalcohols, the volumes of small (8–50 nm) and very large (d > 100 nm) pores diminish and the number of pores with d = 60–80 nm increases sharply, so that the overall pore volume hardly changes and remains ~1 $cm^3 g^{-1}$.

Table 3. Characteristics of the porous structures of modified methacrylate copolymers.[30,40,51,108]

Designation	Aminating agent	S, $m^2 g^{-1}$				V, $cm^3 g^{-1}$				d, nm	
		S_{N_2}	$S_{C_8F_{18}}$	$S'_{C_8F_{18}}$	S_{Hg}	$V_{C_8F_{18}}$	V_{Hg}	$V_{C_6H_{12}}$	$V^L_{C_6H_{12}}$	$d_{C_8F_{18}}$	d_{Hg}
G-60-91/9		63	–	–	–	–	1.03	–	1.47	–	60
G-60-91/9	A	100	106	100	108	1.08	1.13	–	1.28	70	70
G-60-91/9	DETA	69	69	70	54	1.03	0.97	–	1.03	66	80
G-60-91/9	DETA	67	74	–	74	1.02	1.01	1.00	–	70	70
G-60-91/9	DETA(alk)	50	58	41	61	0.88	0.92	0.90	1.31	65	100
G-60-91/9	MEA	60	–	–	–	–	0.93	–	–	–	60
G-60-91/9	EDA	70	–	–	–	–	1.00	–	–	–	60
G-80-91/9	—	36	–	–	–	–	–	–	1.20	–	(132)
G-80-91/9	A	48	35	24	102	0.71	0.99	0.72	1.15	80	100

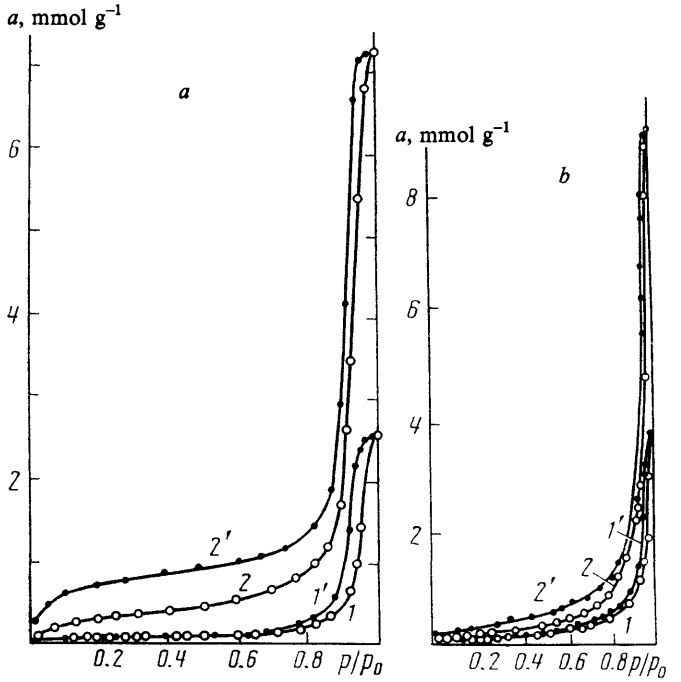


Figure 1. Adsorption (curves *1* and *2*) and desorption (curves *1'* and *2'*) isotherms for n-C_8F_{18} (curves *1* and *1'*) and cyclo-C_6H_{12} (curves *2* and *2'*) vapours at 25 °C: (*a*), on the styrene–divinylbenzene (8%) copolymer modified with diethylenetriamine (AN-511 anion exchanger) obtained in n-decane (100%) as the pore-forming agent; (*b*) on the 2,3-epoxypropyl methacrylate–ethylene dimethacrylate copolymer (60% of 2,3-epoxypropyl methacrylate) modified with diethylenetriamine.

The low-temperature adsorption of nitrogen on specimens of methacrylate polymers with the specimens heated in a closed space have been investigated.[73] For all the specimens, $S_{N_2} = S_2$, i.e. the polymers have a very regular structure. This can be explained by the following causes. Polymers containing in their chains an appreciable number of polar groups are fairly rigid structures. Furthermore, in the synthesis of these polymers it is possible to obtain a uniformly cross-linked framework, which does not contain highly cross-linked microporous sections.

Determination of the pore volume from the adsorption of C_8F_{18} and C_6H_{12} vapours showed that the values of $V_{C_8F_{18}}$ and $V_{C_6H_{12}}$ are virtually identical (Table 3) despite some swelling of the polymers in cyclohexane vapour (Fig. 1). For the highly cross-linked specimen (40% EDMA), $V_{Hg} \simeq V_{ads}$. This shows that either the framework does not change at elevated pressures and the specimen does not contain an appreciable number of macropores with d > 200 nm or the framework is compressed but the specimen contains pores with d > 200 nm, the effects cancelling out. The first hypothesis appears more probable. For the weakly cross-linked specimen, $V_{Hg} > V_{ads}$ ($d_{Hg} > d_{ads}$). Possibly the specimen becomes more coarsely porous under the conditions of mercury porometry.

The method of determining the pore volume from the adsorption of liquid, for example, cyclohexane,[117] yields unduly high results owing to the more extensive swelling of the polymers in liquids than in vapours. However, formal calculation of the average pore diameter $\bar{d}$ using $V^L_{C_6H_{12}}$ and S_{N_2} yields values close to d_{Hg}.

Table 2 and Fig. 2 show that the values of S for the methacrylate polymers increase with increase in the amount of ethylene dimethacrylate and depend on the solvent/precipitant ratio. With increase in the fraction of ethylene dimethacrylate to 40%, the pore volume also increases, but, on still further increase in the fraction of ethylene dimethacrylate (to 60%), it changes little. With increase in the amount of the pore-forming agent (cyclohexanol) in the mixture with the precipitant (dodecanol), S_{N_2} increases, while $V_{C_6H_{12}}$ diminishes, i.e. the specimen acquires a more finely porous structure.

The porous structures of methacrylate copolymers obtained by cross-linking monomers of different polarity with ethylene dimethacrylate have been investigated.[44,49] It was found that the specific surface and the pore volume diminish with increase in the content of the polar monomer: $S_{MMA} > S_{HEMA} > S_{AN}$ (MMA = methyl methacrylate, HEMA = hydroxyethyl methacrylate, AN = acrylonitrile). The polymers contain no pores with $d > 100$ nm and the preferred pore size is $d = 40-80$ nm. The pore structure of sulphur-containing methacrylate copolymers is also regulated by varying the content of ethylene dimethacrylate and the solvent/precipitant ratio. With increase in the amount of ethylene dimethacrylate in the copolymers, S and V increase, while the content of epithio-groups falls.[119,120]

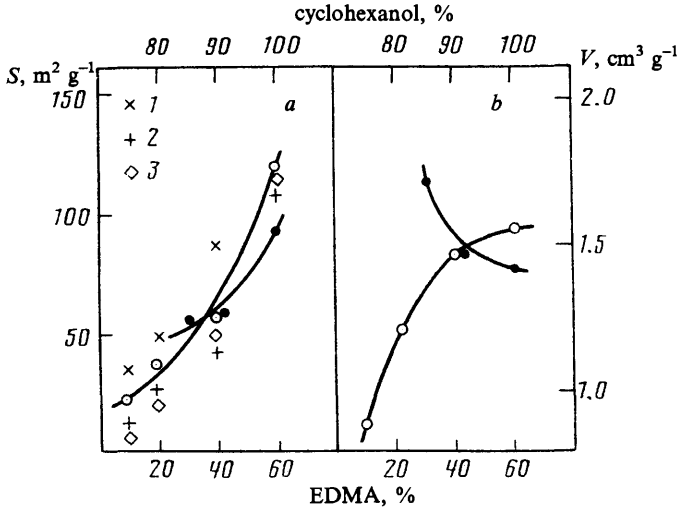


Figure 2. Dependence of the specific surface S (*a*) and pore volume V (*b*) on the content of the cross-linking agent (open symbols) and the solvent (cyclohexanol) (filled symbols) for the epoxypropyl methacrylate–ethylene dimethacrylate copolymers. Fig. 2*a* also presents the values of S for polymers with different degrees of cross-linking modified by ammonia (*1*), ethylenediamine (*2*), and diethylenetriamine (*3*).

Thus methacrylate polymers have an extensive porosity. These are mainly mesoporous adsorbents. The pore structure of the polymers is regulated by varying the amount of the cross-linking agent (ethylene dimethacrylate) and the solvent/precipitant ratio and by introducing a polar monomer. On modification of these copolymers, the parameters of the porous structure do not change greatly.

3. The porous structure of polymers of the styrene – divinylbenzene type

Porous styrene–divinylbenzene copolymers are obtained by the suspension copolymerisation of styrene with divinylbenzene. The principal factors influencing the porosity of these copolymers are the degree of cross-linking of the three-dimensional copolymer framework, which is determined by the amount of the cross-linking agent (divinylbenzene) and by the nature of the pore-forming agent and its concentration in the mixture of the polymerising monomers. The structure of the styrene–divinylbenzene copolymers has been investigated by the adsorption method (from the adsorption isotherms of water vapour and methanol) and by mercury porometry (see the literature references in Table 1). The present review deals primarily with the porous structures of anion exchangers obtained from styrene–divinylbenzene copolymers. The study of the adsorption and desorption isotherms of methanol, n-hexane, perfluorobenzene, and perfluoro-n-octane on the AN-221 anion exchanger containing ethylenediamine groups showed that, as for the epoxypropyl methacrylate–ethylene dimethacrylate copolymers, the anion exchanger does not swell only in the vapour of the fully fluorinated saturated hydrocarbon, the interaction of the molecules of which with the surface of the polymer are not only non-specific but also weak (Fig. 1). The isotherm is fully reversible. At high values of p/p_0, a distinct capillary-condensation hysteresis is observed, as for inorganic adsorbents with a rigid skeleton.

In order to be able to distinguish the geometrical modifications of the styrene–divinylbenzene copolymers, the following notation has been introduced: the ratio of the amounts of the cross-linking agent and the pore-forming agent is stated and then the pore-forming agent is indicated. Thus the 12/80, BR-1 copolymer is obtained by copolymerising 88% of styrene with 12% of divinylbenzene in the presence of 80% of petrol of type BR-1 as the pore forming agent.

The porous structure of a number of anion exchangers has been investigated by various methods (Table 4). The surface area S of the test specimens varies in the range from 11 to 130 m^2g^{-1}, V varies from 0.05 to 1.29 cm^3g^{-1}, and d varies from 24 to 100 nm, which is associated mainly with the nature and amount of the cross-linking and pore-forming agents. The ranges of variation of S, V, and d obtained for 8 specimens of AN-221 (12/80, BR-1) have been published:[26] $S = 75-120$ m^2g^{-1}, $V = 0.4-0.8$ cm^3g^{-1}, and $d = 20-100$ nm; similar data have been published for 12 specimens of AN-511 (8/100, n-decane): $S = 25-40$ m^2g^{-1}, $V = 1.0-1.3$ cm^3g^{-1}, and $d = 100-200$ nm. This indicates some non-reproducibility of the conditions in the synthesis of the given polymers.

Table 4 shows that the specific surfaces of the film S' and S, determined from the adsorption of C_8F_{18}, are virtually identical. Furthermore, the values of S determined from the adsorption of the small nitrogen molecule and the fairly large C_8F_{18} molecule are also similar. This indicates the absence of an appreciable number of micropores in the test specimens.

Comparison of the pore volumes determined by mercury porometry and from the adsorption of vapours shows that, within the limits of the reproducibility of the measurements, $V_{Hg} \simeq V_{ads}$. This indicates the absence of an appreciable number of macropores with $d > 200$ nm in the test specimens. The above conclusion is confirmed also by the pore volume distribution curves. Thus both adsorption methods using adsorbates in which the polymers hardly swell and mercury porometry are applicable to the study of the structures of the test polymers.

In order to elucidate the influence of the polymer-analogue reactions on the structural characteristics of the polymers, measurements were made of the adsorption isotherms of C_8F_{18} on the initial styrene–divinylbenzene copolymer (8/100, n-nonane), the chloromethylated copolymer (CMC) and the anion exchangers AN-221, AN-511, and AN-541 (specimens *1–5* in Table 4). A narrow pore distribution is observed for these substances and virtually all the specimens have $d_{eff} \simeq 60$ nm. Changes in the structure occur mainly in the chloromethylation stage, whereupon V

Table 4. Characteristics of the porous structures of the styrene–divinylbenzene anion exchangers.[73,108]

Specimen	Brand or dessignation	Pore-forming agent	DVB/pore-forming agent	S, $m^2 g^{-1}$				V, $cm^3 g^{-1}$		d, nm	
				S_{N_2}	$S_{C_8F_{18}}$	$S'_{C_8F_{18}}$	S_{Hg}	$V_{C_8F_{18}}$	V_{Hg}	$d_{C_8F_{18}}$	d_{Hg}
1	ST–DVB	n-Nonane	8/100	60	–	62	–	0.84	–	49	–
2	CMC	»	8/100	–	46	50	–	0.73	–	57	–
3	AN-221*	»	8/100	53	55	53	63	0.74	0.79	57	60
4	AN-511*	»	8/100	49	50	55	95	0.79	0.89	57	55
5	AN-541*	»	8/100	–	58	53	–	0.77	–	57	–
6	AN-221	BR-1	8/100	11	–	14	–	0.05	–	24	–
7	AN-221	»	12/80	60	64	54	98	0.56	0.66	30	30
8	AN-221	»	15/100	61	66	61	121	0.60	0.71	40	35
9	AN-221	»	20/80	69	67	61	–	0.68	–	45	–
10	AN-221	»	30/100	130	95	72	–	1.29	–	100	–
11	AN-221	Isooctane	12/80	60	66	59	75	0.61	0.64	40	40
12	AN-511	n-Decane	8/100	31	32	42	–	0.75	–	100	–
13	AN-511	»	8/100	32	27	42	64	0.63	0.70	60	60
14	AN-221	PS	10/10	–	–	7	–	0.13	–	55	–

*The AN-221, AN-511, and AN-541 anion exchangers contain EDA, DETA, and MEA groups respectively.

falls somewhat as a result of the removal of pores with sizes ranging from 20 to 30 nm. On subsequent amination, these parameters hardly change. After the introduction of highly basic groups, the parameters of the porous structure change more appreciably.

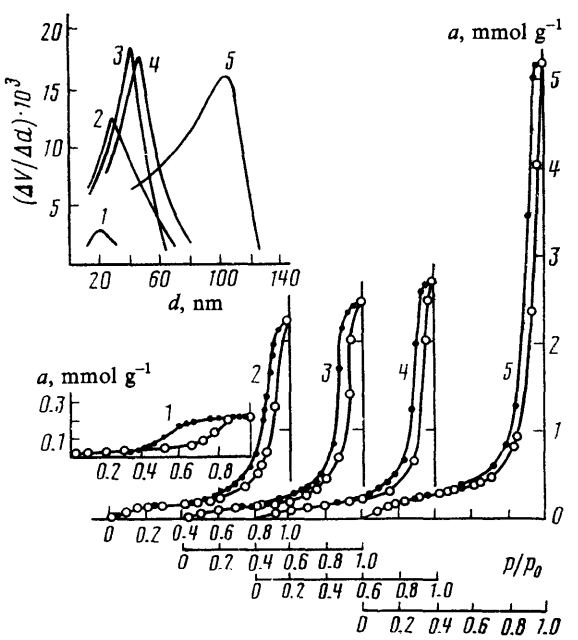


Figure 3. Isotherms for the adsorption (open circles) and desorption (filled circles) of n-C_8F_{18} vapour on the AN-221 anion exchanger (BR-1 pore forming agent, specimens *6–10* in Table 4) at 25 °C. The inset shows the corresponding curves for the distribution of pore volumes with respect to the effective diameters. Amount of divinylbenzene (%): (*1*) 8; (*2*) 12; (*3*) 15; (*4*) 20; (*5*) 30.

The influence of the amount of the cross-linking agent on the structure of the AN-221 anion exchangers has been investigated. Fig. 3 presents the adsorption and desorption isotherms for C_8F_{18} vapour on the anion exchangers with different degrees of cross-linking. The parameters of the porous structure listed in Table 4 were calculated from the isotherms. With increase in the amount of divinylbenzene in the anion exchanger matrix from 8 to 30%, S, V, and the pore size increase. Similar relations have been observed for styrene–divinylbenzene copolymers. With increase in the amount of the cross-linking agent, the polymer framework becomes more rigid and its contraction after the removal of the solvent during synthesis diminishes, which leads to an increase in the size and volume of the pores. The highly cross-linked specimen (30% DVB) contains a larger number of fine pores, which explains its higher value of S.

The dependence of the structure of the AN-221 and AN-511 anion exchangers on the molecular size of an inert solvent (hydrocarbon) has also been investigated. The largest pores ($\geqslant$100 nm) are present in anion exchangers whose matrix has been obtained in the presence of a solvent such as n-decane.[26,73] The porosity of the styrene–divinylbenzene copolymer in the dry state is greater the lower the degree of solvation of the copolymer by the solvent.[64] With increase in the molecular size of the solvent in the series petrol < isooctane < n-nonane < n-decane, the solvating power of the solvent diminishes, as a result of which the contraction of the copolymer on removal of the solvent during synthesis diminishes and the fraction of large pores in the adsorbent increases.

The porous structure of the anion exchangers has also been investigated by the static nitrogen adsorption method at −195 °C with the specimen being warmed during the measurement of the adsorption isotherm. S_{N_2} and S_2 were determined in this way.[73] In contrast to methacrylate polymers, $S_2 > S_{N_2}$ for the styrene–divinylbenzene copolymers and anion exchangers. Thus an appreciable increase (up to 200%) in S after the specimen heating–cooling cycle has been observed for styrene–divinylbenzene copolymers. Apparently, when the specimen is heated, as a result of the increase in the pressure of nitrogen its molecules can

permeate into pores with constrictions or micropores which are inaccessible to the adsorbate under the usual experimental conditions. This phenomenon is analogous to the effect of activated breakthrough, i.e. to the increase in the degree of adsorption with increase in temperature which is characteristic of microporous adsorbents.[118] There is then a possibility of the enforced elastic deformation of the polymer pore walls[121] which persists on subsequent cooling to a greater extent the more elastic the polymer and the smaller its rigidity. In the chloromethylation of the copolymer, a polar group ($-CH_2Cl$) is introduced into the polymer, which leads to the additional cross-linking of the polymer chains[122] and to an increase in the rigidity of the polymer and hence to a decrease in the difference between S_{N_2} and S_2. The introduction of amino-groups into the polymer makes it still more rigid and the enforced elastic deformation on desorption of nitrogen during heating diminishes. With increase in the amount of the cross-linking agent in the anion exchanger matrix, the difference between S_{N_2} and S_2 increases owing to the dominant influence of the factor associated with the increase in the amount of highly cross-linked sections containing micropores in the anion exchangers. The values of S measured by the nitrogen thermal desorption method agree with those of S_{N_2} (with the exception of highly cross-linked specimens).

Thus the application of various methods to the study of the porous structure of polymers permits a more detailed characterisation of the structures of these complex objects. The porous structure is readily regulated by the introduction of different amounts of the cross-linking agent (in the given instance divinylbenzene), by the alteration of the divinylbenzene/pore-forming agent ratio, and by the nature of the pore-forming agent.

4. The porous structure of copolymers of vinylpyridine derivatives and divinylbenzene

Porapak S as well as Polysorb N, which are vinylpyridine–divinylbenzene copolymers, are widely used in chromatography. Porous copolymers of this class are obtained by the suspension copolymerisation of the initial monomers—vinylpyridine derivatives containing ionogenic groups, with divinylbenzene or divinylpyridine. Porous copolymers of 4-vinylpyridine with ethylene dimethacrylate and 2,5-divinylpyridine having specific surfaces up to 400 m^2g^{-1} have also been synthesised and investigated.[103,104] The synthesis of such ion exchangers consists of a single stage and their structure is formed in the copolymerisation stage and does not undergo further changes. The porous structure of such copolymers has been investigated by the adsorption method (in relation to nitrogen and methanol) and by mercury porometry (see the literature references in Table 1). The structure of the vinylpyridine–divinylbenzene anion exchangers has been investigated[73] by the nitrogen thermal desorption method and by the low-temperature adsorption of nitrogen with warming of the specimen in a closed volume. For these copolymers, $S_2 > S_{N_2}$. As for the styrene–divinylbenzene copolymers, the heating of the vinylpyridine–divinylbenzene specimens can entail, as a result of the increased pressure of nitrogen, the penetration of its molecules into the pores with constrictions or micropores which are inaccessible to the sorbate under the usual conditions. The difference between S_{N_2} and S_2 for AN-251, cross-linked by divinylpyridine, is smaller than for AN-251 cross-linked by divinylbenzene, which can be explained by the increased rigidity of the polymer framework when divinylpyridine is used as the cross-linking agent. The introduction of polar groups into the polymer chains increases their rigidity to a greater extent the more polar the group and the greater their number introduced into the chain. On passing from AN-251, containing pyridine nitrogen, to AN-451, containing also tertiary nitrogen, the difference between S_{N_2} and S_2 therefore diminishes.[73] The quantity S, determined by the nitrogen thermal desorption method, corresponds to S_2 and not to S_{N_2}, as in the case of the styrene–divinylbenzene copolymers.

5. The porous structure of ultracross-linked polystyrenes (Styrosorbs)

The macronetwork isoporous polymers based on polystyrenes (see the literature references in Table 1) are porous in the dry state and have an extensive inner surface only in the presence of large amounts of the cross-linking agent (>30%). The Styrosorb (I) sorbents are obtained using a method involving the cross-linking of linear polystyrene (PS) chains dissolved in an organic solvent [in most cases dichloroethane (DCE)] by *p*-xylylene dichloride (XDC), 4,4′-bis(chloromethyl)biphenyl, chloromethyl methyl ether (CMME), or methylal in the presence of a Friedel–Crafts catalyst.

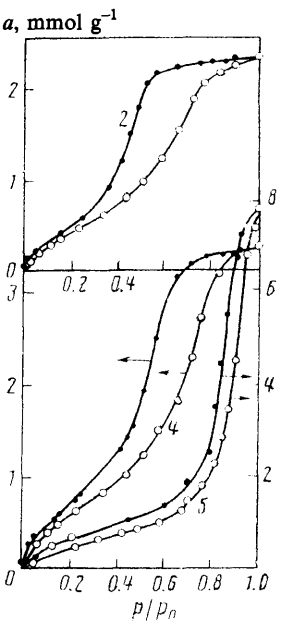


Figure 4. Isotherms for the adsorption (open circles) and desorption (filled circles) of n-C_8F_{18} vapour on Styrosorbs I (specimens *2*, *4*, and *5* in Table 5) at 25 °C.

The study of the structure of Styrosorbs obtained in dichloroethane by electron microscopy, small angle X-ray scattering, and gel permeation chromatography showed that they are microporous sorbents in which the main fraction of pores have diameters of the order of 1 nm.[83,89,90] The Styrosorbs (I) examined in this study were obtained by cross-linking linear polystyrene dissolved in cyclohexane (CH) with chloromethyl methyl ether. The molecular weight of the polymer varied from 13×10^3 to 3×10^6. A Styrosorb (II) specimen, synthesised by the cross-linking with chloromethyl methyl ether of a copolymer of styrene with 2% of divinylbenzene swollen in dichloroethane, was also investigated (Table 5).[90] All the polymers investigated had a degree of cross-linking of 100%. In the study of the porous structure of the Styrosorbs, n-C_8F_{18} was used as the sorbate. In its vapour the Styrosorbs swell to a lesser extent than in other organic solvents.

Table 5. Structural characteristics of Styrosorbs I (specimens *2*–*6*) and II (specimen *1* with 2% DVB).[92]

Specimen	Molecular weight of initial polystyrene × 10^{-3}	Solvent	S, $m^2 g^{-1}$				V, $cm^3 g^{-1}$				d, nm	
			S_{Ar}	$S_{C_8F_{18}}$	$S'_{C_8F_{18}}$	S_{meso}	$V^{b.d.}$ (V^{ρ})	$V_{C_8F_{18}}$	V_{micro}	V_{meso}	d_{eff}	$\bar{d}$
1	300	DCE	1000	650	–	–	0.20	–	0.20	–	–	1
2	3000	CH	330	300	235	–	0.74	0.6	0.17	0.57	7	8
3	300	CH	545	400	280	280	0.78	0.4	0.42	0.36	4	4
							(0.70)	0.4	0.34	0.36	4	4
3a *	300	CH	–	510	–	–	–	0.6	–	–	4	4
4	80	CH	405	400	285	280	(0.90)	0.9	0.04	0.86	9	9
5	17	CH	430	250	–	240	1.94	1.9	0.03	1.91	30	30
6	13	CH	330	280	200	200	1.30	1.1	0.23	1.07	20	16

**3a* represents specimen *3* chloromethylated and aminated by DETA.

Fig. 4 presents the n-C_8F_{18} sorption isotherms on three specimens of Styrosorbs (specimens *2*, *4*, and *5*, Table 5) obtained in cyclohexane by cross-linking polystyrenes having different molecular weights. They differ in the position and form of the hysteresis loop, which can provide some idea about the size and shape of the pores present in the given sorbents. It is possible to distinguish two varieties of Styrosorbs I. The first includes polymers obtained by cross-linking polystyrene having a high molecular weight ($3 \times 10^6 - 8 \times 10^4$) dissolved in cyclohexanes. Such Styrosorbs have sorption isotherms with a hysteresis loop which belongs to the H2 type according to de Boer's classification. The second variety of Styrosorbs I is obtained by structure formation in polystyrene having a low molecular weight ($13-17 \times 10^3$). Their sorption isotherms exhibit a narrow capillary-condensation hysteresis of the H1 type. The comparatively large degrees of sorption of n-C_8F_{18} on Styrosorbs for low values of p/p_0 and the slight irreversibility of the isotherms in the initial region are striking. The latter feature may be associated both with the low degree of swelling of the polymers in the given sorbate and with the slow rate of sorption of n-C_8F_{18} in the micropores present in these specimens.

Analysis of the data in Table 5 permits the following conclusions. The cross-linking of polystyrene chains in dichloroethane, which is a thermodynamically effective solvent, leads to the formation of microporous sorbents with $d \simeq 1$ (specimen *1*). This is also indicated by the low value of $S_{C_8F_{18}}$ compared with S_{Ar}. It is noteworthy that solvents such as hexane and methanol, in which polystyrene does not dissolve, are capable of solvating vigorously the polymer chains of ultra-cross-linked polystyrene, as a result of which $V^L_{C_6H_{14}}$ and $V^L_{CH_3OH}$ reach 4 $cm^3 g^{-1}$.[83,89,90] The appearance of micropores in the given Styrosorbs is a consequence of the loose packing of the polymer chains in the single-phase network cross-linked by a large number of rigid bridges, which hinder the mutual approach of the polymer chains when the solvent is removed from the swollen polymer produced. The high strain in the structure of Styrosorbs in the dry state imparts to them a unique capacity to swell in any medium even in inert media such as perfluorooctane.[90]

When the thermodynamically effective solvent dichloroethane is replaced by cyclohexane (a solvent with a lower affinity for polystyrene), the structure of the sorbents changes. They contain not only micropores but also mesopores (specimens *2*–*6* in Table 5 and Fig. 4). Such Styrosorbs swell least in the n-C_8F_{18} vapour. The rigid n-C_5F_{12} fills the cavities in the polymer, whereupon the specimen hardly swells. The weak swelling of Styrosorbs I in fluorinated hydrocarbons is indicated primarily by the form of the isotherms and the closeness of the values of $V_{C_8F_{18}}$ to V^{ρ} or $V^{b.d.}$ (specimen *3* containing a large number of micropores is an exception). For specimens *2*–*4*, $V < 1$ $cm^3 g^{-1}$, while S_{meso} is the same as S' and less than $S_{C_8F_{18}}$, which indicates the presence in the specimen of fine pores ($d \simeq 3$ nm) accessible to C_8F_{18} molecules. Specimens *5* and *6* have $V > 1$ $cm^3 g^{-1}$. Their effective pore diameter is much greater than for specimens *2*–*4* and amounts to 20–30 nm. As in the case of specimens *2*–*4*, S_{meso} for specimens *5* and *6* is approximately equal to S' and is less than $S_{C_8F_{18}}$, while V_{micro} is not large.

Fig. 5 presents the dependence of the effective pore diameters of the Styrosorbs on the molecular weight of the initial polystyrene. A decrease in the polymer chain length leads to an increase in d. The high mobility of the low-molecular-weight polystyrene facilitates the phase decomposition of the solution. Pores whose size amounts to several tens of nanometers therefore arise in the final polymer. If the rate of the chemical reaction is sufficiently high while the mobility of the chains is, on the other hand, limited (a polystyrene with a fairly high molecular weight), then the chains are fixed in the three-dimensional structure very rapidly and in such a system there are no favourable conditions for microlayer formation. The mesopores in the given Styrosorbs consist of gaps between individual coils of polystyrene macromolecules (or their aggregates), which exist in the initial solution and are fixed by cross-links.[92,93]

Thus the nature of the porous structure of the Styrosorbs can vary within wide limits and depends both on the nature of the solvent and on the molecular weight of the polystyrene.

In the chloromethylation and amination of Styrosorb (I) by DETA, its structure (specimen *3a*, Table 5) changes, $S_{C_8F_{18}}$ and $V_{C_8F_{18}}$ increase, while d_{eff} remains unchanged. The polymer-

analogue reactions probably involve the formation of small ($d \simeq$ 3 nm) pores, which are nevertheless still accessible to C_8F_{18} molecules.

The anion exchanger obtained from Styrosorb I by chloromethylation and amination using ethylene and diamine and additionally ammonia has been investigated by the low-temperature nitrogen adsorption method with the specimen being warmed in a closed space. In this case, S increases by only 14%, i.e. the specimen has very regular cross-links, because the reactivity of all the polystyrene units is the same and the network polymer obtained has statistically distributed cross-links. Furthermore, the anion exchanger framework is cross-linked to the extent of 100%, i.e. it is rigid, and the enforced elastic deformation is small, which is manifested by the significant increase in S on heating the specimen.

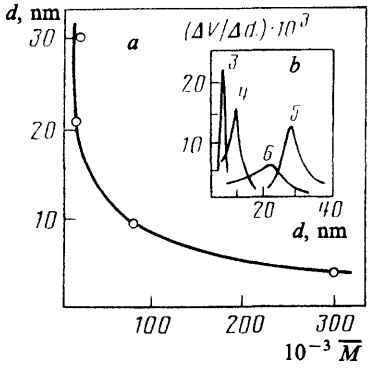


Figure 5. Dependence of the pore diameter for Styrosorbs I on the molecular weight of the initial polystyrene (*a*) [points corresponding to the maxima on the curves for the distribution of the pore volumes with respect to the diameters (*b*)].

When the Styrosorb is sulphonated, it becomes non-porous. This probably takes place as a result of the increase in the volume of the sulpho-groups caused by the binding of the water molecules and as a result of the high cohesion energy, which holds together the highly cross-linked but mobile polymer network.

IV. The influence of the porous structure of polymers on their adsorption and chromatographic properties

1. Characteristic features of the adsorption of organic vapours

The study of the influence of the porous structure of methacrylate polymers on their gas-chromatographic properties has shown that the less cross-linked polymers possess better chromatographic properties (more symmetrical peaks, lower retention times of all substances and lower heights equivalent to the theoretical plate) since they contain the smallest number of bottle-shaped pores and pores with $d < 5$ nm.[38,43–47,49–52,54] With increase in the specific surface of the methacrylate polymers, the specific retention volumes of all the substances also increase. The relative retention volumes of the non-specifically sorbed n-hydrocarbons increase with increase in the amount of the cross-linking agent (ethylene dimethacrylate) (owing to the increase in S and in the contribution of dispersion interactions), while those of specifically sorbed substances (for example, benzene, alcohols, ethyl methyl ketone, nitromethane, and pyridine) fall, which can be explained by the decrease, with increased S, in the concentration of surface functional groups responsible for the specific interactions with these molecules.[25,47,120,123]

The gas-chromatographic properties of vinylpyridine–divinylbenzene copolymers have been investigated in relation to the AN-251 anion exchangers obtained with the same amount of n-heptane as the pore-forming agent (80% of the total monomers) for different contents of divinylbenzene.[124] The retention volumes V_R of n-hydrocarbons increase on passing from the AN-251-15/80 specimen to the AN-25-30/80 specimen and diminish somewhat for the AN-251-40/80 specimen, while the specific surfaces of this series increase monotonically. The decrease in retention volumes for the AN-251-40/80 specimen can probably be accounted for by the decrease in the degree of swelling and in the overall pore volume of this highly cross-linked ion exchanger. The values of V_R for the specifically adsorbed molecules are appreciably higher than those for the non-specifically adsorbed molecules and, on passing to highly cross-linked specimens, they decrease owing to the decrease in the number of functional groups in the polymer.

The methacrylate and styrene–divinylbenzene polymers poorly sorb hydrocarbon vapours and undergo partial swelling in C_6H_{14} vapour; the C_6H_{14} adsorption isotherms on the initial (S = 25 m^2g^{-1}) and chloromethylated (S = 32 m^2g^{-1}) copolymers as well as the copolymer aminated by ethylenediamine (S = 31 m^2g^{-1}) are the same, i.e. the introduction of functional groups into the polymer does not alter the sorption of the n-alkane, since the sorption takes place as a result of a non-specific interaction. The same features have been observed for the sorption of CH_3OH, i.e. the contribution of specific interactions is in this case small.

Styrosorbs, which have a more extensive porous structure, effectively sorb hydrocarbon vapours.[84,90] In a study[125] of the kinetics of the sorption of n-heptane and n-hexane by Styrosorb, it has been shown that the process takes place in two stages: the first, rapid stage involves a rearrangement of the sorbent structure and the second, slow stage is associated with the permeation of the n-C_5H_{12} and n-C_6H_{14} molecules into the microcavities formed as a result of the segmental mobility of the polymer chain units. The degree of sorption of CH_3OH and H_2O vapours by Styrosorbs is not high. The CH_3OH vapour sorption isotherm on Styrosorb II (a microporous specimen) lies above that on Styrosorb I (a biporous specimen containing micropores and mesopores) and has a different form—it is linear up to $p/p_0 = 0.6$. On the other hand, on being immersed in CH_3OH or H_2O, these polymers absorb up to 6.0 and 4.0 cm^3g^{-1} of these liquids respectively.[92]

The cyclohexane sorption isotherms on the initial and DETA-modified polymers of this type are similar up to $p/p_0 \simeq 0.8$; for higher values of p/p_0, the sorption isotherm on the initial copolymer lies in a much higher position, evidently due to its greater swellability at high pressures. On sulphonation, the specimen becomes non-porous and the degree of sorption of n-C_6H_{14} and cyclo-C_6H_{12} diminishes almost to zero.[80]

Thus the study of the sorption of organic substances on the test specimens showed that their capacity is determined to a large extent by the geometrical structure of the sorbent. Styrosorbs exhibit a high capacity with respect to organic compounds.

2. Characteristic features of the absorption of carbon and sulphur dioxides

It was shown above that the geometrical structure of the polymeric sorbents is determined by the amount and nature of the components involved in their synthesis. The influence of these factors on the adsorption and chromatography of certain adsorbates,

in particular carbon and sulphur dioxides, has therefore been investigated. These gases were selected because they are, firstly, of interest from the practical point of view and, secondly, they are effectively adsorbed by polymers containing amino-groups.

(a) The influence of the amount and nature of the cross-linking agent

Anion exchangers based on styrene–divinylbenzene and vinylpyridine–divinylbenzene (divinylpyridine) copolymers and Styrosorbs.[1,80,126–130] Measurements were made of the CO_2 adsorption isotherms by the static volumetric method and of the output curves (frontal chromatograms) for CO_2 and SO_2 on AN-221 specimens with different degrees of cross-linking (Fig. 6). Table 6 presents the ratios of the amounts of divinylbenzene and of the pore-forming agent for the AN-221 anion exchanger containing ethylenediamine groups, the static exchange capacities (SEC) with respect to 0.1 M HCl, S_{N_2}, S_{CO_2}, as well as the capacities with respect to CO_2 and SO_2 before break-through (E_0); data for anion exchangers based on Styrosorbs are not included. For styrene–divinylbenzene copolymers not containing functional groups, an increase in capacity before the break-through of SO_2 is observed with increase in the amount of divinylbenzene (with increase in S), since the molecules are adsorbed mainly as a result of dispersion interactions. Figs. 6 and 7 show that the capacities of the AN-221 anion exchangers with respect to CO_2 and SO_2 diminish with increase in the amount of cross-linking agent in them and that the same behaviour is observed for the AN-251 exchangers (Fig. 8). With increase in the divinylbenzene content, S_{N_2} and the overall pore volume (V) of the anion exchangers increase. On the other hand, with increase in divinylbenzene content in the polymerising system, the number of monomer units carrying functional groups diminishes. In the styrene–divinylbenzene copolymers, these are styrene rings, which are subsequently chloromethylated and aminated, while in the vinylpyridine–divinylbenzene copolymers these are vinylpyridine rings. As a result, an increase in the divinylbenzene content in the anion exchangers entails a diminution of the overall number of functional groups (the SEC characterises the content of functional groups in the swollen ion exchanger, i.e. virtually the total number of functional groups). The decrease in the number of functional groups entails a decrease in the degree of adsorption of CO_2 and SO_2 adsorbed on anion exchangers as a result of dispersion interaction with the anion exchanger framework and specific interactions with the functional groups, i.e. the dominant factor is the interaction with functional groups. Therefore, a decrease in the SEC of the anion exchanger entails, despite the increase in S, a diminution in the degrees of adsorption of CO_2 and SO_2. Similar variations in the degrees of adsorption by the dry AN-221 anion exchangers have been obtained for SiF_4 [131] and the acrylonitrile–divinylbenzene copolymer (or acrylonitrile) in relation to phenol and aniline.[25] The weaker dependence of the capacity of the AN-251 anion exchanger before the break-through of SO_2 on the amount of divinylbenzene compared with the dependence of the total capacity shows that the capacity before break-through depends to a greater extent on S than the total capacity, which is mainly determined by the SEC of the anion exchangers (Fig. 8).

The absorption of SO_2 on the AN-251 anion exchangers cross-linked not by divinylbenzene but by divinylpyridine i.e. anion exchangers in which both the cross-linking agent and the monomer contain pyridine nitrogen, has also been investigated. For specimens with a similar structure, it has been shown that the time of the protecting action and hence also $E_0^{SO_2}$ for the AN-251-DVP,15/50 anion exchanger is greater than for AN-251-DVB,15/50, i.e. the use of divinylpyridine as the cross-linking agent increases the number of functional groups in the anion exchanger and its capacity with respect to SO_2.

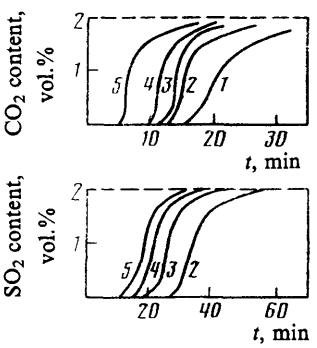


Figure 6. CO_2 and SO_2 output curves on the AN-221 anion exchanger (BR-1 pore-forming agent). Experimental conditions: carrier gas flow rate 250 cm^3 min^{-1}, CO_2 or SO_2 content in the carrier gas 2 vol.%, column diameter 15 mm, column length 50 mm for CO_2 and 25 mm for SO_2 and column temperature 20 °C. Amount of divinylbenzene (%): (*1*) 8; (*2*) 12; (*3*) 15; (*4*) 20; (*5*) 30.

Table 6. Characteristics of the AN-221 anion exchangers with different geometrical structures (specimens *1–8*) and anion exchangers based on Styrosorb I (specimens *9–11*) and their capacities with respect to CO_2 and SO_2.[80,126–130]

Specimen	Solvent	DVB/solvent	S_{N_2}, m^2 g^{-1}	S_{CO_2}, m^2 g^{-1}	SEC, mequiv. g^{-1}	$E_0^{CO_2*}$, mg g^{-1}	$E_0^{SO_2*}$, mg g^{-1}
1	BR-1	8/100	51	142	6.7	40	147
2	BR-1	12/80	65	124	6.4	30	173
3	n-Heptane	15/100	61	101	5.5	24	134
4	BR-1	15/100	75	–	5.3	–	–
5	BR-1	15/100	62	–	5.5	25	–
6	BR-1	20/80	90	92	4.1	18	126
7	BR-1	30/100	140	–	3.0	12	–
8	BR-1	30/100	150	64	3.4	20	92
9	DCE	MCDE/100-EDTA + NH_3	664	64	3.5	18	–
10	DCE	MCDE/100-EDA	–	64	3.0	16	–
11	DCE	XDC/100-EDA	710	64	3.0	18	–

For the highly cross-linked macronetwork polystyrene ion exchangers (Styrosorbs containing ethylene diamine groups—specimens *9–11* in Table 6), the values of $E_0^{CO_2}$ are close to those for highly cross-linked AN-221 anion exchangers.[80] The CO_2 adsorption isotherms on the macronetwork anion exchanger and on AN-221-30/100, having identical ethylenediamine groups and similar values of SEC (3.0–3.5 mequiv.g^{-1}), are identical despite the fact that the value of S for the macronetwork anion exchanger is almost 5 times greater than that for the AN-221 anion exchanger. The CO_2

adsorption isotherm on AN-221-15/100 (specimens 3), having a value of S smaller by a factor of 10 than the macronetwork specimen but a higher value of SEC, lies above the CO_2 adsorption isotherm on the macronetwork anion exchanger.

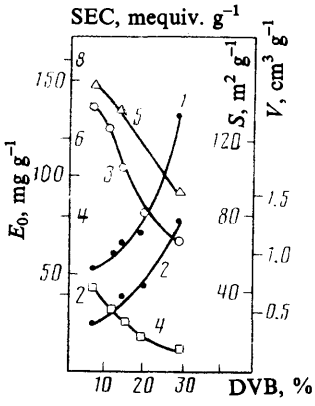


Figure 7. Dependence of the specific surface (curve *1*), pore volume (curve *2*), static exchange capacity (curve *3*), and capacities before the break-through of CO_2 (curve *4*) and SO_2 (curve *5*) on the divinylbenzene content in the AN-221 anion exchangers.

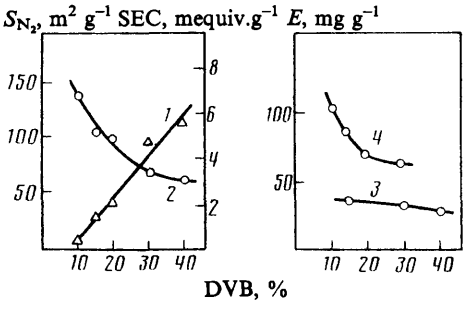


Figure 8. Dependence of the specific surface (curve *1*), static exchange capacity (curve *2*), the capacity before the break-through of $SO_2(E_0^{SO_2})$ (curve *3*), and the total capacity (E^{SO_2}) (curve *4*) on the divinylbenzene content in the AN-251 anion exchangers.

The CO_2 and SO_2 adsorption isotherms on the anion exchangers investigated are described approximately by the Langmuir equation. The monolayer capacity a_m were determined from the slopes of the linear plots of p/a against p and S_{CO_2} and S_{SO_2} were calculated (the values of S_{CO_2} are listed in Table 6; the area per CO_2 molecule in the monolayer is 0.171 nm^2). In the case of the weakly cross-linked polymer (specimen *1*), S_{CO_2} exceeds S_{N_2} almost by a factor of three, while in the case of the highly cross-linked anion exchangers it is much lower. This indicates an appreciable local interaction of CO_2 molecules with the amino-groups of the anion exchangers and, in the case of the weakly cross-linked anion exchangers, the adsorbed molecules permeate into the matrix. Calculations showed that the fraction of the amino-groups participating in the adsorption of CO_2 on the least cross-linked specimen (8% DVP) is somewhat greater than on the remaining specimens and hardly changes with increase in the amount of divinylbenzene to 30%. The static exchange capacity is by no means fully utilised in the adsorption of CO_2—at best to the extent of 50%. In the case of SO_2, it is possible to attain 100% utilisation of the amino-groups of the anion exchangers, which can be accounted for by the stronger acid properties of the SO_2 molecule compared with CO_2.

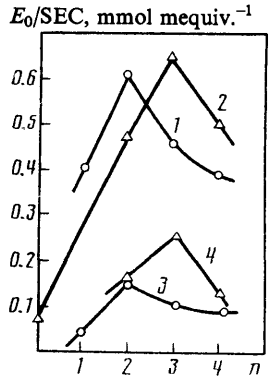


Figure 9. Dependence of the capacities of the anion exchangers before break-through (calculated per unit SEC) with respect to SO_2 (curves *1* and *2*) and CO_2 (curves *3* and *4*) on the number of amino-groups (n) in the aminating agent: (*1*) and (*3*) anion exchangers obtained from the styrene–divinylbenzene copolymer with d = 30 nm (12/80, isooctane); (*2*) and (*4*) ditto for the styrene–divinylbenzene copolymer with d = 60 nm (8/100, n-nonane).

(b) The influence of the amount and nature of the pore-forming agent

Anion exchangers based on styrene–divinylbenzene and vinylpyridine–divinylbenzene copolymers.[124,129,130,132] The change in the porous structure of the polymers induced by the change in the content and nature of the pore-forming agent influences appreciably their adsorption capacity. Firstly, the increase in the volume and size of the polymer pores with increase in the size of the hydrocarbon (pore-forming agent) molecule increases the accessibility of the functional groups to the molecules being adsorbed. Secondly, an increase in the size of the copolymer pores makes it possible to modify the copolymer by larger molecules containing several amino-groups. Fig. 9 presents the dependences of $E_0^{CO_2}$ and $E_0^{SO_2}$, referred to the SEC, on the number of amino-groups in the functional unit of the styrene–divinylbenzene anion exchangers having different pore sizes. An increased number of amino-groups in the molecule of the aminating agent increases the capacity of the anion exchanger, but the introduction of larger molecules (for example diethylenetriamine) into the copolymer with d = 30 nm is difficult. Furthermore, the configuration of the diethylenetriamine molecules in the pores is such that the amino-groups are inaccessible to the molecules being adsorbed. As a result, the capacity of the AN-511 anion exchanger with d = 30 nm diminishes. In the case of the more coarsely porous specimen with d = 60 nm, the configuration of the large molecule of the aminating agent (diethylenetriamine) in the copolymer pores is favourable for the molecules undergoing adsorption and the capacity of the anion exchanger increases.

The dynamics of the adsorption of CO_2 on different beds (ranging from 7 to 90 cm) of the AN-221 anion exchangers obtained in the presence of pore-forming agents of different natures (PR-1 petrol, n-heptane, isooctane, and n-decane) has been investigated. It has been shown that the anion exchanger whose matrix has been synthesised in n-decane (having the largest pores among the polymers investigated) exhibits the best dynamic characteristics together with a high capacity with respect to CO_2.

The influence of the nature and amount of the pore-forming agent on the absorption of SO_2 has been studied for anion exchangers of different types containing different amino-groups.[1,130] For the same divinylbenzene content (for the virtually identical value of SEC), the capacity of the anion exchangers before the breakthrough of SO_2 passes through a maximum as the amount of the solvent (pore-forming agent) increases. It is known that S also passes through a maximum under these conditions, while V and d increase. In the region of the SO_2 absorption maximum, the optimum ratios of the values of S, V, and d for the anion exchangers are apparently attained. The use of a solvent with a larger molecular size (white spirit instead of heptane) for AN-251 shifts the maximum towards lower concentrations of the pore-forming agent.

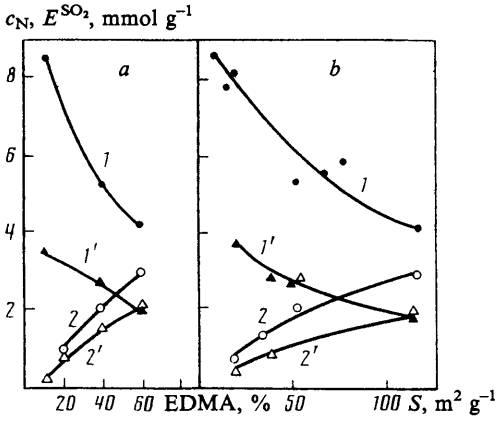


Figure 10. Dependence of the concentration of the amino-groups c_N (curves *1* and *1'*) and of the capacity with respect to SO_2 (E_0) (curves *2* and *2'*) on the amount of the cross-linking agent (*a*) and S (*b*) in the epoxypropyl methacrylate–ethylene dimethacrylate copolymers modified by dithylene triamine (curves *1* and *2*) and ethylmethylamine (curves *1'* and *2'*).

(c) The influence of the amount of the cross-linking agent and of the solvent/precipitant ratio

Methacrylate polymers.[40] Fig. 10 presents the dependences of $E_0^{SO_2}$ and of the concentration of amino-groups c_N on the percentage content of ethylene dimethacrylate and S. They differ from the similar dependences for the anion exchangers of the styrene–divinylbenzene series (Figs. 7 and 8). For the methacrylate polymers, an increase in the amount of the cross-linking agent (simultaneously with an increase in S and V and a decrease in c_N) in the polymers increases their capacity with respect to SO_2. The amount of SO_2 adsorbed by a weakly cross-linked polymer is much smaller than the amount of amino-groups, apparently because the values of S and V for such polymers are small and most of the amino-groups are not accessible to the SO_2 molecules undergoing adsorption. As a consequence of the increase in S and V, an increase in the amount of ethylene dimethacrylate entails an increase also in the content of the surface amino-groups and in their accessibility, so that the capacity with respect to SO_2 increases. This is confirmed by the fact that, with increase in the ethylene dimethacrylate content, the number of surface epoxy-groups rises.[30] It is important to note that, as the content of ethylene dimethacrylate increases, the ratio E_0/c_N tends to unity, i.e. the complete utilisation of the amino-groups is attained.

For the polymers differing in the cyclohexanol/dodecanol ratio, an increase in the adsorption capacity with respect to SO_2 with increase in S is also observed (Fig. 10*b*).

It is noteworthy that, despite the different forms of the dependences of E_0 on the amount of cross-linking agent for AN-221 and epoxypropyl methacrylate–ethylene dimethacrylate–ethylenediamine, containing identical functional groups, the optimum (as regards the absorption of CO_2 and SO_2) structure of the specimens is the same: $S \simeq 50$ m^{2}g^{-1} and $d \simeq 100$ nm, although in the former case the copolymer was obtained with 8% of the cross-linking agent (divinylbenzene), while in the latter case 40% of the cross-linking agent (ethylene dimethacrylate) was used. For such structural parameters, the maximum accessibility of the amino-groups to the molecule being adsorbed is apparently achieved regardless of the nature of the polymer matrix.

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Thus the study of the porous structures of polymeric sorbents of different structural types by a set of physicochemical methods and the determination of the dependences of the parameters of the porous structure on the conditions of synthesis (the amount and nature of the cross-linking agent, the amount and nature of the pore-forming agent, and the molecular weight of polystyrene) permits the specific synthesis of porous polymers with a particular structure. It has been shown that, with increase in the amount of the cross-linking agent in the anion exchanger matrix, the specific surface and the pore volume and size increase; an increase in the molecular size of the pore-forming hydrocarbons also entails an increase in the size of the anion exchanger pores. The nature of the porous structure of Styrosorbs depends likewise on the nature of the solvent in which the cross-linked copolymer is formed and on the molecular weight of the initial polystyrene. The polymer-analogue reactions of the mesoporous styrene–divinylbenzene and epoxypropyl methacrylate–ethylene dimethacrylate copolymers do not lead to significant changes in their porous structure. The relations established for the adsorption of carbon and sulphur dioxides by modified polymers of different structure make it possible to optimise their porosity, for which the maximum accessibility of the functional groups to the molecules undergoing adsorption is ensured.

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Translated from *Uspekhi Khimii* 60 398–429 (1991) U.D.C. 541.64:539/2+3

Emulsion polymerisation in the absence of an emulsifying agent and latexes based on it

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ABSTRACT. The results of studies on the emulsion polymerisation of monomers of different chemical nature in the absence of an emulsifying agent are analysed and treated systematically. When the physicochemical properties of the latexes are considered attention is concentrated on factors influencing their stability, especially in concentrated systems. Questions concerning film formation and the specific properties of films, which are important in the technology of the manufacture of glues and adhesives, are also touched upon.

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I. Introduction

The chlorides obtained by the traditional emulsion polymerisation (EP) have found applications in various branches of science and engineering—as calibration standards in electron and optical microscopy, light scattering, and ultracentrifugation, in the counting of aerosol particles and small angle X-ray diffraction,[1] in the medical diagnosis of a number of diseases,[2–5] in the counting of viral particles, in the determination of the pore size in filters and biological membranes, for the stimulation of the growth of antibodies and their purification,[1] as model colloids in the study of their rheological behaviour, stability, flocculation, and adsorption,[6] and in the study of the mechanism and kinetics of the formation of films from latexes. However, the use for the above purposes of latexes obtained in the presence of emulsifying agents is difficult because of the need to seek special conditions for the attainment of a specified particle size, the poor reproducibility of the results, and also the presence of the emulsifying agent on the surfaces of the particles, whose removal involves complex procedures.

The latexes obtained with the aid of emulsifier-free emulsion polymerisation (EFEP) did in fact initially attract the attention of investigators as colloids with identical particle sizes and a "clean" surface. Other characteristics of the latexes are important for the above purposes: resistance to various influences, the chemical nature of the surfaces of the particles, their charge, etc. Recently, the number of studies devoted to the preparation of emulsifier-free latexes (EFL) with the required properties has been growing steadily. New advantages of EFEP, associated in particular, with the prospects for the industrial synthesis of latexes without the use of the surfactants employed in traditional emulsion polymerisation, have been discovered. This is very important ecologically: the pollution of industrial waste water and water-containing areas is prevented and, in addition, the properties of the polymers isolated are improved as regards their practical use.[7]

In each application, specific requirements must be met by the EFL. Whereas monodisparity and a controllable particle size are essential when they are used as calibration standards, for model colloids there is a need, apart from the above factors, to characterise the chemistry of the surface of the polymer phase; for immunodiagnosis, the surface must contain specific functional groups [in all these cases systems with low concentrations (up to 10 wt.%) are suitable]. For the EFL used for industrial purposes, for example for glues and adhesives, a necessary condition is a high polymer concentration (~50 wt.%) combined with a low content of electrolytes and other water-soluble substances. Ideally, such systems are hydrophobic polymer sols, whose particles, suspended in a pure dispersion medium, are stabilised solely by the chemical nature of the surface. The complexity of the production of industrial EFL on a large scale is associated with the need to overcome technological difficulties arising due to the inadequate colloidal stability towards various influences.

The present review analyses and treats systematically the results of studies on the EFEP of monomers of different chemical nature. When the physicochemical properties of the latexes obtained are considered, attention is concentrated on factors influencing their stability, in particular in concentrated systems. The questions concerning film formation and the physicochemical properties of films obtained, which are important in the technology of the manufacture of glues and adhesives, are also touched upon.

The possibility of obtaining relatively dilute latexes in the absence of an emulsifying agent was first demonstrated in the polymerisation, initiated by persulphuric acid salts, in the aqueous phase of monomers which are appreciably soluble in water, such as vinyl acetate[8] and methyl acrylate.[9] Subsequently, the range of monomers used for this purpose was expanded by including hydrophobic monomers such as styrene.[10] The tabulation of monodisperse polystyrene latexes with a controllable particle diameter in the range 97–5000 nm has been reported.[11–14] EFL have been obtained also in the copolymerisation of vinyl monomers with a small amount of comonomers containing ionisable groups: sulphate,[15–17] carboxy-,[18] and amino-groups.[19] In all cases persulphate was used as the initiator. It was assumed that the particles formed are stabilised by the ionisable surface groups of the macromolecules (in the initiation of the process by radical-ions) or by copolymerisation with ionisable monomers. EFL have also been obtained by

polymerisation initiated by azo-compounds—2,2′-azobisisobutyramidine,[20] 2,2′-azo-bis(2-amidinopropane)hydrochloride,[21] and 2,2′azobis-*N*,*N*′-di-methyleneisobutyramidine.[22] On decomposition of such compounds, nitrogen is evolved and free radicals containing positively charged amidine groups are formed. They apparently impart stability to the particles. Subsequently studies on the preparation of highly concentrated EFL began to develop. Thus, 50% latexes of styrene–butadiene copolymers with unsaturated acids have been obtained.[23] Other studies[24,25] produced 30% EFL based on ethyl acrylate and its copolymers.

The absence from the polymerisation system of a specially introduced emulsifying agent, to which a decisive importance has been attributed in the study of the mechanism and kinetics of emulsion polymerisation,[26,27] faced investigators with the task of elucidating the mechanism of the nucleation, growth, and stabilisation of particles on formation of EFL based on both polar and non-polar monomers.

II. Polymerisation of polar monomers in the absence of an emulsifying agent

1. Nucleation mechanism

The theory of the formation of particles via the micellar mechanism in traditional emulsion polymerisation[26–31] is apparently not applicable to monomers which are appreciably[32–39] and even slightly soluble in water.[38] It is assumed that, in the case of persulphate initiation, polymerisation begins not in the emulsifer micelles, but in the aqueous solution with formation of oligomeric radicals. The oligomeric radicals can participate in several reactions: they can combine with the molecules of the monomers soluble in the aqueous phase and can be precipitated after the attainment of a critical degree of polymerisation, n_{cr}, giving rise to primary charged particles; they can recombine with other dissolved radicals with formation of neutral surfactants; they can flocculate with other dissolved radicals on chain termination; they can be absorbed by particles or they can be adsorbed on their surfaces. Under these conditions, the emulsifier plays merely a stabilising function and increases the solubility of oligomeric radicals.[38] A particular reaction can introduce a greater or smaller contribution to the nucleation process depending on the solubility of the monomer (and the radical) in water.

The mechanism of the nucleation of particles in the EFEP of methyl methacrylate (MMA) (solubility in water 1.5×10^{-1} mol/litre at 319 K) and styrene (St) (2.6×10^{-3} mol/litre at 298 K) has been most thoroughly investigated.

As a result of studies on the EFEM of MMA in very dilute solutions (from 0.03 to 0.09 M) in the presence of Fenton's initiating system [potassium persulphate (PPS) (7.4×10^{-4} mol/litre H_2O) + sodium bisulphite (1.2×10^{-3} mol/litre H_2O) + Fe^{II}], the authors[39] concluded that each oligomeric radical $SO_4^-(M)_{\bar{n}}$ "coils up" after the attainment of $n_{cr} = 65-70$, forming a particle. The rate of formation of particles in this initial instant is equal to the effective rate of initiation W_{in}. The oligomeric radicals formed are subsequently captured by the particles at a rate W_c, whereupon the rate of formation of the particles dN/dt becomes

$$dN/dt = W_{in} - W_c. \quad (1)$$

The number of particles can be calculated by integrating this equation with respect to time.

It has been suggested[39] that W_c is proportional to the overall surface area of the captured particles with a radius r_p:

$$E_c = W_{in}\pi r_p^2 LN, \quad (2)$$

where L is the distance over which the oligomeric radical is able to diffuse before losing its solubility and precipitating from the solution. The probability of the capture of the growing radical before it forms a new particle increases with increase in L, i.e. the number of particles falls.

It follows from Eqn. (1) that the number of particles should increase with increase in the rate of initiation and should diminish with increase in the rate of capture. However, Eqns. (1) and (2) have certain limitations associated with the colloidal instability of the particles formed, which leads to their flocculation. Flocculation takes place at a high rate and is limited by the density of the surface charged groups for which the electrostatic potential barrier becomes sufficiently high to ensure the stability of the particles.[40] In view of this, the authors[39] supplement Eqn. (1) by a new term—the rate of flocculation W_f:

$$dN/dt = W_{in} - W_c - W_f. \quad (3)$$

The hypothesis that the rate of formation of radicals with n_{cr} is equal to the rate of formation of primary radicals[39] (see above) can be valid only for a very low rate of chain termination in the aqueous phase.

In considering the polymerisation of MMA in aqueous solution at a monomer concentration C_m ranging from 0.1 to 0.15 mol/litre H_2O (the limiting solubility of MMA), Arai et al.[41] assumed that the total number of particles is equal to the sum of the reactive (N_1) and inactive (N_0) particles: $N = N_1 + N_0$. In constrast to Fitch,[39] Arai et al.[41] and Barrett and Thomas[42] assume that, owing to the small size of the particles, at the beginning of the process the rate of capture of the radicals by the particles is not proportional to their overall surface area [see Eqn. (2)] and is controlled by the diffusion of the radicals, being expressed by the equation

$$W_c = 4\pi r \sum_{n=1}^{n=n_{cr}} D_n R_n, \quad (4)$$

where D_n is the diffusion coefficient and R_n is the concentration of the growing radicals. Neglecting the difference between the sizes of the primary particles, the authors[41] take into account the difference between the average numbers of reactive and inactive particles, the rate of formation of which is described by the following equations:

$$dN_1/dt = k_p M_L R_J N_A + 4\pi(r_0 N_0 - r_1 N_1) \sum_{n=1}^{J} D_n R_n N_A, \quad (5)$$

$$dN_0/dt = (1-\lambda)\frac{k_t}{2} \sum_{n=1}^{J} R_{n_{cr}+1} \sum_{n}^{n_{cr}} R_n N_A + 4\pi (r_1 N_1 - r_0 N_0) \sum_{n=1}^{n_{cr}} D_n R_n N_A, \quad (6)$$

where J is the length of the growing radical, t the time, k_p and K_t are the rates of chain propagation and termination, M_L is the monomer concentration in the aqueous phase (since the formation of the particles terminates at a low degree of conversion, M_L is assumed equal to the initial value of C_m), N_A the Avogadro number, and λ the ratio of the rate of the disproportionation reaction to the overall rate of the termination reaction.

The first terms in Eqns. (5) and (6) express the rate of nucleation of new particles and the second terms express the change in their number on capture of radicals. By setting up differential balance equations for the rate of increase of the overall volume of the reactive and inactive particles and by solving these equations in a system with known values of λ, M_L, k_{in}, k_p, and k_t (assuming that the rate of initiation is unity under these conditions), the authors[41] obtained the dependence of N on time for different values of n_{cr}. It follows from these relations that the particle formation process is rapid and terminates after several seconds. After this, the number of particles N remains constant, i.e. there is no flocculation of particles. For M_L = 0.15 M and C_{in} = 1 × 10^{-3} mol/litre H_2O, the final value of N depends little on the chosen value of n_{cr} (diminishing somewhat with increase of the latter) and is N = (4–6) × 10^{-14} H_2O molecules. In the region where C_{in} = 10^{-3}–10^{-2} M, the number of particles increases with increase in C_{in} and, for C_{in} > 10^{-2} M, the relation becomes weaker. The latter finding is attributed to the fact that, with increase in C_{in}, mainly "dead" particles are formed as a result of the termination of the growing radicals.

The number of particles calculated on the basis of the model proposed by Arai et al.[41] is much smaller than that found by Fitch.[39]

On comparing the theoretical[41] and experimental[43] results obtained in the polymerisation of MMA, Arai et al.[41] were unable to assess accurately the model which they proposed because of the approximate nature of the experimental value of N. However, N_{exp} is appreciably closer to the value obtained from the model of Arai et al.[41] than the value yielded by Fitch's model.[39] The approximate agreement between the theoretical[41] and experimental[43] values shows that, under the conditions employed (C_m = 0.9 M, C_{in} = 5 × 10^{-3} M, and T = 333 K [43]), the particles do not flocculate during the formation process.

Both models considered (Fitch's model[39] as well as that of Arai et al.[41]) refer to very dilute systems and, although they provide an idea about the possible mechanisms of the formation of colloids in the course of polymerisation, they do not simplify them significantly. Thus in the above models no account is taken of the possible presence of the monomeric phase and of neutral electrolytes; the probability of the new predominance of the rate of growth of radicals before their precipitation from the aqueous phase over the rate of termination is not estimated but is merely assumed on a speculative basis. As a consequence of this, the possible formation of water-soluble oligomers in the course of the mutual termination of radicals, which is an important factor, is not taken into account. Nevertheless, the presence of oligomers having the properties of surfactants, especially in the initial phase of the process where their formation is most likely, affects both the mechanism of the nucleation and the number of particles generated. Thus the mechanism of the nucleation and growth of particles in the absence of an emulsifying agent in real reaction systems and of the formation under these conditions of stable latexes appears much more complex than in the models.[39,41] This follows from the further consideration of the factors influencing the above mechanism.

2. Stability factors

(a) Surface-active oligomers

In the emulsifier-free polymerisation of MMA (C_m = 0.5 M, in the presence of the monomeric phase), initiated by 2.2 × 10^{-3} M ammonium persulphate (APS) at 353 K, yielded a latex with the following characteristics: concentration 4.7%, particle diameter d_p = 175 nm, surface tension σ = 60.5 mJ m^{-2},[45] and content of the sol fraction 1.4% relative to the mass of the polymer.[46] The nature of the surface tension isotherm for the sol fraction $\sigma = f(C)$ (Fig. 1) indicates the similarity of the water-soluble oligomers isolated to low-molecular-weight surfactants with a critical micelle-formation concentration (CMC) amounting to 1.4 wt.%. This indicates an appreciable contribution to the MMA polymerisation by the radical termination process in the aqueous phase involving the formation of water-soluble oligomers capable of micelle formation. Indeed, according to Solov'ev and Zuikov,[47] the instant of the formation of particles in the polymerisation of MMA coincides with the instant of the attainment of the CMC for the oligomeric surfactant.

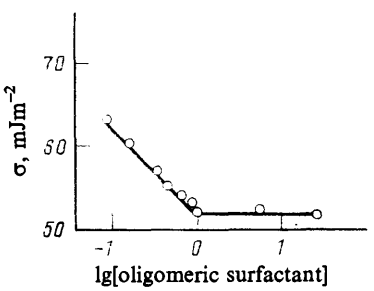


Figure 1. The surface tension isotherm for the sol fraction of the emulsifier-free PMMA latex (C_m = 0.5 M) synthesised in the presence of ammonium persulphate (C_{in} = 2.2 × 10^{-3} mol/litre H_2O) at 353 K.[46]

When higher concentrations of the monomers are employed (C_m = 1 M) and for lower potassium persulphate concentrations [C_{in} = (3.3–4.8) × 10^{-4} M] in the emulsifier-free polymerisation of MMA[48] (T = 353 K), latexes of a high-molecular-weight [MW = (0.98–1.25) × 10^6] with d_p = 288–300 nm and resistant to aggregation are produced; the surface tension σ = 67.8–68.5 mJ m^{-2} of these latexes indicates the presence in them of water-soluble surfactants. The content of surfactants in the aqueous phase found experimentally[48] is lower than the value obtained by Bogdanova et al.[45] in view of the lower value of C_{in}, while the volume and surface area of the disperse phase, adsorbing the surfactants, are higher, which leads to their more extensive exhaustion as a result of adsorption. Indeed, with increase in C_m to 1.5 M for the same value of C_{in}, the surface tension σ of the latex increases to 70 mJ m^{-2}.[49]

In the study of the conditions governing the formation of stable monodisperse MMA latexes, it was shown that oligomeric and polymeric surfactants, formed during the process and removed on dialysis of the latexes, participate in the stabilisation of the particles.[50] It has been demonstrated with the aid of gel permeation chromatography that the molecular weights of the polymer latexes isolated vary from 1.1 × 10^3 to 1 × 10^5, the fraction with MW = 4.9 × 10^3, corresponding to n = 49, predominating. These data refer to the latex obtained by the polymerisation of MMA (C_{in} = 5 × 10^{-3} M, T = 343 K) and indicate a radical termination

reaction in the aqueous phase with formation of oligomers, the degree of polymerisation of which is significantly lower than n_{cr} = 65–70 according to Fitch.[39]

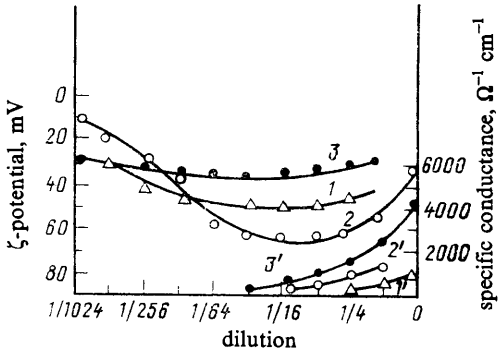


Figure 2. The ζ-potential of the particles (curves *1*–*3*) and the specific conductances (curves *1'*–*3'*) of PMMA latexes synthesised under the following conditions: *1* and *1'*, *T* = °4° K, potassium persulphate initiator; *2* and *2'*, °4° K, potassium persulphate + Cu^{2+}; and *3* and *3'*, °0° K, potassium persulphate + Cu^{2+} + sodium bisulphite.[50]

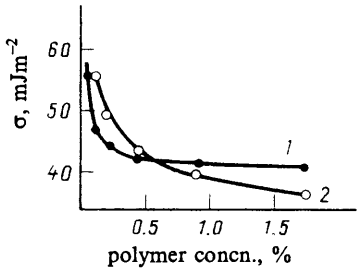


Figure 3. Surface tension isotherm for the butyl acrylate–methacrylic acid (80:20) copolymer at different pH: *1*, 2.7; *2*, 7.8.[18]

In order to analyse the surface activity of the oligomers present in the MMA latexes, the variation of their specific conductance and the ζ-potential of the particles on dilution with water containing the dispersion medium was investigated (Fig. 2).[50] The absolute value of the ζ-potential of the negatively charged particles increases on dilution with water, which is accompanied by a decrease in the specific conductance and then, after the attainment of the conductivity minimum, the ζ-potential falls. This relation shows that the dispersion medium contains a non-indifferent electrolyte, one of the ions of which (oligomeric) is capable of being adsorbed on the surface of the particles.[51]

Surface-active oligomers are or are not capable of forming micelles, for example in the copolymerisation of hydrophobic and ionising comonomers. Thus the low-molecular-weight copolymers (MW ≃ 2 × 10^4), formed on the emulsion-free copolymerisation (EFC) of lower alkyl acrylates with methacrylic acid (MAA) in the presence of ammonium persulphate, exhibit a pronounced surface activity associated with the diphilic nature of their molecules.[18,52] The form of the σ = *f*(*C*) isotherms for these products depends on the pH of the medium (Fig. 3); at pH 2.7, where the carboxy-groups are hardly dissociated and the oligomer molecules have a coiled conformation, the form of the isotherm is similar to that for micelle-forming surfactants: CMC ≃ 0.1–0.2 wt.%. On raising the pH to 7–8, the dispersions dissolve as a result of the dissociation of the carboxy-groups. The σ = *f*(*C*) isotherm steadily decreases with increase in the concentration and becomes similar to the isotherms for the non-micelle-forming low-molecular-weight surface-active homologues.[18,52]

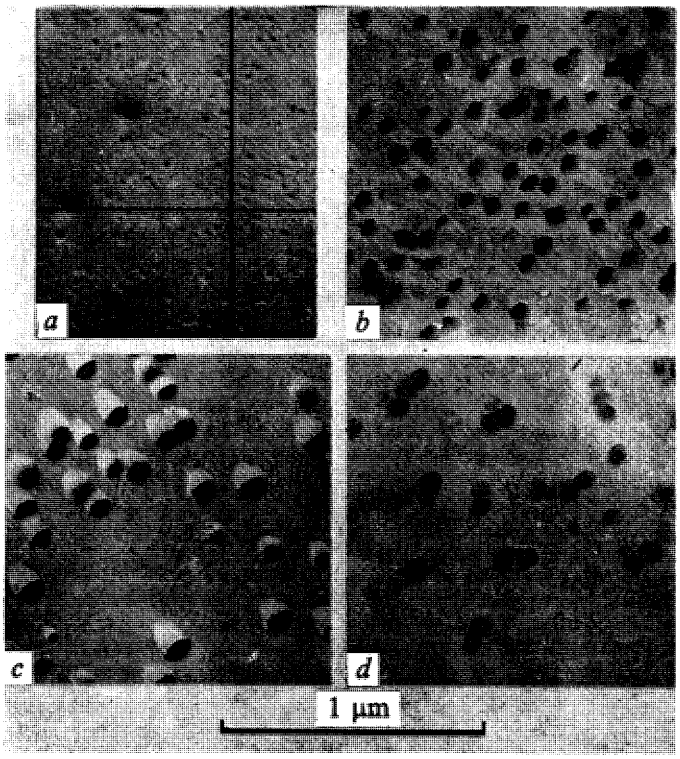


Figure 4. Electron photomicrographs of the latex particles formed in the emulsifier-free copolymerisation of butyl methacrylate and dimethylaminoethyl methacrylate (85:15) for different conversions (%): *a*, 9.9; *b*, 45; *c*, 65.5; *d*, 65.5 (after dialysis).[53]

The formation of non-micelle-forming surface-active electrolytes has been observed in the emulsifer-free copolymerisation of butyl methacrylate (BMA) with the water-soluble hydrochloride of dimethylaminoethyl methacrylate (DMAEMA) [85:15 (mol%)] at pH 5.4–5.5 in the presence of potassium persulphate as the initiator (6 × 10^{-3} mol/litre H_2O).[53,54] The water-soluble copolymer fraction

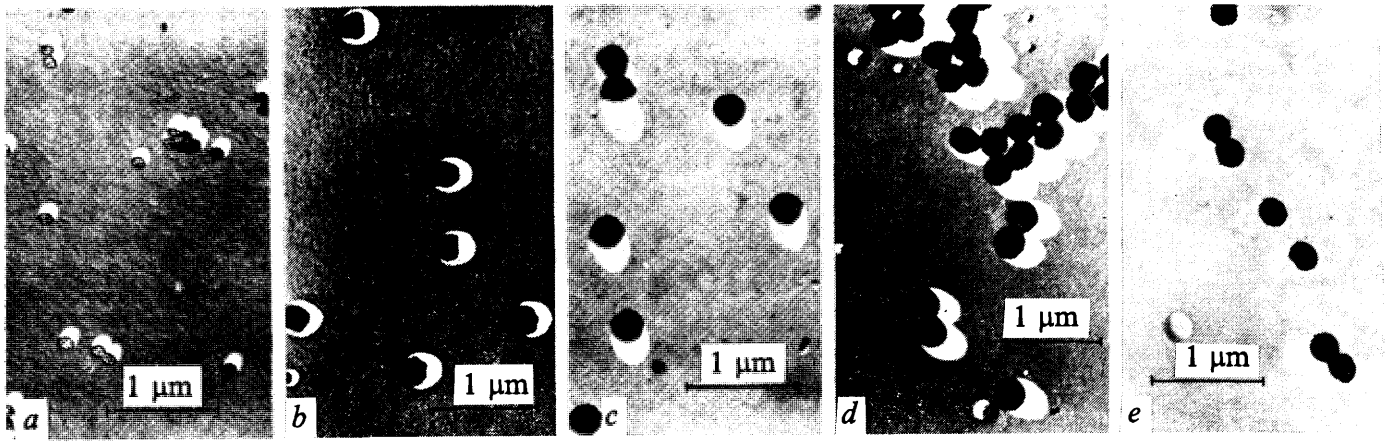


Figure 5. Electron photomicrographs of the latex particles formed in the emulsifier-free polymerisation of methyl methacrylate for different conversions (%): *a*, 5; *b*, 12; *c*, 42; *d*, 75; *e*, 100.[48]

enriched in DMAEMA [47:53 (mol%)] is formed initially; the surface tension of its aqueous solution (4 wt.%) is σ = 49 mJ m^{-2}. After the dialysis of the final latex, the BMA:DMAEMA = 87:13 (mol%) copolymer with a high molecular weight (intrinsic viscosity in benzene η = 2.5) remains. The latex formed at the beginning of the process is characterised by a high polydispersity (the ratio of the volume-average and number-average diameters is d_{vol}/d_{numb} = 1.4), while the final latex is fairly monodisperse (d_{vol}/d_{numb} = 1.1) (Fig. 4). A change in the polydispersity of the latex during polymerisation has been observed also in the study of the emulsifier-free copolymerisation of another hydrophobic monomer (styrene) with the sodium salts of styrene-*p*-sulphonic acid and 2-ethanesulphonylmethyl methacrylate.[55] Presumably the polymerisation in such systems begins in a molecular aqueous solution with formation of surface-active electrolytes enriched in the water-soluble ionised comonomer. After the attainment of very high molecular weights and a high degree of hydrophobicity, some of them are precipitated, forming associated species solubilising the hydrophobic monomer. The subsequent polymerisation process takes place in such associated species. The long duration of the nucleation process leads to a high polydispersity of the latex at the beginning of the process; it then diminishes as a result of the flocculation of the small particles.[40] The particles are stabilised by virtue of the diphilic nature of the macromolecules and the adsorption of the surface-active electrolytes. The latter stability factor is indicated by the partial flocculation of the latex on prolonged dialysis, which results in the desorption of the surfactant (Fig. 4*d*). In the emulsifier-free polymerisation of MMA (pH 3.7; C_{in} = 3.3 × 10^{-4} mol/litre H_2O), where the surface-active oligomers are capable of micelle formation, the particles are monodisperse already at the beginning of the process,[48] which indicates a high rate of nucleation (Fig. 5).

(b) The electrostatic factor

In order to obtain latexes differing in the charge of the particles, use is made of the emulsifer-free polymerisation of MMA (C_m = 1 M, T = 343 K) with different potassium persulphate concentrations (from 1.85 × 10^{-4} to 5.5 × 10^{-3} mol/litre H_2O).[56] The latexes were purified by dialysis and on ion-exchange resins.[1] Conductimetric titration of the purified latexes with alkali demonstrated the presence on the surfaces of the particles of only highly acid groups ($-SO_4^-$); the charge density on the particles varied from 0.53 to 6.6 mC m^{-2}. Its dependence on the concentration of the initiator consumed proved to be almost linear, while the ζ-potential of the particles, determined by microelectrophoresis, varied much less—from −20.7 to −33.7 mV.

A significant correlation has been established between the critical coagulation concentration (CCC) and the charge density as well as a very slight correlation between the CCC and the ζ-potential.[57] This shows that the stability of latexes in relation to electrolytes is influenced primarily by the SO_4^- groups bound covalently to the macromolecules and located on the surface of the particles.

The data quoted were obtained for latexes freed from electrolytes. However, in initiation with persulphate the unpurified latexes always contain low-molecular-weight electrolytes, which affects their stability and particle size. Thus, with increase in C_{in} from 1.85 × 10^{-4} to 5.5 × 10^{-3} mol/litre H_2O, a non-monotonic variation of d_p was observed: there was an initial decrease (from 212 to 167 nm) followed by a gradual increase (to 252 nm).[56] The behaviour was established in the polymerisation of ethyl acrylate (C_m = 1 M, T = 343 K):[24] with increase in C_{in} from 0.2 × 10^{-4} to 1.1 × 10^{-2} mol/litre H_2O, d_p initially fell from 430 to 416 nm and then increased monotonically to 510 nm. The number of surface charges increased under these conditions by a factor of 13. Since the ionic strength of the medium was not regulated,[24,56] the extremum in the dependence of the particle size on C_{in} can be explained by the salting-out effect of the neutral electrolytes with increase in C_{in}. At low values of C_{in}, an increase in the charge on the particles entails a diminution in their diameter, since there is no salting-out effect. The salting-out effect is manifested particularly strikingly in concentrated systems. Thus in the polymerisation of ethyl acrylate (3 M), when C_{in} is varied within the same limits (see above[24]), the maximum stability of the latexes during polymerisation and storage was attained for C_{in}(PPS) = 4.4 × 10^{-4} mol/litre H_2O.

The influence of potassium persulphate in the emulsifier-free copolymerisation of butyl acrylate with methyl methacrylate (T = 353 K) on the stability of the latexes, the ζ-potential of the

particles, the surface tension, and the electrical conductivity of dispersions at a concentration of 17–18% has been investigated.[58] It was shown that an increase in the potassium persulphate concentration from 1.18×10^{-3} to 5.9×10^{-3} mol/litre H_2O increases the ζ-potential, lowers the surface tension, and leads to a strong increase in the electrical conductivity, but has little effect on the stability and size of the particles. The inconsistency of these results with earlier data[56] can be associated, on the one hand, with the different chemical nature of the surface-active oligomers, which eliminated the salting-out effect of the neutral electrolytes and, on the other hand, with the higher polymerisation temperature.

An increase in temperature (increase in the rate of initiation) is important for the stability of the latexes. Thus an increase in the polymerisation temperature of ethyl acrylate (C_m = 3 M) from 343 to 359 K entailed an increase in the charge on the particles, a decrease in their size, and a sharp increase in the stability of the latex particles in the polymerisation process (a decrease in the coagulated component).[24] This result can be explained by the high rate of nucleation and stabilisation of the particles by the rapidly formed radicals. The same effect, associated with the increase in the rate of nucleation, occurs also when the potassium persulphate–sodium bisulphite–copper(II) oxidation-reduction system is used as the initiator (more disperse latexes with d_p = 170 nm compared with those obtained on initiation with potassium persulphate alone and having d_p = 600 nm are then formed).[59] The higher stability can also be explained by the increase in the rate of radical formation and in the rate of appearance of particles whose surfaces rapidly capture the primary and oligomeric radicals from the aqueous phase and are stabilised by the terminal SO_4^- groups of the macromolecules.

An increase in the potassium persulphate concentration from 4.8×10^{-5} to 2.2×10^{-3} M in the emulsifier-free polymerisation of ethyl acrylate (~30 vol.%) leads to an increase in the mechanical stability of the latexes;[25] the latter also increases with increasing process temperature. This has been explained by the increase in the concentration of the SO_4^- groups on the surfaces of the particles. However, latexes sufficiently resistant to mechanical influences could not be obtained by a further increase in C_{in} and T. In order to attain the desired effect, it is sufficient to achieve additional stabilisation, for example, as a result of the copolymerisation of the main monomer with a small fraction of an unsaturated acid.[25]

(c) The structural factor

The polarity of the polymer is known[60–62] to influence the stability of latexes synthesised in the presence of an emulsifier; however, the dependence of the stability of the emulsifier-free latexes on the nature of the polymer has not been examined. Evidently, the polarity of the polymer adjoining the aqueous phase is responsible for interfacial polar interactions,[63] which, by reducing the interfacial energy, influence the stability of the system as regards aggregation. A recent study of the emulsifier-free copolymerisation of methyl methacrylate and butyl acrylate, differing in their solubilities in the aqueous phase, established[64] that, with increase in the hydrophilicity of the polymer surface, estimated from the wetting angle θ_r (wetting by water) on the surfaces of latex films (modelling the surfaces of the particles), the stability of the dispersions during polymerisation increases and, conversely, diminishes as the surface becomes more hydrophobic. The hydrophilic-hydrophobic properties of the latex polymer were varied by varying its monomer composition. Under identical polymerisation conditions but for a lower concentration (or activity) of the intrinsic surfactant (i.e. for a higher value of σ), the latexes based on methyl methacrylate are more stable than those based on butyl acrylate, but their stability diminishes after the introduction of the butyl acrylate units into the polymer composition (Table 1). Since the ζ-potentials of the particles of poly(butyl acrylate) and poly(methyl methacrylate) latexes are approximately the same, −30 and −24 mV respectively, the observed difference between the stabilities of the latexes cannot be accounted for by electrostatic forces.

Table 1. Physicochemical properties of methyl methacrylate–butyl acrylate copolymers and of the films based on them.[64]

Monomer : H_2O	C_{in}^*, mg litre H_2O	C_m in latex, %	MMA : BA (by volume)	C_m in aqueous phase, %	Coagulated component, % (m_c)	r, nm	σ, mJ m^{-2}	pH	$10^3\chi$, Ω^{-1} cm^{-1}	θ_r, deg
20 : 80	180	18.6	1 : 0	1.5	0	166	68.2	3.27	0.69	63.0
			2 : 8	0.428	0.5	165	61.8	3.02	0.71	82.0
			0 : 1	0.16	2.0	135	54.4	3.17	0.67	84.5
30 : 70	270	27.7	1 : 0	1.5	1.5	185	68.5	3.01	0.54	72.5
			1 : 2	0.595	5.9	–	–	2.96	0.84	89.1
			0 : 1	0.16	15.9	153	57.3	2.88	0.92	89.0

* C_{in} per monomer was in all cases 810 mg litre^{-1}.

The dispersion components of poly(methyl methacrylate) and poly(butyl acrylate) should be similar, since their absorption spectra hardly differ (the Hanaker constants are in both cases in the range 4×10^{-21} to 1×10^{-20} J [65]). Thus the difference between the stabilities of the latexes cannot be explained by dispersion forces either. However, a correlation is observed between the stability of the latex and the hydrophobicity of the polymer (the angle for the wetting of the films by water). This suggests that the structural component of the stability plays a significant role in the stabilisation of the emulsifier-free latexes.[66,67] A theoretical calculation, carried out in order to achieve a semiquantitative test of this hypothesis, confirmed its validity.

If it is supposed that the mass of the precipitated coagulated components m_c is determined by the total number of particles N with a radius r falling into the nearest potential well per unit time, proportional to the number of collisions N, and the probability of overcoming the potential barrier V_{max},[68] then we have

$$m_c \sim Nr^3 \sim r^3 N_1 \exp(-V^{max}/kT) = n^2 \exp(-V^{max}/kT) r^3, \quad (7)$$

where n is the concentration of the particles. The ratio of the masses of the coagulated component in experiments i and l is given by

$$m_c/m_{c_l} = (n_i^2/n_l^2) \exp[-(V_i^{max} - V_l^{max})/kT]. \quad (8)$$

Eqn. (8), combined with the known expressions for the structural attraction of hydrophobic surfaces,[66,67,69] explains semiquantitatively the difference between the stabilities of the latexes presented in Table 1, provided that one attributes the change in the height of the potential barrier to the change in the structural component of the energy of attraction of the spherical particles. The latter can be formulated approximately[66,69] (for particles whose wetting angle is in the range 65–69°) as follows:

$$V_s^{max} = -k_a r \exp(-H^{max}/H_s), \quad (9)$$

where H_s is the scale length of the descent (the distance between the particles for which the energy of their interaction diminishes by a factor of e), H^{max} the distance corresponding to the potential barrier, and k_a the coefficient of structural energy which depends on the hydrophobicity of the particle. Fig. 6 shows that the values of k_a are in general correlated with the wetting angles, increasing in parallel with increase in the latter. It follows from the foregoing that the stability of the particles falls with increase in their wetting angle, which is correlated with the hydrophobic attraction forces and, conversely, increases with increase in the hydrophilicity of the surfaces of the particles, which is equivalent to an increase in the hydrophilicity of the polymer in the case of the emulsifier-free latexes. These data show that the monomeric composition of the emulsifier-free latexes influences their stability.

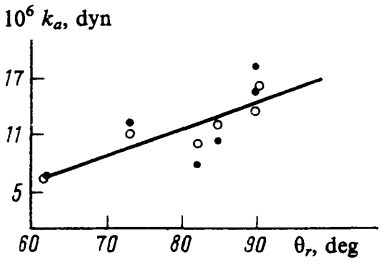


Figure 6. Dependence of the structural forces coefficients k_a on the wetting angle θ_r on the surfaces of polymers. Filled circles—calculation using Eqn. (8); open circles—calculation taking into account Eqn. (9).

3. Polymerisation kinetics

Comparison of the emulsifier-free and classical emulsion polymerisations[2] reveals significant differences between the kinetics of these processes.

Three stages are characteristic of emulsion polymerisation in the presence of an emulsifying agent: (1) a brief increase in the rate of polymerisation associated with the formation of the primary particles; (2) the constancy of the rate of polymerisation up to the disappearance of the monomer phase, which is associated with a constant concentration of the monomer and the radicals in small particles (on average 0.5 of a radical per particle); (3) the dependence of the rate on the balance between the decreasing C_m and the increasing concentration of the radicals in the particles (for the approximate mutual compensation of these factors, the rate continues to remain constant[70] until the process passes into the diffusion region).

The same stages are characteristic also of the emulsifier-free emulsion polymerisation, but their course and duration depend on the individual monomers, the recipe, and the polymerisation conditions.

A comparative dilatometric study of the kinetics of the polymerisation of ethyl acrylate (C_m = 1 M, C_{in} = 3.3 × 10^{-3} M, T = 318 K) in the absence and presence of the emulsifying agent E-30 (1.5% relative to the monomer) established that in the former case the rate at the beginning of the process is lower by more than an order of magnitude than in the latter case (Fig. 7).[71] However, with increase in the degree of conversion, it increases in the former case. Since the emulsifier-free latexes obtained were characterised under these conditions by a small particle diameter (~200 nm), the increase in rate during the polymerisation process was explained not by an increase in the number of radicals per particle but by the fact that in the absence of emulsifier the reaction takes place initially in the aqueous solution migrating into the polymeric-monomeric particles (PMP) as the polymer phase is formed: the rate of termination of the growing radicals diminishes sharply under these conditions, as a result of which the process is accelerated. The same explanation of the increase in the rate of the emulsifier-free polymerisation of styrene with increase in the degree of conversion has been put forward.[72] This idea has also been confirmed by the overall activation energy for the initial stage of the polymerisation of ethyl acrylate at T = 304–333 K: in the presence of an emulsifer, its value is 12.9 kcal mol^{-1}, which is characteristic of traditional emulsion polymerisation while in its absence it is 27.1 kcal mol^{-1},[72] which indicates polymerisation in solution.

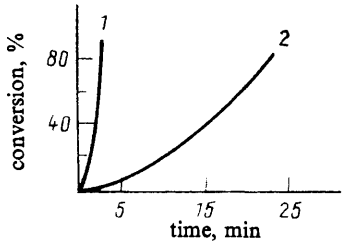


Figure 7. Kinetic curves for the polymerisation of ethyl acrylate in the presence of 1.5% of the E-30 emulsifier (curve *1*) and in its absence (curve *2*).[71]

The region where the rate of polymerisation increases may involve a variation in the surface tension of the system with an alternating sign (Fig. 8).[53] In the initial stages of the emulsifer-free copolymerisation of butyl methacrylate with dimethylaminoethyl methacrylate, the surface tension σ falls sharply due to the accumulation in the system of oligomeric surfactants as a result of the aqueous phase polymerisation. After the formation of the polymeric-monomeric particles, the surface-active oligomers are adsorbed by the polymer phase, which is accompanied by an increase in σ up to the equilibrium value. The duration of the formation of the surface-active oligomers depends on the solubility of the monomer, the initiator concentration, and temperature. For a low solubility of the monomer, a low initiator concentration, and a high rate of radical formation (high temperature), the nucleation is so rapid that this period cannot be detected on the kinetic curves (Fig. 9). This was observed in the polymerisation of methyl methacrylate (C_m = 1.5 M, C_{in} = 3.3 × 10^{-4} M, T = 348–353 K):[48] the process occurred at a constant rate virtually from the beginning and up to the exhaustion of the monomer phase (28% conversion). After this, a decrease in rate was observed, being particularly pronounced at advanced stages of the

reaction. The absence of a period with a low rate at the beginning of the process, in contrast to other data,[53,71] can be explained by the rapid migration of the process to the polymeric-monomeric particles formed, in which further polymerisation takes place. This is confirmed by the constancy of the number of particles ($\sim$°.5 × 10^{13} cm^{-3}), whose diameter increases (from 50 to °00 nm), and the high molecular weight ($\sim$1.4 × 10^6) of the polymer. The retardation of the polymerisation process in the final stages is associated with its transition to the diffusion region.

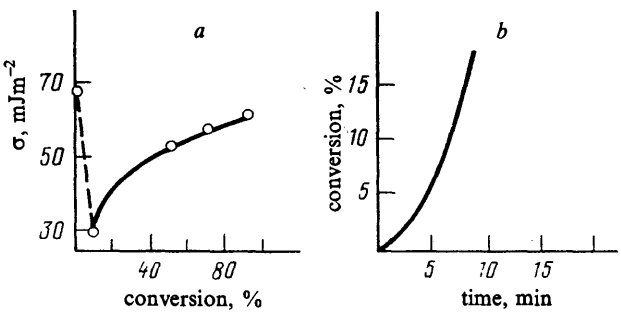


Figure 8. Variation of the surface tension of the system σ with conversion in the emulsifier-free copolymerisation of butyl methacrylate with dimethylaminoethyl methacrylate in the presence of potassium persulphate (*a*) (BMA : DMAEMA = 85 : 15, C_{in} = 7.4 × 10^{-3} mol/litre H_2O, T = 323 K, C_m = 2.5 M) and time variation of the conversion in the emulsifier-free copolymerisation of butyl methacrylate with dimethylaminoethyl methacrylate under the same conditions (*b*).[53]

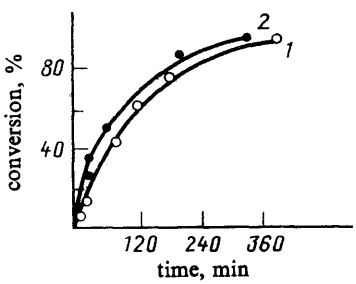


Figure 9. Kinetic curves of the polymerisation of methyl methacrylate in the presence of potassium persulphate (C_m = 1 M; 353 K):[48] *1*, C_{in} = 3.3 × 10^{-4} M; *2*, C_{in} = 6.6 × 10^{-4} M.

On formation of very large particles, the polymerisation kinetics are influenced by the accumulation of radicals within the bulk of the particles. Thus, in the analysis of the mechanism of the emulsifier-free polymerisation of methyl methacrylate, a theoretical calculation of the molecular weight of the polymer and of the rate of polymerisation was carried out on the assumption that the particle size is much greater than in the usual emulsion polymerisation;[73] the authors used the Stockmayer equation[74] to calculate the number of radicals as a function of the particle size taking into account the rates of diffusion and chain termination of the new radical within the particle. Calculation showed that the radical concentration in the particle can increase in the initial stages at a constant monomer concentration in the particle. The calculated and experimental data, obtained for the emulsifer-free polymerisation of methyl methacrylate (C_m = 1 M, C_{in} = 2.5 × 10^{-4}–4 × 10^{-3} M, T = 323 K), are compared in Fig. 10. The observed acceleration of the polymerisation (which is greater the higher the value of C_{in}) is attributed[73] to the accumulation of radicals in the particles.

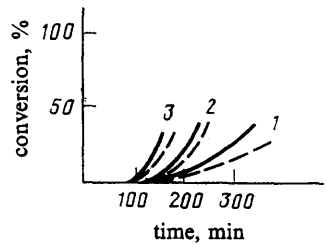


Figure 10. Experimental (continuous curves) and theoretical (dashed curve) time dependences of the conversion of the emulsifer-free polymerisation of methyl methacrylate in the presence of potassium persulphate (C_m = 1M, 323 K) for different concentrations of the latter 10^3 C_{in} (mol/litre H_2O): *1*, 0.25; *2*, 2.0; *3*, 4.0.[41]

(a) The influence of the hydrodynamic effect

It has been shown that the influence of stirring on the rate of the emulsifer-free polymerisation of methyl methacrylate (C_{in} = 1 × 10^{-3} mol/litre H_2O, T = 338 K) depends on C_m.[75] For C_m below saturation (10^{-1} M), the increase in the rate of rotation of the stirrer from 200 to 500 rev min^{-1} lowers the rate of the process slightly. In the presence of the monomer phase (C_m = 1 M), the rate decreases significantly following such a change in the rate of rotation. The number of particles and the molecular weight of the polymer are hardly altered in both cases when the rate of rotation is changed. It was concluded that the rate of transfer of the monomer from the drops to the aqueous phase (E_m), on which depends its concentration in the particles (M_p), is an important factor. (It is usually assumed the M_p retains its equilibrium value in the presence of drops[76]):

$$E_m = k_L A N_m (M_w^* - M_w), \qquad (10)$$

where k_L is the coefficient of the transfer of the monomer from the drop to the aqueous phase, A and N_m are the average specific surface of the drop and the number of drops per unit volume, and M_w^* and M_w are the saturation and non-stationary concentrations of the monomer in the aqueous phase. The relation between the parameters of Eqn. (10) and the rate E_m was analysed for different values of k_L. It was shown that a decrease in E_m entails a decrease in M_w and M_p. A slight decrease in M_p diminishes the degree of polymerisation, while an appreciable decrease leads to the reverse effect by virtue of the gel effect. The ratio $M_w/M_p = m$ depends on

the rate of rotation of the stirrer and is assumed to be constant for different degrees of conversion. An attempt was made to calculate theoretically the conversion–time curves for m ranging from 0.0231 to 0.329, which are values corresponding to rates of rotation of the stirrer from 200 to 400 rev min^{-1}. It was shown that the rate of polymerisation diminishes with increase in m.[76]

The influence of the rate of stirring on the kinetics of the emulsifier-free polymerisation of methyl methacrylate (C_m = 2.5 M, C_{in} = 10^{-3}–5 × 10^{-2} mol/litre H_2O, T = 333 K) has been investigated[77] with the rate of rotation of the stirrer varied within wide limits (from 0 to 960 rev min^{-1}). It was shown that the initial rate of the process passes through a maximum at 360 rev min^{-1}. The authors explained the increase in the initial rate of the process for low rates of rotation by the decrease in the drop size and hence by the acceleration of the transport of the monomer from the drop to the aqueous phase, where initiation and chain propagation takes place initially. The decrease in the rate of polymerisation after the attainment of the rate of stirring indicated is explained by the capture of the particles formed by the monomer drops or microdrops, which leads to the suppression of the gel effect. The latter is confirmed by the fact that the extremum in the initial rate is smoothed out with increase in C_{in} (from 5 × 10^{-3} to 10^{-2} mol/litre H_2O) as a result of its salting-out effect on the monomer drops.

(b) The influence of the solid phase

The emulsifer-free polymerisation of vinyl and diene monomers in the presence of organic and inorganic powders of different kinds has been described in a number of studies.[75,76,78–85] Powders encapsulated in the polymer and reinforced composites with a uniform distribution of the filler in the matrix are then obtained. In the polymerisation of methyl methacrylate, calcium sulphite,[75,76,78] barium sulphate,[85] graphite,[79,84] various metal oxides,[81–83] and aluminium and copper[80,82] powders were employed.

The emulsifier-free polymerisation of methyl methacrylate at a $CaSO_3$ concentration below and above the limit of its solubility (3 × 10^{-4} M), i.e. in the absence and presence of a solid phase, has been investigated.[75] In the first case, the kinetic curves for the polymerisation of methyl methacrylate have the same shape as those for the emulsifier-free polymerisation of pure methyl methacrylate (Fig. 11);[73] an increase in the $CaSO_3$ concentration entails an increase in the rate of polymerisation. The authors explained the latter by the promoting effect of calcium sulphite on the persulphate initiation reaction. Furthermore, $CaSO_3$ can itself exert an initiating effect on the polymerisation process.

In the presence of solid $CaSO_3$, the rate initially diminishes, increasing with increase in the calcium sulphite concentration (Fig. 12). This is accompanied by a change in the nature of the kinetic curves (cf. Fig. 10) whose shape becomes closer to that of the kinetic curve for emulsion polymerisation in the presence of an emulsifying agent. The initial retardation of the process can be attributed to the distribution of the monomer and initiator between the aqueous and solid phases.

It has been shown that the aqueous phase of latexes contains only a small amount of polymer particles, whose size is comparable to the size d_p in emulsion polymerisation in the presence of an emulsifier. This permits the assumption that the primary particles are adsorbed on the surface of the powder, which is apparently the main polymer formation region. It is known that the size of the polymethacrylate particles and their monomer content in the usual emulsion polymerisation are determined thermodynamically by the particle–water interfacial energy (σ_{12}).[86] This was also established in a later study of the polymerisation of methyl methacrylate.[87] After the adsorption of the polymethacrylate particles by the surface of the solid phase, the particles were in contact not only with the aqueous medium but also with the surface of the powder, i.e. σ_{12} and the overall area of the interface change, which influences the particle size and the content of the monomer in the particles, these being reflected in the rate of polymerisation. It has been shown[76] that on a solid surface there are two varieties of polymers, one of which is readily removed while the other is virtually inseparable from the powder even after prolonged extraction. It has been suggested that the latter variety is firmly bound to the surface via the electrostatic interaction between the latter and the terminal ionic groups of the macromolecules forming the nuclei of the particles directly on the surface; with increase in surface area, the number of particles also increases, as a result of which the process is accelerated. Another nucleation process takes place in the aqueous phase, whereupon the nuclei formed are adsorbed by the solid surface when they continue to grow.

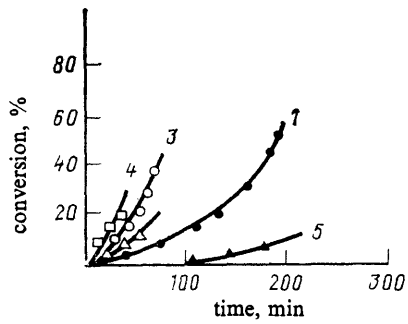


Figure 11. Kinetic curves for the emulsifier-free polymerisation of methyl methacrylate in the presence of potassium persulphate (C_{in} = 4 × 10^{-3} mol/litre H_2O) (curves *1*–*4*) and different calcium sulphite concentrations ($10^4 C_{CaSO_3}$, mol/litre H_2O) [*1*, 0; *2*, 1.34; *3*, 2.28; *4*, 3.44] and without potassium persulphate but in the presence of $CaSO_3$ at a concentration of 2.28 × 10^{-4} M (curve *5*). T = 323 K; C_m = 1 M.[73]

Thus the introduction of a highly disperse solid phase into the system alters its physicochemical characteristics and influences the process kinetics. In the emulsifier-free polymerisation of methyl methacrylate initiated by potassium persulphate (C_m = 0.5 M, T = 333 K) the presence of the inert $BaSO_4$ powder, which is almost insoluble in water, is reflected in the rate of polymerisation.[85]

The chemical nature of the solid surface influences the polymerisation process via the possible heterogeneous interactions with the reaction components.[75] Thus a relation between the chemistry of the surface and the crystallinity of the structure of the filler (highly disperse pyrophyllite and kaolinite powders) has been traced in the polymerisation in the aqueous phase of butyl methacrylate initiated by azobisisobutyrohydrazide in the course of the elementary polymerisation reactions—initiation and termination. With increase in the specific surfaces of these powders (up to 60 m^2 $litre^{-1}$ for pyrophyllite and up to 240 m^2 $litre^{-1}$ for kaolinite), the rate of polymerisation rises sharply.[88]

(c) The influence of the surface activity of the initiator

A number of studies on emulsion polymerisation in the presence of initiators exhibits a stabilising effect by virtue of the diphilic structure of their molecules have been published recently.[58,89–96] Although the polymerisation in such systems cannot be rigorously defined as emulsifier-free polymerisation, nevertheless under the conditions of a high degree of involvement of the surface-active initiator in the reaction one may expect the formation of latexes which virtually contain no free emulsifier and which are in this sense close to emulsifier-free latexes.

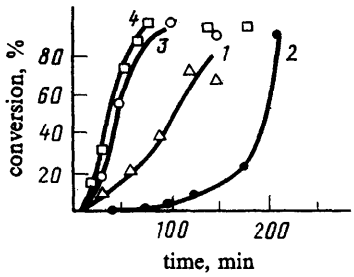


Figure 12. Kinetic curves for the emulsifier-free polymerisation of methyl methacrylate in the presence of potassium persulphate (C_{in} = 4 × 10^{-3} mol/litre H_2O) and a solid phase [$10^4 C_{CaSO_3}$ (mol/litre H_2O) *1*, 0; *2*, 0.1; *3*, 0.25; *4*, 0.57] at T = 323 K and C_m = 1 M.[73]

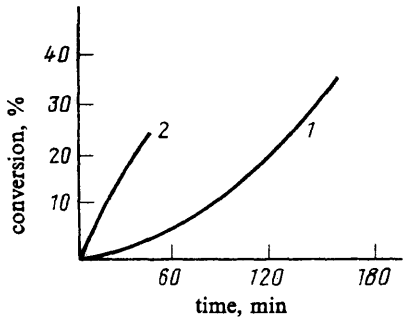


Figure 13. Kinetic curves for the polymerisation of methyl methacrylate in the presence of potassium persulphate (curve *1*) and the PAAI initiator (curve *2*). C_{in} = 6.58 × 10^{-4} mol/litre H_2O; T = 353 K; C_m = 2.4 M.[58]

Surface-active initiators contain in their molecules peroxide[90–94] and azo-groups,[58,95,96] which are typical for radical polymerisation initiators; the surface activity is imparted to the molecules of these compounds by fragments which usually represent residues of a poly(hydroxyethylated) alcohol or poly(ethylene glycol).

A series of studies, surveyed in two reviews,[91,93] have been devoted to the topochemistry and mechanism of the emulsion polymerisation of styrene in the presence of surface-active peroxides. It was shown that the rate constant for the decomposition of the micelle-forming peroxide k_d exceeds appreciably the rate constant for the decomposition of its non-micelle forming analogue, which is evidence that micellar catalysis has an effect. However, the efficiency of the initiation by surface-active peroxides is very low in view of the localisation of the rapidly formed radicals in a small volume in the reaction zone—adsorption layers; thus the overall effect of surface-active peroxides on the rate of initiation may be small.

We carried out a comparative study[58] of the characteristics of the emulsifier-free polymerisation of methyl methacrylate initiated by potassium persulphate and a sulphated poly(ethylene glycol)-azo-initiator (PAAI)[95] having a molecular weight of 780 and exhibiting surface activity. The polymerisation kinetics were investigated in the presence of equimolar concentrations of both initiators at C_{in} = 6.58 × 10^{-4} M (this value is lower than the critical micelle formation concentration for PAAI), which ruled out the micellar effect. It is seen from the kinetic curves (Fig. 13) that the initial rate of the process initiated by PAAI is higher than that of the process initiated by potassium persulphate. The efficiency of the initiation by both initiators was assumed close to unity, since they decompose in aqueous solutions into radical-ions bearing like (negative) charges; the cage effect is unlikely.[73] It follows from the calculated rate constants for the decomposition of potassium persulphate and the azo-initiator[24,58,97] that the observed difference between the initial rates of polymerisation (by a factor of 2.2) is associated not only with the different rates of initiation (difference by a factor of 1.5) but also with the difference between the mechanisms of nucleation and between the stabilising capacities of both initiators. The disposition of the peaks on the chromatograms of the molecular weight distribution (MWD) of the polymers isolated from the latexes (Fig. 14) shows that, for identical initiator and monomer concentrations, the molecular weight is higher and the distribution narrower in the case of polymers synthesised in the presence of PAAI compared with those synthesised in the presence of potassium persulphate. This indicates a greater contribution of the polymerisation in the rapidly stabilised polymethacrylate particles in the case of initiation by PAAI and a greater contribution of polymerisation in the aqueous solution on initiation by potassium persulphate. Electron miscroscope study of the latexes obtained using both initiators showed that the particle size in the case of PAAI initiation is smaller than that for initiation with potassium persulphate. The difference between the particle sizes and hence between the number of particles may be attributed to the different rates of nucleation; in both cases, the process begins in the aqueous solution with formation of the $SO_4^-[M]_n^\cdot$ and $PAAI[M]_m^\cdot$ radical species; in view of the decrease in the solubility of the high-molecular-weight azo-initiator following the addition of one or several monomeric methyl methacrylate units, the critical micelle formation concentration for the adducts diminishes rapidly, which leads to a high rate of formation of micelles, which become the predominant polymerisation zone. In order to impart surface activity to the $SO_4^-[M]_n^\cdot$ radical species, it is necessary to add to them a large number of monomer units (CMC = 1.4 wt.%),[45] which lengthens the period of polymerisation in the aqueous phase and lowers the rate of nucleation.

4. Emulsifier-free latexes on film forming systems

Film-forming emulsifier-free latexes must satisfy a series of specific conditions, which are sometimes difficult to fulfil, in order to obtain high-quality glues and adhesives from them. Thus the polymers based on such emulsifier-free latexes must be characterised

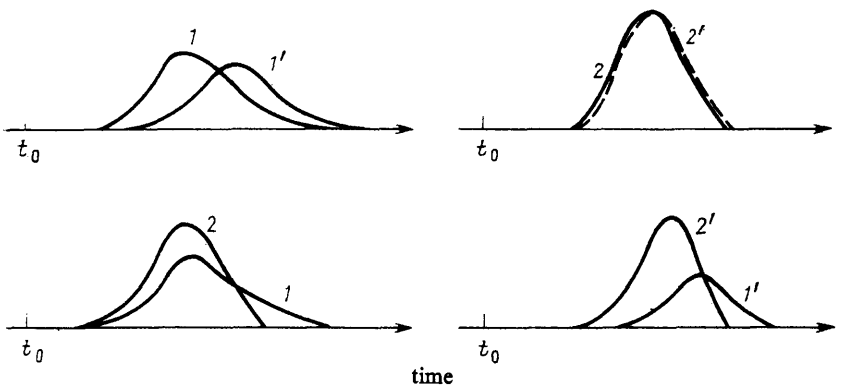


Figure 14. Gel-chromatographic curves for the molecular weight distribution of PMMA synthesised in the presence of potassium persulphate (curves *1* and *1'*) and the PAAI initiator (curves *2'* and *2'*). C_{in} = 3.29 × 10^{-4} M (curves *1* and *2*) and 6.58 × 10^{-4} M (curves *1'* and *2'*); T = 353 K; C_m = 1.0 M (curves *1* and *2*) and 2.4 M curves *1'* and *2'*).[58]

by the necessary elasticity (T_s) and hence by a minimal film formation temperature, a high resistance to water, and effective adhesion and dielectric properties. The latexes must be resistant to various influences, for example, mechanical influences, freezing, etc. When monomers, such as the widely employed alkyl methacrylates and acrylates, are used to obtain the traditional latexes, the problem of sedimentation stability arises (the density of PMA, PEA, PBA, and PMMA are respectively 1.23, 1.15, 1.06, and 1.19 [98]).

Alkyl methacrylates and acrylates as well as their copolymers having a fairly low T_s, namely ethyl acrylate[24,25,59] and the methyl methacrylate–butyl acrylate copolyer,[58] have been mainly used as monomers for film-forming emulsifier-free latexes

In the study of the resistance of the emulsifier-free latexes to mechanism influences, sedimentation, and freezing, it has been shown[25] that stabilisation solely by the initiator (the terminal ionised groups of the macromolecules) is insufficient and that additional hydration of the surface is necessary, for example, by introducing surface carboxy-groups into the particles. In the case of the ethyl acrylate latex, this is achieved either by the hydrolysis of ester groups by the sulphuric acid formed on decomposition of potassium persulphate[99] or by the copolymerisation of ethyl acrylate with the necessary amount (5 mol%) of acrylic acid (AA). The concentration of carboxy-groups on the surface of the particles formed as a result of the acid hydrolysis (heating at 348 K for 30 h) is only 0.13 mol%. An important factor in impairing stability to the latex is not the content of these groups in the copolymer itself but their location on the surface, i.e. the structure of the particles. It is known[100,101] that, in the copolymerisation of ethyl acrylate with acrylic acid, the carboxy-groups are distributed over the entire surface layer of the particle but the fraction of the groups localised directly on this surface is then very low, while in the case of hydrolysis the chemically bound carboxy-groups are directly on the surfaces of the particles.[102]

It has been shown[58] that the main sedimentation stability of the acrylate latexes obtained using PAAI as the initiator is ensured by the introduction into the surface layer of the particles of highly hydrated groups (polyoxyethylene) which apparently induce an increase in the local viscosity of the hydrated surface layers.

An important criterion of the quality of the film forming emulsifier-free latexes is the adhesion and water resistance of the film. The studies carried out on these lines[7] indicate that the effective adhesion properties of such films, is apparently associated with the absence of an emulsifier, which is deposited at the interface between the polymer and the support.

The water resistance of such polymers is due to the content in the latex of neutral electrolytes and other water-soluble substances, which is in its turn determined by the conditions in the synthesis of the emulsifier-free latex. This can be traced clearly on the basis of the curves for the water absorption by the films (Fig. 15) obtained from methyl methacrylate–butyl acrylate latexes;[58] the water absorption is greater the higher the concentration of the initiator employed in the preparation of the latex. Thus the absorption of water after 90 days by films obtained from a latex synthesised in the presence of potassium persulphate ($C_{in} \simeq 12 \times 10^{-4}$ mol/litre H_2O) is 4% and increases to 70% for films from a latex synthesised in the presence of $C_{in} \simeq 6 \times 10^{-3}$ M. The same rule holds also for ethyl acrylate latexes;[24,25] at a constant potassium persulphate concentration and with increase in polymerisation temperature, the degree of absorption of water diminishes, which is apparently associated with the increase in the fraction of potassium persulphate consumed in nucleation and with the decrease in its fraction involved in the formation of surface-active oligomers and electrolysis.

An increase in the concentration of PAAI (by a factor of 5) in the synthesis of latexes, accompanied by its accumulation in the dispersion medium, leads to an increase in the water absorption by the films from 3 to 25%.

Latex films are known to be bleached when they are immersed in water as a consequence of the diffusion of water molecules into the interparticle boundary region;[103] this effect occurs also for films of emulsifier-free latexes despite the low water absorption.[58]

Summarising the data presented, one may conclude that, in order to obtain film-forming emulsifier-free latexes with the required properties, one must employ in their synthesis factors which increase their stability as regards the state of aggregation, on the one hand, and factors promoting the suppression of the formation of electrolytes and other water-soluble substances, on the other. One of the conditions for the optimisation of the process is a decrease in the initiator concentration to the minimum necessary value with the simultaneous increase in the rate of radical formation by increasing the temperature or by using oxidation-reduction systems. Since the

ionisation of the surface of the particles involving solely the ionisable SO_4^- groups is insufficient to impart to concentrated latexes the necessary sedimentation stability and resistance to mechanical influences and freezing, their additional stabilisation as a result of the hydration of the surface of the particles, for example, by introducing carboxy-groups or polyoxyethylene units into the latter, is necessary.

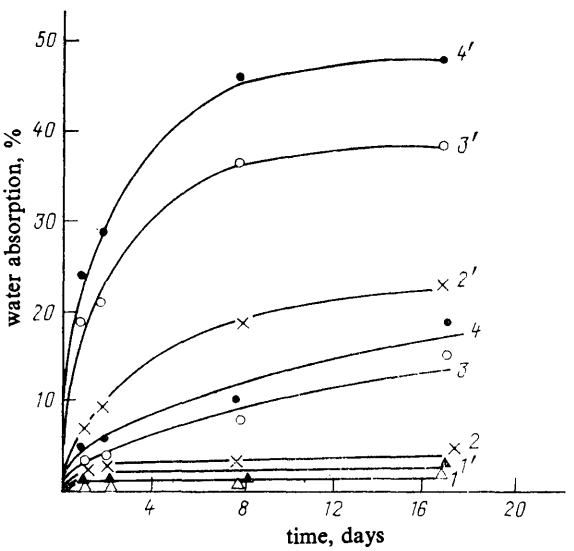


Figure 15. Kinetic curves for the absorption of water by films of methyl methacrylate–butyl acrylate latexes synthesised for equalised rates of decomposition [$10^9 V_d$ (mol litre^{-1} s^{-1}): *1* and *1'*, 0.82; *2* and *2'*, 1.64; *3* and *3'*, 3.28; *4* and *4'*, 4.10] at T = 353 K and C_m = 1.9 M in the presence of PAAI [$10^4 C_{in}$ (mol/litre H_2O): *1*, 8; *2*, 16; *3*, 32; *4*, 40] and potassium persulphate [$10^4 C_{in}$ (mol/litre H_2O): *1'*, 11.8; *2'*, 23.6; *3'*, 57.2; *4'*, 59.0].[58]

III. Polymerisation of non-polar monomers in the absence of an emulsifying agent

1. Mechanism of the nucleation and growth of particles

As already mentioned above, the mechanism of nucleation in the emulsifier-free polymerisation of polar monomers depends significantly on the nature of the monomers and the process parameters. This also applies to the emulsifier-free polymerisation of hydrophobic monomers, but their low solubility in water leads to significant differences in the process.

A study[104] of the emulsifier-free polymerisation of styrene (C_m = 0.87, C_{in} = 10^{-3} M, T = 343 K) showed that a large number of primary particles (5 × 10^{12} ml^{-1}) are formed initially. They are flocculated until the attainment of a constant number (10^{11}–10^{12} ml^{-1}). It has been established by gel chromatography that the molecular weight in the primary polymer particles is approximately 10^3 with a small content of the polymer having a molecular weight of $\sim 10^6$. The oligomer is present also in the finished latex. This permitted the assumption that nucleation takes place via micelles incorporating the surface-active oligomers formed as a result of the recombination of short-chain free radicals. The micelles formed absorb the monomers from the aqueous phase, after which the process migrates to the polymethacrylate particles. The question how the particles grow and are stabilised in the subsequent course of the polymerisation remains unelucidated.

The nucleation of the particles in the polymerisation of styrene initiated by potassium persulphate has been studied from the light scattering intensity and by photocorrelation spectroscopy at 333 K.[105] Three stages were observed in the light scattering intensity as a function of time: in the first stage, it remained unaltered, in the second it increased very rapidly (which could be explained by the formation of aggregates but not by the growth of particles or the absorption of the monomer by the latter), while in the third it increased slowly. Electron microscope data and granulometric analysis showed that in the initial stages the number of particles diminishes rapidly and then remains constant. The flocculation of the particles in the initial stage was not attributed[104] to their stability (in contrast to the study[39] of the polymerisation of methyl methacrylate). It is assumed that the "micelles", formed from the products of the recombination of soluble radicals with n = 2–4, are stable, but, as macromolecules having a high molecular weight accumulate in them, the nuclei lose their stability, since this entails a decrease in the concentration of charged groups on the surfaces of the growing particles. Theoretical calculation of the charge density on the nuclei of polystyrene particles after the introduction into the latter of polymers having different molecular weights, carried out on the assumption that the nuclei consist of 100 chains having a molecular weight of 10^3, that the macromolecules are formed as a result of the recombination of the radicals growing in the particles, and that their terminal SO_4^- groups are located on the surface, showed that the macromolecules with a molecular weight of 10^4–10^6 initially induce (before the attainment of d = 30 nm) a decrease in the charge (the particles flocculate) and then its increase—which is greater the higher the molecular weight of the added macromolecules; for a molecular weight of 10^6, the charge remains constant until the attainment of d = 126 nm (the number of the particles remains constant).[105] This calculation was performed for an ideal system without taking into account the real conditions, in particular, the ionic strength of the aqueous phase, which depends on the initiator concentration.

Among the three possible mechanisms of the nucleation of particles, namely association of surface-active radicals with formation of micelles, the adsorption of radicals on monomer drops, and the recombination (or growth) of radicals with formation of colloidally unstable macromolecules (RSO_4^-), preference is nevertheless given to the last mechanism.[106] In view of the colloidal instability of the insoluble macromolecules, they undergo association. The particles formed immediately absorb the monomer, and, in view of the low content of the chains, they have a low surface charge, as a result of which they rapidly flocculate; flocculation continues until the attainment of the surface charge density and particle radius necessary for their colloidal stability. The rate of flocculation is

$$W_f = -[dN/dt]_f = k_0 N^2/F,$$

where k_0 is the rate constant for the diffusion controlling flocculation and F is the Fuchs stability factor.[107] In order to achieve a qualitative understanding of the relevant questions, namely what is the size of the particles when the latter become stable, what is their charge under these conditions, and how many polymer chains are contained in the particle, a number of assumptions have been

made:[106] the particles are spherical, all the molecules have the same molecular weight (M_c), and each has two terminal (charged) groups located on the surfaces of the particles. Calculations of the stability of the hydrophobic sols carried out on the basis of the assumptions made, taking into account the ionic strength of the aqueous phase, make it possible to assume that

$$N_c = 4\pi r^3 \rho_L N_A / 3M_c = M_L / M_c,$$

where N_A is the Avogadro number, N_c the number of chains in the particle when its molecular weight is M_L, r the radius, and ρ_L the density. The number of charges on the end groups of the particle is

$$N_e = 2N_c = \frac{8\pi r^3 \rho_L N_A}{3M_c},$$

and the charge density

$$\sigma_s = \frac{N_e e}{4\pi r^2} = \frac{2\rho_L e N_A r}{3M_c}$$

is directly proportional to the particle radius. Assuming that $M_c = 1.5 \times 10^5$ (the usual value for the emulsifier-free polymerisation of styrene), it is possible to calculate σ_s for different values of r. The surface potential is[108]

$$\psi_s = \frac{4\pi r \sigma_s}{\varepsilon (1 + k_z)},$$

where ε is the dielectric constant of the medium and $k_z = 3.4 \times 10^7 I^{1/2}$ is the reciprocal of the thickness of the diffuse electrical double layer (I is the ionic strength). Next, plots of $\lg F$ against r (5–20 nm) were constructed for different ionic strengths I of the system (4.24×10^{-4}, 9.33×10^{-4} and 4.0×10^{-3}) on the basis of the values of ψ_s obtained, the Fuchs stability factor, and the Deryagin–Landau–Verley–Overbeek (DVLO) stability theory.[40,109,110] Assuming that the latexes are stable when only 1% of the particles flocculate after 1 h, it is easy to show that $\lg F = 6.26$. Hence it follows from the dependence of $\lg F$ on r obtained at different ionic strengths I that a sufficient stability of the particles is attained at the given ionic strength of the aqueous phase for a specific particle radius. Thus the particle size and hence the concentration of particles can be controlled by the ionic strength, which indicates, in its turn, the importance of the stage involving the flocculation of the primary particles for the final value of the radius obtained.

An empirical equation for the dependence of the particle size of the styrene latex on the parameters C_m, C_{in}, T, and I has been derived:[111]

$$\lg d = 0.238 \lg I + 0.41 \lg[M] - 0.238 \lg[PPS] + 1173T^{-1} - 0.827.$$

It has been shown[13] that, in the emulsifier-free polymerisation of styrene initiated by potassium persulphate, the size of the particles of the final latexes depends on the ionic strength of the aqueous phase, temperature, and the monomer and initiator concentrations. For the given $I = 2.22 \times 10^{-2}$ and $C_m = 0.87$ M, the particle diameter varies from 967 to 643 nm when the temperature is raised from 328 to 363 K. At the same monomer concentration and ionic strength $I = 11.3 \times 10^{-3}$, the particle diameter diminishes from 864 to 526 nm with increase in C_{in} from 0.34×10^{-3} to 2.76×10^{-3} mol/litre H_2O (the molecular weight increases from 1.41×10^5 to 5.46×10^5 with increase in the particle diameter). At $I = 1.92 \times 10^{-2}$ and $C_{in} = 2.76 \times 10^{-3}$ mol/litre H_2O, an increase in C_m from 2.2×10^{-3} to 8.71×10^{-1} M leads to an increase in d_p from 40 to 643 nm.

Monodisperse 10% polystyrene latexes with d_p ranging from 141 to 967 nm have been obtained.[13] An increase in temperature leads to more highly disperse latexes, while the application of seeded polymerisation leads to latexes with particles whose diameters are in excess of 4 μm. The hydrodynamic polymerisation conditions are important for the reproducibility of the results: the rate of stirring must ensure a sufficiently high dispersity of the monomer drops in order to maintain the saturation of the aqueous phase by the latter.

The presence on the surfaces of the particles of both sulphate and carboxy-groups has been established by the conductimetric titration method for styrene emulsifier-free latexes.[112] A large number of hydroxy-groups have also been detected. These evidently appear as a result of the tendency of the sulphate groups to hydrolyse; the oxidation of the hydroxyls leads to the formation of carboxy-groups:

$$RCH_2SO_4^- \rightarrow RCH_2OH \rightarrow RCOOH.$$

All these groups participate in the stabilisation of the particles mainly via the electrostatic factor (SO_4^- as well as COOH and OH). The structural factor is also important. The stability of the latexes obtained using potassium persulphate is sufficiently only for relatively dilute (10%) sols. This is associated with the insufficient content of ionised and hydrophilic groups on the surface of the particles. Thus, according to Goodwin et al.,[13] the surface area of the particles per SO_4^- and COOH groups varies (depending on the method of preparation of the latex) from 700 to 2000 Å and from 218 to 700 Å^2 respectively, which apparently does not ensure the stability of concentrated sols of the highly hydrophobic polymer. The degree of saturation of the emulsifier of the usual styrene and the styrene–butadiene latexes is known to be higher than 50%, which corresponds to an absorption area of the anionic emulsifier molecule of ~100 Å^2. The low degree of saturation of the particles of styrene emulsifier-free latexes by the end groups can be attributed to the very low solubility of the monomer in the aqueous phase, where initiation and nucleation take place.

2. Principles governing the increase in stability

A general principle governing the increase in the stability of emulsifier-free latexes obtained using initiation by persulphate is an increase in the charge and degree of hydration of the surfaces of the particles. The methods used for this purpose reduce to an increase in the solubility of the monomer in the dispersion medium, copolymerisation with monomeric acids[113–125] and their amides,[126,127] or the addition to the aqueous phase of an organic solvent.[128–130] The increase in the solubility of the monomer induces an increase in the fraction of the initiator consumed in initiation and the acceleration of the process, on the one hand, and an increase in the concentration of the surface SO_4^- groups as well as surface-active oligomers, on the other. This lyophilises the surfaces of the particles, reduces the hydrophobic interaction factor, and hence increases the resistance of the latex to aggregation.

(a) Copolymerisation with unsaturated acids

The copolymerisation of hydrophobic monomers with monomeric acids in emulsifier-free systems induces the acceleration of the process and leads to additional stabilisation via the carboxy-groups. Depending on the degree of hydrophilicity of the acid and its distribution between the monomeric and aqueous phases, the rate of the process and the location of the carboxy-groups differ greatly. Thus, in the copolymerisation of styrene with 2.4 mol% of acrylic acid, methacrylic acid (MAA), and itaconic acid (IC), methacrylic acid increases the initial rate to the greatest extent, while

itaconic acid is least effective (Fig. 16).[113] The observed difference is associated with the topochemical characteristics of the process: although in all cases polymerisation begins in the aqueous phase with formation of highly carboxylated oligomers, for the more hydrophobic methacrylic acid nucleation takes place at a higher rate and polymerisation migrates more rapidly into the particles, which accelerates the process. On the other hand, in the case of acrylic and itaconic acids, which are more soluble in water, the nucleation of the more hydrophilic oligomer is slower, which diminishes the overall rate of the process. It is striking that, in the course of the copolymerisation of styrene and with acrylic and itaconic acid, where the process migrates to highly hydrophilised particles, its rate not only attains but also exceeds the rate of copolymerisation of styrene with methacrylic acid, which takes place more uniformly (Fig. 16).

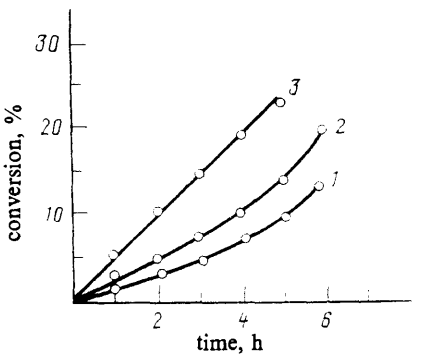


Figure 16. Kinetic curves for the emulsifier-free polymerisation in the presence of equimolar amounts (2.4 mol%) of acrylic (curve *1*), itaconic (curve *2*), and methacrylic (curve *3*) acids as well as potassium persulphate (3.7×10^{-4} mol/litre H_2O) at 343 K.[113]

Only the carboxy-groups localised on the surfaces of the particles are important for the stability of carboxylated emulsifier-free latexes (see above). It has been established that, in the emulsifier-free copolymerisation of ethyl acrylate[114] and styrene[115,116] with methacrylic and acrylic acids, the latter tends to concentrate in the surface region of the particles while the more hydrophobic methacrylic acid tends to be distributed throughout their bulk. The copolymerisation with the most hydrophilic itaconic acid leads to its preferential homopolymerisation in the aqueous phase.[117]

In terms of their influence on the resistance to electrolytes and the mechanical stability of highly concentrated butadiene–styrene latexes, dibasic acids [maleic, fumaric (FA), and itaconic acids] are significantly superior to monobasic acids (methacrylic and acrylic acids).[119]

Thus the individual characteristics of the acids are important for the stability of the latex.

In order to achieve the maximum fixation on the surface of the particles of the carboxy-groups of the acids, which ensure the formation of stable highly concentrated styrene–butadiene emulsifier-free latexes, the method of seeded polymerisation with variation of the pH of the medium during synthesis was employed.[118] In the first stage, carried out at a low pH, all the ingredients (including the acid) are introduced but only a proportion of the principal monomers are added in order to obtain a stable system at a reduced concentration. With increase in the pH of the seeding latex, the carboxy-groups introduced into the polymer ionise; the highly charged particles obtained in this process constitute the region of the subsequent polymerisation of the monomers introduced in the second stage. The high hydrophilicity of the carboxylate anions induces their localisation on the surfaces of the particles adjoining the aqueous phase, which imparts adequate stability to the final latexes. After the introduction of 2 wt.% of itaconic acid and an increase in the pH in the first and second stages from 2.5 to 9.5, a polydisperse 40% latex with $d_p = 50-130$ nm is obtained.

In order to compare the stabilities of styrene–butadiene copolymer latexes containing 4 mol% of methacrylic and acrylic acids (the partition coefficients between styrene and water are respectively 1.94 and 0.175 [120]), latexes with a 50% concentration were obtained; however, only in the copolymerisation with acrylic acid do they possess the necessary mechanical stability, which is associated with the high concentration of surface carboxy-groups.

The migration of the carboxy-groups in the particles is influenced by the mobility of the segments of the macromolecules. This has been observed[121] in the alkaline and subsequently acid treatments of the styrene–butyl acrylate–methacrylic acid terpolymer latexes (T_s = 343 K) during their heating. The number of surface COOH groups (A_s) was determined by conductimetric titration. It was shown that A_s increases as a result of heating the latexes at pH 10 to a greater extent the higher the temperature (293–343 K) and the more prolonged the heating process (1–3 h). The concentration of the acrylic acid dissolved in the aqueous phase changes very little under these conditions. On the other hand, as a result of the subsequent heating of the latexes at pH 3, A_s diminishes to a greater extent the higher the temperature and the longer the heating process. The observed changes are associated with the tendency of the ionised carboxy-groups to migrate to the interface with the aqueous phase; on their deionisation (neutralisation) and on decrease in the degree of hydration, the carboxyl-containing segments tend to return to the bulk of the particles.[121]

The influence of the degree of ionisation of acrylic and fumaric acids on the stability of 50% styrene latexes has been investigated.[122,123] The emulsifier-free polymerisation was carried out in the presence of a small amount (0.05 wt.%) of sodium dodecyl sulphate. The degree of neutralisation of the acid groups was regulated by adding $NaHCO_3$. It was shown that the degree of neutralisation, which influences the solubility of the oligomeric radicals formed in the aqueous phase, is very important for the rate of the process, the particle size, and the stability of the latex. The degree of neutralisation optimal for the stability of the latexes is 0.89–0.87, which corresponds to the highest concentration of the surface COOH groups; under these conditions, the area of the particle surface corresponding to each COOH group is 16–19 Å^2. For a degree of neutralisation of 0.85, the maximum rate is observed apparently as a consequence of the maximum degree of hydration of the surface and the smallest interfacial surface, which is the reason for the maximum concentration of the monomer in the particles.[86] With increase in the acrylic acid concentration from 0.5 to 5 wt.%, the rate of the process increases and the particle size diminishes.

The frost resistance of the carboxyl-containing styrene–isoprene emulsifier-free latexes also depends on the density of the distribution of the COOH groups on the surfaces of the particles and on the degree of their neutralisation.[127] Frost resistance is achieved if the

area per COOH group is 30–60 Å^2. The resistance of carboxyl-containing polystyrene latexes to electrolytes obeys the theory of the stability of hydrophobic sols[110,111] according to Sakota and Okayo.[125]

(b) Copolymerisation with acid amides and their derivatives

The use of the amides of acrylic and methacrylic acids as comonomers for the synthesis of stable emulsifier-free latexes is based on the increase in the hydrophilicity of the oligomeric radicals growing in the aqueous phase and on the involvement under these conditions of a greater proportion of the persulphate SO_4^- groups participating in the stabilisation process. The capacity of the NH_2 groups for the formation of strong hydrogen bonds with water increases not only the stability but also the viscosity of the sols formed.

The emulsifier-free copolymerisation of butadiene and styrene with the amide (AMA) and hydroxymethylamide (HMAMA) of acrylic acid (2 wt.%) in 50% systems with a high ammonium persulphate concentration (0.5–1.25 mol% H_2O) has been investigated.[115] In two-stage polymerisation (T = 353 K) and with the introduction of the functional comonomer only in the second stage (into the seeding 25% latex), electrolyte-resistant ($CaCl_2$) latexes are formed. In the case of the hydroxymethylamide of acrylic acid, a high resistance to mechanical influences is also achieved apparently as a consequence of the more effective interaction of the hydroxymethylamide groups with water.

The emulsifer-free copolymerisation of styrene with 0.1–0.5 parts of acrylamide by weight at pH 9 (C_{in} = 5 × 10^{-3} M, T = 343 K, phase rate 20:150) can be divided into three stages depending on the topochemistry of the process;[126] (1) copolymerisation in the aqueous phase with formation of oligomers which are rapidly rendered hydrophobic and are nucleated; (2) polymerisation of styrene in the particles formed until its almost complete exhaustion; (3) continuation of the copolymerisation of acrylamide with the styrene dissolved in the aqueous phase to form radicals with an increased hydrophilicity as a consequence of the low concentration of styrene. The kinetic curves for the overall rate of acrylamide–styrene copolymerisation and for the acrylamide content in the copolymer corresponding to different degrees of conversion are presented in Fig. 17, which also illustrates the variation of the viscosity of the system. The latexes obtained are stable and highly disperse (d_p = 150–300 nm). Depending on the ratio of the acrylamide and styrene, the initial stage of the process shifts to a greater or lesser extent into the aqueous phase, which influences the rate of nucleation and the particle size. With increase in the fraction of the dissolved monomer, the rate of initiation also rises and there is an increase in the number and a decrease in the size of the particles. This also occurs with increase in temperature. On reducing the pH from 9 to 3, at which acrylamide exhibits basic properties, the radicals formed in the first stage acquire an open-chain conformation, which decreases the number of nuclei in which styrene polymerises and hence increases the particle size (190–430 nm). The increase in C_{in} induces an increase in the charge on the particles, which alters the degree of hydration of the amide units. This leads to a decrease in the stability of the latex. Appreciable hydrolysis of the NH_2 groups at high pH is not observed during the reaction time (less than 6 h). In view of the high hydrophilicity of acrylamide, the latexes contain a large proportion of a water-soluble polymer; it has been suggested that the use of less water-soluble acrylamide derivatives leads to its diminution.[126]

Acrylamide and its derivatives, differing in the partition coefficients k at the styrene–water interface, have been investigated in copolymerisation with styrene:[127] acrylamide (k = 0.093), N-hydroxymethylacrylamide (k = 0.089), methacrylamide (MAMA, k = 0.159), N,N-dimethylacrylamide (DMAMA) (k = 0.293). Fig. 18 shows that the composition–conversion curves for the N-hydroxymethylacrylamide–styrene and N,N-dimethylacrylamide–styrene copolymers resemble the curve for the acrylamide–styrene copolymer (Fig. 17), i.e. for all three comonomers, the three-stage copolymerisation mechanism described above operates. On the other hand, the composition–conversion curve for the styrene–methacrylamide copolymer differs from them appreciably.

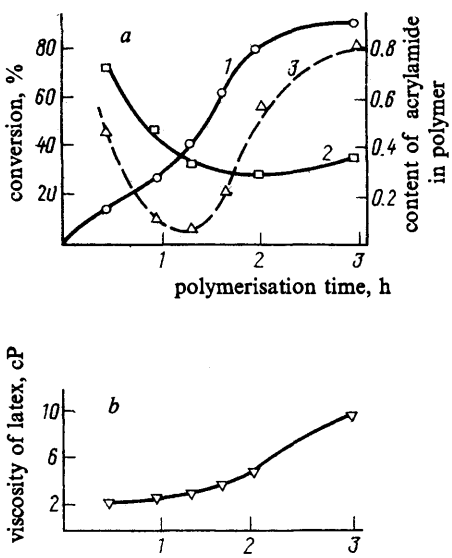


Figure 17. Time variation of the conversion (curve *1*) and of the fractions of acrylamide in the accumulated (curve *2*) and instantly formed (curve *3*) polymers in the emulsifier-free copolymerisation of styrene and acrylamide in the presence of potassium persulphate and at 343 K (C_m = 1.1 M) (*a*) and time variation of the viscosity of the finished latex (*b*).[126]

Certain characteristics of the emulsifier-free copolymerisation of the first three systems can be accounted for by the difference between the hydrophilic-hydrophobic properties of the comonomers and their reactivities in relation to styrene. The low value of k for acrylamide and N-hydroxymethylacrylamide, indicating a high concentration of the amide dissolved in the aqueous phase, induces an increase in the duration of the first stage as a result of the extensive growth of the water-soluble radicals. On the other hand, the high value of k for N,N-dimethylacrylamide is associated with a short first stage and the rapid precipitation of the radicals, which accelerates the transition of the process to the second stage. However, this entails the formation of larger particles (d_p = 329 nm) than in the first two stages (d_p = 144–147 nm), which can be

explained by the inadequate stability (lower degree of hydration) and flocculation of the styrene–*N*,*N*-dimethylacrylamide nuclei. The monomeric composition of this polymer, formed in the second stage mainly in the polymeric-monomeric particles, depends on the reactivity of the amides in relation to styrene and on *k*. The unfavourable constants for the copolymerisation of styrene and *N*,*N*-dimethylacrylamide are responsible for the low content of the latter in the copolymer.

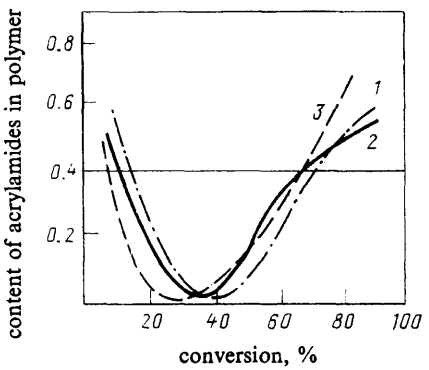


Figure 18. Variation of the composition of the polymer in the emulsifier-free copolymerisation of styrene with acrylamide (curve *1*), *N*-hydroxymethylacrylamide (curve *2*), and *N*,*N*-dimethylacrylamide (curve *3*) in the presence of ammonium persulphate (5×10^{-3} mol/litre H_2O) at 343 K and C_m = 1.25 M.[127]

The observed difference in the nature of the copolymerisation of styrene with acrylamide and *N*-hydroxymethylacrylamide (Fig. 17) is inconsistent with the closeness of the values of *k*; while the solubility of *N*-hydroxymethylacrylamide in water is somewhat greater, the duration of the first stage of the copolymerisation with this comonomer is shorter. This is associated with the different fractional composition of its copolymer, which contains a smaller water-soluble fraction appreciably enriched (to the extent of 97%) in the amide compared with the styrene–acrylamide copolymer.[126] The latter may be explained, in its turn, by the different reactivities in the aqueous phase of the copolymers being compared.

Pure monodisperse styrene–*N*-hydroxymethylacrylamide copolymer latexes containing a weight fraction of the latter comonomer of 0.09 have been obtained.[127]

(c) The addition of an organic solvent

The influence of methanol on the emulsifier-free copolymerisation of styrene in the presence of potassium persulphate and the properties of the latexes obtained from them has been investigated.[128] Methanol was chosen because of its unlimited miscibility with water and styrene and its inability to dissolve the polymer. It was shown that, after the addition of methanol to the extent of 60%, the rate of polymerisation as well as the degree of conversion increased significantly. The time of attainment of a high degree of conversion increases with increase in C_m (from 10 to 40%) and the particle size increases from 0.7 to 1.2 μm (C_{in} = 4.6×10^{-3} M). At a given concentration of the electrolytes, the particle diameter falls with increase in the initiator concentration.

The mechanism of the formation of particles is similar to that in the polymerisation of polar monomers (appreciably soluble in water) (see above). A constant rate is retained up to the attainment of 50% conversion, after which it increases,[128] which can be associated with the gel effect in view of the presence of more than one radical in the large particles.

The possibility of another mechanism for the increase in the rate of polymerisation in the presence of methanol has been postulated.[129] It consists in the interaction of methanol with potassium persulphate, which predominates over the thermal decomposition of the latter and is accompanied by the formation of the $^{\cdot}CH_2OH$ radical. This increases the concentration of surface OH groups with increase in the content of methanol and the latter can in turn promote the lyophilisation and an increase in the stability of the particles.

Okubo et al.[130] used acetone (up to 40 vol.%) instead of methanol in the emulsifier-free polymerisation of styrene. Acetone is also infinitely miscible with water and the monomer, but, in contrast to methanol, it can dissolve the polymer. Therefore, when acetone at a concentration in excess of 40% is introduced, a latex is not formed. A characteristic feature of acetone is an increase in the rate of decomposition of the initiator, which rises by a factor of 3.5 (compared with water) when the content of the solvent is 40 vol.%.[130] The rate of polymerisation of styrene increases with increase in acetone concentration from 0 to 40%, while the particle diameter diminishes under these conditions from 0.5 to 0.17 μm. The latter behaviour is also observed when C_{in}(PPS) increases from 10^{-4} to 10^{-2} M, and is attributed to an increase in the rate of nucleation of the particles. Conditions for the formation of highly stable 70% latexes with narrow particle size (d_p = 0.16 μm) and molecular weight distributions have been found. When such latexes are ultracentrifuged (27 000 rev min^{-1}), the precipitation of the deposit is not observed; after the removal of acetone, the stability of the latexes persists.

IV. Conclusion

The development and introduction into industry of the emulsifier-free polymerisation technology eliminates the pollution of wash waters and water reservoirs. The latexes obtained by this method are of great interest for a wide variety of purposes.

The principal problem in the preparation of such systems, which consist of hydrophobic sols, is their colloidal stability, which is achieved in traditional emulsion polymerisation by introducing an emulsifying agent into the system. For the formation of a colloidally stable emulsifier-free latex, it is essential to produce particles with a definite morphology as a result of the modification of their hydrophobic bulk by covalently bound highly hydrophilic surface groups, which are ionised or (and) capable of generating a sufficiently powerful hydration layer on interaction with the aqueous phase. An increase in the stability of the particles by the adsorption on their surface of the "intrinsic" diphilic low-molecular-weight oligomers is of some importance.

If the modification of the surfaces of the particles leads to a sufficient decrease in the interfacial Gibbs free energy, then stable polymeric sols are formed. In practice this is achieved when interfacial polymerisation of hydrophobic monomers is initiated by radical-ions and (or) when they are copolymerised with ionisable or highly hydrophilic comonomers.

Three stages are characteristic of emulsifier-free (as well as traditional) emulsion polymerisation: nucleation, particle growth, and polymerisation within the particles until its completion. The principal difference between emulsifier-free and classical emulsion polymerisation[26–30] involves the first stage — nucleation. Since this stage alway begins with polymerisation in the aqueous solution and the formation of diphilic oligomers, the rate and mechanism of nucleation depend on the solubility of the latter in water and their behaviour in the reaction system: chain propagation and termination by other radicals with formation of either the nuclei of particles (after the attainment of n_{cr}) or of water-soluble oligomeric surfactants and micelle-like aggregates, which constitute the nucleation zone.

In emulsifier-free emulsion polymerisation in very dilute systems — in the absence of the monomer phase — there is a possibility of homogeneous nucleation as a result of the "coiling up" of the growing radicals or their termination by reaction with other radicals on attainment of n_{cr}.[39,41] The monomer remaining in aqueous solution tends to pass into the nuclei because of the difference between its activity coefficients in the aqueous and organic phases.[130] When the entire solution has been exhausted, nucleation ceases. It has been suggested that the particles formed are stabilised by covalently bound surface ionised groups;[41] if the stabilisation is insufficient, then the particles flocculate until the size and charge density on the surface necessary for their stability are attained.[39,105]

Emulsifier-free polymerisation in very dilute systems[39,41] is of theoretical interest, but it does not model the real process occurring in the presence of the monomeric phase: in the latter case, the concentration of the monomer dissolved in water is kept constant until its equilibrium absorption by the particles as a result of mass transfer from the monomer drops through the aqueous solution. Nucleation via the formation of associated oligomeric species, which lose their solubility in water after the attainment of n_{cr} [105] or are characterised by micelle-forming properties,[14] acquires dominant importance; the associated species, which immediately solubilise the monomer, are converted into polymeric-monomeric particles in which the second and third polymerisation stages take place. The nucleation period, associated with the accumulation of water-soluble oligomers, becomes longer with increase in their solubility in water[53] and shorter with increase in the rate of radical formation and temperature, which promote the rapid displacement of the process into the particles.[24,25] The second stage (particle growth) can both proceed via the classical mechanism[26–30] and can be determined by the flocculation process for which the concentration of the electrolyte in the system plays an important role.[103–105] The first mechanism is more characteristic of polar monomers (methyl methacrylate, ethyl acrylate, etc.),[41,48] while the second is more characteristic of non-polar monomers (styrene). This difference can be accounted for by the structural factor governing the stability of colloids — the high degree of hydration of the particles of polar polymers, and, conversely, by the large contribution due to the forces associated with the hydrophobic interaction of the polystyrene particles.[64]

The concluding stage of the process with formation of the polymer-monomeric particles after the disappearance of the monomeric phase depends on their size and the initiator concentration. For a large volume of the polymeric-monomeric particles and a sufficiently high initiator concentration, when there is a possibility of the coexistence of several radicals in the particle, polymerisation is accelerated.[41] For a particle size characteristic of classical emulsion polymerisation,[26–30] at a low initiator concentration and at a high rate of radical formation (at a high temperature), where not more than one radical is present in the particles, the process in the concluding stage proceeds at a constant rate with subsequent transfer to the diffusion region.[48]

The electrostatic stability factor, determined solely by the persulphate initiation of emulsifier-free polymerisation, plays an important role in the preparation of latexes with limiting stability and a comparatively low concentration (~10 wt.%).[13,103,105] If it is necessary to increase the stability and to obtain more concentrated emulsifier-free latexes from high-molecular-weight polymers, it is essential to resort to an additional structural stabilisation factor, which depends on the hydration of the surface of the particles. This is achieved in different ways: by introducing into the aqueous phase an organic solvent which increases the solubility of the monomer,[127–129] by using an initiator whose molecules have surface-active properties,[58] and by the hydrolysis of the ester groups of the polymer (polymethacrylate or polyacrylate).[25,120] However, in practice the copolymerisation with hydrophilic[125,126] and especially with ionisable comonomers[25,112,117,118] is most often used for this purpose. In the latter case, a necessary condition is the localisation of the hydrophilic groups on the surface of the particles. In selecting the comonomer, for example a monomeric acid, its partition coefficient between the monomeric and aqueous phases[119] becomes important as do the mobility of the carboxyl-containing segments of the macromolecules, which is responsible for the possibility of their migration in the bulk of the particles and their localisation at the interface with the aqueous phase.[120]

Concentrated emulsifier-free polymer latexes with sufficiently low T_g, characterised by a low content of oligomers and electrolytes, can be used as glues and adhesives, since they exhibit an increased hydrophilicity and are capable of adhering to various supports more effectively than traditional latexes.[7]

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Translated from *Uspekhi Khimii* **60** 430–447 (1991) U.D.C. 541.64.678.046

Catalytic degradation of polyolefins—a promising method for the regeneration of monomers

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ABSTRACT. The catalytic degradation of polyolefins, which in contrast to the purely thermal process takes place selectively, can help solve the problem of the regeneration of monomers.

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I. Introduction

The kinetics of the catalytic degradation of polyolefins in the presence of electrophilic reagents differ considerably from the kinetics of their thermal degradation.[1,2] This is due primarily to differences in the initiation of decomposition reactions of the polymer products. In general, in both thermal[3–5] and catalytic[6,9] reactions of polyolefins two mechanisms of initiation can be distinguished: a) initiation of depolymerisation of the macromolecules on the terminal groups; b) initiation of decomposition of macromolecules randomly. To date it has not been possible to determine the contribution of each of these mechanisms using the existing theoretical and experimental approach to a study of the kinetic reaction parameters.[10] A new method of determining the apparent constants of initiation and length of the kinetic chain of competing processes[11] has made it possible to bring closer the development of a general theory concerning the processes of selective catalytic degradation of polyolefins.

II. Thermal degradation of polyolefins

The thermal degradation of polyolefins as an independent process became a topic of interest for research workers at the end of the 1940's, primarily in order to achieve the selective extraction of valuable gaseous hydrocarbons from a polymer feedstock.[12–14] However, with rare exceptions [poly(α-methylstyrene), poly(methylmethacrylate)] very low selectivity with respect to the yield of monomer has been recorded in the thermal degradation of polyolefins. For the majority of polyolefins the formation of a wide range of low-molecular weight products—gaseous, liquid, and waxy—during degradation was typical.[15] The experimental data, in particular the change in molecular weight of the polymer as a function of the temperature and degree of degradation, the observed composition of volatile and nonvolatile degradation products, and the rate of the process, showed that reactions involving chain scission with hydrogen transfer and depolymerisation of the macromolecules are the most probable.[4,15] The degradation of polyolefins can in a number of cases be accompanied by side reactions, such as cross-linking of macromolecules. Moreover in some cases, particularly in the degradation of polyethylene, an active site is formed at a point of branching followed by detachment of a side-chain residue.

The combination of successive parallel reactions that form the basis of the complex chemical process of thermal degradation of polyolefins predetermines the complex task of studying and defining the process. Nevertheless, in relation to the decomposition of polyolefins the main reactions that determine the chemical nature of the overall process are: chain depolymerisation to form the corresponding monomer and its isomerisation and hydrogenation products and random decomposition of the macromolecules with the formation of sequences of polymer molecules of different length (degradation) resulting in a decrease in the molecular weight of the polymer.

As a rule initiation of decomposition of macromolecules is related to the occurrence of various kinds of defects in the polymer chain (structural irregularities) that are formed, for example, during polymerisation. Groups that are formed by addition of a monomer according to the "tail-to-tail" principle, and when there are side-chain substituents, internal double bonds of various types,[15] etc. can become labile. The resulting primary macroradicals decompose in chain propagation reactions, undergoing β-cleavage (Rice's rule) to form lower olefins, and also decompose in chain transfer and chain termination reactions leading to the formation of heavier hydrocarbons. Typically, during the thermal decomposition of polymer products the role of chain transfer to the polymer is very important,[10] which is a determining factor in the formation of a series of reaction products of variable composition.

Of the reactions that occur during the thermal degradation of polyolefins, the three most typical reactions that govern the yield and distribution of products can be distinguished: 1) radical decomposition (degradation) of macromolecules; 2) reactions that occur with hydrogen transfer; 3) radical substitution reactions (chain transfer to the polymer). The role of these reactions can vary according to the chemical structure of the polyolefins. Thus, for

Table 1. Yield and composition of gaseous products from thermal and catalytic degradation of polyolefins.

Catalyst	Polyolefin	T, K	Yield of gas, wt.%	Composition of gaseous products*, wt.%							
				C_1-C_3	iso-C_4H_{10}	n-C_4H_{10}	α-C_4H_8	iso-C_4H_8	β-C_4H_8	$C_4H_8+C_4H_{10}$	C_5 and higher
No catalyst	PE	673	40.8	52.9	18.7	7.5	–	1.1	19.8	47.1	–
	PIB	653	75.9	1.9	2.1	–	0.1	16.0	0.9	19.1	79.0
	BR	653	50.4	2.7	w	0.5	3.0	2.9	30.3	36.7	60.6
$AlCl_3$	PE	643	47.6	5.7	22.4	–	0.1	15.7	2.7	40.9	53.4
	PIB	643	62.7	1.5	2.1	–	w	19.1	1.0	22.2	76.3
	BR	643	85.0	14.3	59.0	–	0.1	0.6	0.2	59.9	25.8
$NaAlCl_4$	PE	643	84.8	24.8	54.9	0.8	–	19.7	0.3	75.5	–
	PIB	583	47.9	1.1	7.8	w	0.3	88.8	2.0	98.9	–
	BR	573	38.8	16.4	23.6	0.4	0.5	39.0	12.4	62.6	7.7
$MgCl_2 \cdot AlCl_3$	PE	643	88.2	15.0	42.5	6.7	–	21.8	14.0	85.0	–
	PIB	573	93.8	1.4	24.9	0.1	0.1	73.4	0.1	98.6	–
	BR	573	75.4	1.7	2.1	0.2	0.5	93.8	0.6	95.9	1.1

*Traces of hydrogen were identified in the gaseous products.

example, for polyethylene (PE) all three types of reaction are equally probable, while for polyisobutylene (PIB), which has two methyl substituents on every second carbon atom, only reactions 1) and 3) are typical. This has the result that in the degradation of PE formation of the monomer in appreciable quantities is improbable and, moreover, is thermodynamically unfavourable, while in the degradation of PIB up to 20% monomer is formed (Table 1). When internal double bonds occur in the polyolefin, such as in butyl rubber (BR), the role of hydrogen transfer reactions once again increases (Table 1). As a consequence the yield of monomer is very small.

Chain transfer reactions with removal of a hydrogen atom from the main chain and a substituent (for PE, branching, which in the vast majority of cases consists of ethyl or *n*-butyl groups, should be regarded as a substituent) during the thermal degradation of PE and BR are of equal probability. For PIB, on the other hand, chain transfer reactions with removal of a hydrogen atom from the internal hydrocarbon atoms are typical, with the result that hydrocarbons of an isomeric structure are mainly formed (Table 1).

On the whole it can be seen that the thermal decomposition of PE, PIB, and BR, as for the majority of other polyolefins, leads equally to the formation of such a wide range of reaction products that the concept of selectivity in relation to the thermal degradation of polyolefins loses its meaning. Nevertheless, from a practical viewpoint, the derivation of hydrocarbon fractions by thermal degradation may be of interest not only as a method of processing various polymer waste products in order to destroy them but also as one of the methods of obtaining liquid hydrocarbons for use as solvents, additives, or fuel.[16] Catalytic methods of treating polyolefins to obtain gaseous and liquid fuels are also possible.[17,18]

III. Catalytic degradation of polyolefins

The electrophilic catalytic degradation of polyolefins that occurs by a cationic mechanism[8] is very interesting from the theoretical viewpoint as an example of the decomposition of polymer products by terminal group or random mechanisms.

Compared to a purely thermal process, the electrophilic catalytic degradation of polyolefins in the presence of $AlCl_3$ takes place with a higher yield of low-molecular weight products (Table 1) at considerably lower temperatures, but it is insufficiently selective with respect to the yield of monomer. In the presence of strongly acidic systems there is an intensification not only of the decomposition processes of the macromolecules but also of secondary processes, in particular isomerisation and cross-linking. The formation of primary polymer carbocations on treatment with aluminium chloride (probably in the form of $H^+(AlCl_3 \cdot OH^-)$),[19] occurs in the degradation of PE with the random removal of a hydride ion:

$$R{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}R' + H^+[AlCl_3 \cdot OH]^- \rightarrow$$

$$\rightarrow R{-}CH_2{-}\overset{+}{C}(CH_3){-}CH_2{-}R'[AlCl_3 \cdot OH]^- + H_2,$$

$$R{-}CH_2{-}CH(CH_3){-}CH_2{-}R' + H^+[AlCl_3 \cdot OH]^- \xrightarrow[-H_2]{}$$

$$\rightarrow R{-}CH_2{-}CH(\overset{+}{C}H_2){-}CH_2{-}R'[AlCl_3 \cdot OH]^- \rightarrow$$

$$\rightarrow R{-}\overset{+}{C}H_2 \cdot [AlCl_3 \cdot OH]^- + CH_2{=}CH{-}CH_2{-}R'.$$

Initiation of degradation of polyolefins is also probable on the defect groups of macromolecules, for example, on vinylidene double bonds:

$$RR'C{=}CH_2 + H^+[AlCl_3 \cdot OH]^- \rightarrow RR'CH{-}\overset{+}{C}H_2[AlCl_3 \cdot OH]^-.$$

The primary ion isomerises to give a more stable tertiary carbocation:

$$RR'CH-\overset{+}{C}H_2[AlCl_3\cdot OH]^- \rightleftharpoons R-\overset{R'}{\underset{CH_3}{\overset{|}{\underset{|}{\overset{+}{C}}}}}[AlCl_3\cdot OH]^-.$$

In the decomposition of polymer carbocations a wide range of products is formed: gaseous products from CH_4 (detachment of methyl branches) to C_4H_8 (skeletal isomerisation of a macroion followed by β-cleavage) and liquid and waxy products from C_5 hydrocarbons and above (Table 1). A typical feature is that in the degradation of PE the yield of just the monomer (ethylene) is low.

Terminal double bonds play a considerable role in chain initiation reactions. However, the proportion of reactions that occur on the terminal groups is small in the case of PE degradation because of the high content of internal defect groups. An increase in the content of the terminal double bonds in PIB and BR macromolecules increases the probability of initiation of the process by a terminal group mechanism, although the expected increse in selectivity of the process also does not occur (Table 1). It is evident that successive chain-transfer reactions to the polymer by the random mechanism play a fairly large part in degradation processes of polyolefins in the presence of strongly acidic catalysts.

Side reactions are usually suppressed in electrophilic processes when the acidity of the catalyst is reduced. This phenomenon together with a high activity and selectivity has been established in the catalytic degradation of polyolefins in the presence of complexes of the type $MCl_n\cdot AlCl_3$ (M = Li, Na, K, Mg, Ca, Ba, n = 1–2).[20–22] Fused $MCl\cdot AlCl_3$ salts, which are familiar as ionic media,[23,24] exhibit properties of weakly acidic catalysts. The decrease in the ionic strength of the outer-sphere cation of an $MCl\cdot AlCl_3$ complex on going from Li^+ to Na^+ is consistent with the order of change in rate of conversion of the polymer (Table 1). A decrease in acidity of the catalysts relative to $AlCl_3$ has a favourable effect on the ratio of chain propagation to chain transfer by considerably reducing the contribution of chain transfer reactions. This in turn results in a considerbale increase in selectivity of the process with respect to the yield of C_4 hydrocarbons. The gaseous reaction products contain up to 90–95% hydrocarbons (Table 1).

Amongst individual salts—metal chlorides of Groups I and II of the Mendeleev Periodic Table—$MgCl_2$ has high activity and selectivity with respect to the yield of monomer during catalytic degradation of PIB and BR (Table 2). The water of crystallisation plays an important role in the formation of catalytically active magnesium chlorides.[25] The aqua complexes $MgCl_2\cdot H_2O$ and $MgCl_2\cdot 2H_2O$ proved to be the most effective. Quantum-chemical calculations confirmed the possibility of the water of crystallisation having an activating effect (Table 3). The catalytic activity of the aqua complexes $MCl\cdot AlCl_3\cdot H_2O$ and $MgCl_2\cdot H_2O$ is caused by the fairly large positive charges on the hydrogen atoms. The stability of the $MAlCl_4\cdot H_2O$ aqua complex, determined from the energy of complexation with water, is somewhat less than for aqua complexes of magnesium chlorides. Therefore, despite the higher charges on the hydrogen atoms, the activity of $MAlCl_4\cdot H_2O$ during the degradation of polyolefins is somewhat lower than that of $MgCl_2\cdot H_2O$ (Table 3). It should also be noted that the quantum-chemical calculations are in agreement with the experimentally determined series of activity of $MAlCl_4$ catlaysts: $LiAlCl_4$ > $NaAlCl_4$ > $KAlCl_4$, namely, the acidity $P_{k\alpha}$ and charges q_{H^+} on the hydrogen atoms of the aqua complexes diminish with an increase in ionic radius of the cation.

Thus, weakly acidic complex catalysts of the type $MCl_n\cdot AlCl_3\cdot H_2O$ and $MgCl_2\cdot H_2O$ are fairly active and selective during the electrophilic catalytic degradation of polyolefins.

Table 2. Catalytic degradation of polyolefins in the presence of some aqua complexes of metal chlorides.

Catalyst	T, K	Yield of gas, wt.%			Yield of monomer, wt.%		
		PIB	BR	PE	PIB	BR	PE*
$MgCl_2\cdot nH_2O$	583	12.4	27.4	8.7	96.2	96.0	76.5
n=1–2	603	81.9	92.0	24.5	99.5	96.4	77.1
	623	100.0	100.0	33.9	99.5	97.0	78.3
$MgCl_2\cdot 4H_2O$	583	11.4	19.7	–	90.1	93.1	–
	603	36.2	31.6	21.4	92.4	92.0	73.0
	623	62.0	35.9	–	98.6	97.0	–
$BaCl_2\cdot 2H_2O$	583	3.8	4.0	2.2	23.5	19.0	53.2

*Total yield of C_4 hydrocarbons given.

Table 3. Quantum-chemical calculations of polyolefin degradation catalysts (LCAO MO method with CNDO/2 approximation).

Catalyst	$P_{k\alpha}$	q_{H^+}	Energy of complexation, kJ mol^{-1}	Yield of gas, wt.% (603 K)		
				PIB	BR	PE
$LiCl\cdot H_2O$	10.5	0.182 0.182	131	9.1	21.2	–
MgOHCl	23.0	0.070	–	8.5	23.4	–
$MgCl_2\cdot H_2O$	12.7 15.4	0.166 0.185	265	100.0	100.0	49.5
$MgCl_2\cdot 2H_2O$	15.4 10.0	0.146 0.185	260 260	100.0 100.0	100.0 100.0	45.0 45.0
$MgCl_2\cdot 4H_2O$	13.7 12.5	0.158 0.165	216	59.5	45.2	21.4
$LiAlCl_4$	5.6	0.253 0.217	88	61.1	96.5	57.4
$NaAlCl_4$	4.5	0.226 0.229	249	55.0	46.7	55.9
$KAlCl_4$	–	–	–	6.3	18.0	12.3

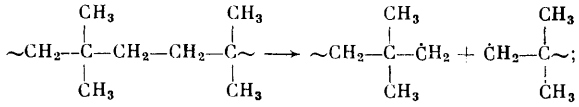
IV. Mechanism of catalytic degradation

The mechanisms of the thermal and thermocatalytic degradation of polyolefins differ. The purely thermal decomposition of polymer products takes place by a radical mechanism,[5] while for the degradation of polyolefins in the presence of electrophilic catalysts an ionic mechanism occurs.[26,27]

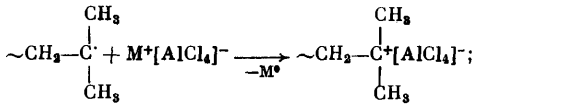
In early studies on the catalytic degradation of polyolefins in the presence of $MAlCl_4$ complexes, a cationic process mechanism was interpreted on the basis of a possible single-electron oxidation of primary radicals formed by the action of heat on the polymer:[1,2]

a) thermal decomposition by the random mechanism, preferentially on the defect groups ("head-to-head" addition of

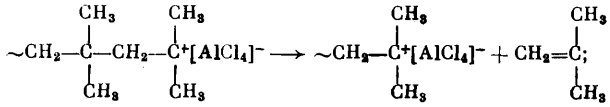
monomer) contained in the macromolecules, for example



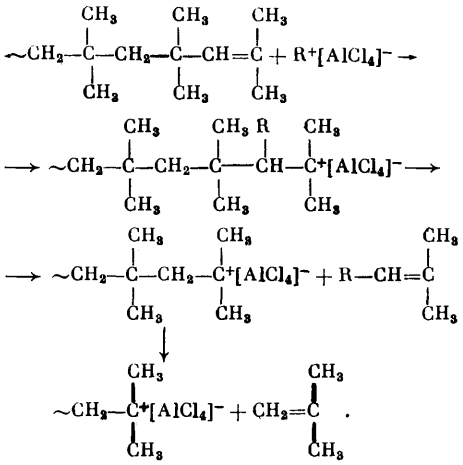
b) a redox reaction with the formation of a polymer carbocation



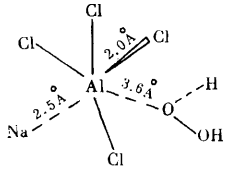
c) depolymerisation of macroions to form the monomer



d) chain transfer to the polymer followed by depolymerisation of the macroions by the terminal group mechanism

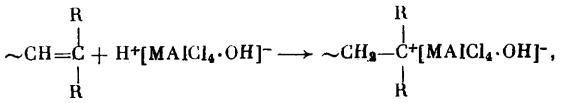


When $MAlCl_4 \cdot H_2O$ aqua complexes are used, initiation of degradation of polyolefins takes place on $H^+(MAlCl_4 \cdot OH)^-$, which has the structure



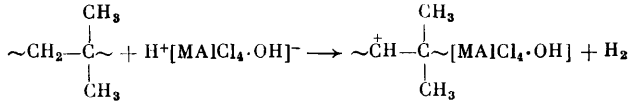
An aqua complex can initiate decomposition both randomly and on the terminal groups. Interaction of the catalyst with the weak bonds of the polymer chain by the random mechanism is governed by the structure of the polyolefin. In PE, degradation of macromolecules is initiated mainly on vinylidene and *trans*-vinylene internal double bonds, while for BR it occurs on the sites where the isobutyl residues are connected to an isoprenyl unit. Initiation by the terminal group mechanism occurs on the terminal double bonds.

a) Terminal group mechanism

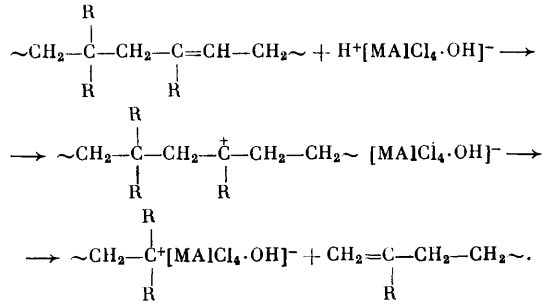


where R = CH_3 PIB, BR) or H (PE).

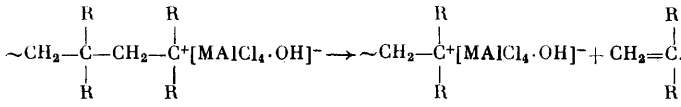
b) Random mechanism



or (what is more probable for BR and PE)

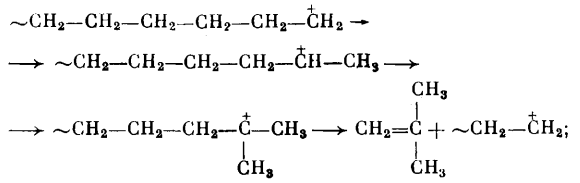


Chain propagation reactions of macrocations can differ considerably according to the chemical nature of the polymer used. For example, for PIB and BR the resulting carbocations mainly undergo β-cleavage with elimination of an isobutylene monomer (Table 1):

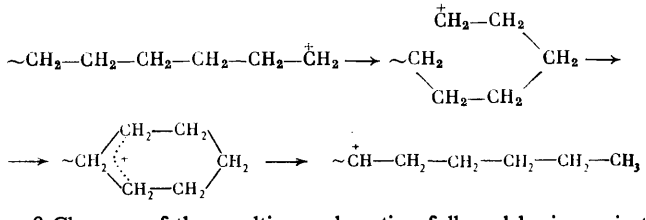


A linear carbocation $R-\overset{+}{C}H_2$ formed during the degradation of PE undergoes conversions by two main routes:

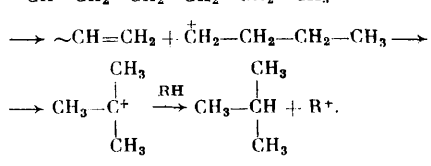
1) skeletal isomerisation with the formation of a tertiary carbocation that subsequently undergoes β-cleavage to give isobutylene



2) isomerisation of a macroion with transfer of excess positive charge to the sixth carbon atom via an intermediate cyclisation reaction of "flexible" methylene sequences

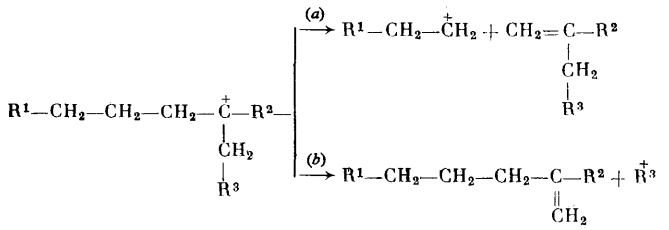


β-Cleavage of the resulting carbocation followed by isomerisation and removal of a hydrogen atom from a neutral molecule gives isobutane:



This reaction does not correspond to the classical route for depolymerisation and can be defined as an associated reaction of degradation and chain transfer.

In the case of the thermocatalytic degradation of PE, which always contains branching, the formation of carbocations can occur on a tertiary carbon atom. The subsequent decomposition of the macrocation occurs by two routes: decomposition of the main chain (*a*) and elimination of the side chain (*b*).



In both cases a new carbocation which undergoes further decomposition and an "inert" polymer with a vinylidene double bond are formed.

Thus, initiation of thermocatalytic destruction of polyolefins with different chemical structures in the presence of $MAlCl_4 \cdot H_2O$ and $MCl_n \cdot H_2O$ aqua complexes has the general characteristics: formation of an active site on the terminal double bonds of the macromolecule (terminal group mechanism) and random scission of the macrochains on defect groups and weak bonds. The mechanism of the chain propagation reaction is determined by the structure of the polyolefin; the presence of bulky substituents results either in depolymerisation reactions mainly occurring (PIB, BR) or depolymerisation (in parallel) with initial isomerisation of the carbocation. The absence of such groups in a linear polymer (PE) results in degradation with chain transfer to the polymer.

V. Kinetic features of the catalytic degradation of polyolefins

The chemical nature of the catalyst determines the sequence of degradation reactions of polyolefins and hence also the characteristics of the kinetic scheme of the process. When weakly acidic ionic catalysts of the type $MAlCl_4$, $MAlCl_4 \cdot H_2O$, and $MCl_n \cdot H_2O$ are used, the kinetics of the process are given by the following scheme:

$$\left.\begin{array}{l} P \xrightarrow{W_r} 2R^{\cdot} \\ P + cat \xrightarrow{k} 2R^{\cdot} \\ R^{\cdot} + cat \xrightarrow{k_{in}} R^{+} \end{array}\right\} \text{(random mechanism)}$$

$$P + cat \xrightarrow{k_{in}} R^{+} \text{ (terminal group mechanism)}$$

$$R_n^{+} \xrightarrow{k'_{dep}} R^{+}_{n-z} + zM; \quad R_n \xrightarrow{k_{dep}} R^{\cdot}_{n-z} + zM$$

$$R^{\cdot} \xrightarrow{k_{deg}} R_n^{\cdot} + R_m; \quad R^{+} \xrightarrow{k'_{deg}} R_n^{+} + R_m$$

$$R^{\cdot} + P \xrightarrow{k_{ct}} RH + P^{\cdot}; \quad R^{+} + P \xrightarrow{k'_{ct}} RH + P^{+} \quad + \Pi^{+}$$

$$R^{+} \xrightarrow{k_t} P.$$

In this case k'_{in}, k_{in}, k'_{dep}, k_{dep}, k'_{deg}, k_{deg}, k'_{ct}, k_{ct} and k_t are the rate constants of initiation, depolymerisation, and degradation by ionic and radical sites, chain transfer of ionic and radical sites, and chain termination respectively.

For degradation of the polymer by the random mechanism, the change in concentration of macrocations $[R^+]$ is given by the equation

$$d[R^+]/dt = k_{in}[cat][R^{\cdot}] - k_t[R^+]. \quad (1)$$

For a steady state

$$[R^+] = k_{in}[cat][R^{\cdot}]/k_t,$$

where

$$[R^{\cdot}] = -\frac{k_{in}[cat]}{2k_1} + \sqrt{\left(\frac{k_{in}[cat]}{2k_1}\right)^2 + \frac{W_r}{k_1}} =$$

$$= \frac{k_{in}[cat]}{2k_1}\left[\sqrt{\frac{4k_1(W_t + k_1[cat])}{(k_{in}[cat])^2}} + 1 - 1\right]. \quad (2)$$

Here $W_r = W_t + k_1[cat]$ is the rate of formation of radicals as a result of thermal scission of the polymer chain and by catalytic action.

Let us consider two limiting cases:[1]

a) There is only a small quantity of catalyst, in other words, only a small proportion of the radicals that are formed is converted to polymer carbocations. This corresponds to the condition

$$4k_1(W_t + k_1[cat])/(k_{in}[cat])^2 \gg 1, \quad (3)$$

then

$$[R^{\cdot}] = \sqrt{(W_t + k_1[cat])/k_1},$$

and the expression for the rate of random decomposition of polyolefins takes the form

$$V_1 = (k'_{dep} + K'_{deg})\frac{k_{in}[cat]}{k_t}\sqrt{\frac{W_t + k_1[cat]}{k_1}} +$$

$$+ (k_{dep} + k_{deg})\sqrt{\frac{W_t + K_1[cat]}{k_1}}. \quad (4)$$

In this case the rate-limiting stage of the process is the interaction of catalyst with a radical;

b) there is a considerable quantity of catalyst in the system, in other words, all of the radicals formed are converted to carbocations

$$4k_1(W_t + k_1[cat])/(k_{in}[cat])^2 \ll 1.$$

In this case the concentration of macroradicals in the system is defined by the relationship

$$[R^{\cdot}] = (W_t + k_1[cat])/(k_{in}[cat]), \quad (5)$$

and the rate of process is in the form of

$$V_1 = (k'_{dep} + k'_{deg})(W_t + 2k_1[cat])/k_t. \quad (6)$$

In the initiation of depolymerisation of PIB by the terminal group mechanism, the concentration of active sites $[R^+]$ is defined by the relationship

$$d[R^+]/dt = k_{in}[cat]C_n - k_t[R^+],$$

where $C_n = A_0/\overline{P}_n$ is the concentration of double bonds in the polymer (A_0 is the concentration of polymer, $\overline{P}_n$ is the degree of polymerisation of the polymer).

The equation for the rate of depolymerisation of PIB by the terminal group mechanism has the form

$$V_2 = k_r[R^+] = \frac{(k'_{dep} + k'_{deg})k_{in}[cat]C_n}{k_t} = \frac{(k'_{dep} + k'_{deg})k'_{in}A_0[cat]}{k_t\overline{P}_n}. \quad (7)$$

Then the rate of depolymerisation in general form is given by the equation

$$V = V_1 + V_2 = (k'_{dep} + k'_{deg}) \frac{k_{in}[cat]}{k_t} \sqrt{\frac{W_t + k_l[cat]}{k_l}} + \\ + (k_{dep} + k_{deg}) \sqrt{\frac{W_t + k_l[cat]}{k_l}} + \frac{(k'_{dep} + k'_{deg}) k'_{in} A_0[cat]}{k_t \overline{P}_n} \quad (8)$$

The equation obtained takes into account the concurrent reactions of degradation and depolymerisation on active ionic and radical sites but cannot elucidate the reasons for the difference in selectivity of the process with respect to the yield of monomer in the presence of catalysts. The selectivity of the catalyst can be determined quantitatively from the values of z (z is the length of the kinetic chain, representing the number of monomer units eliminated on average per macromolecular cleavage):

$$z = \frac{k'_{dep}[R^+] + k_{deg}[R^\cdot] + k'_{deg}[R^+] + k_{dep}[R^\cdot]}{W_t + k'[cat] + k_{ct}[R^\cdot] + k'_{ct}[R^+]}. \quad (9)$$

Table 4. Overall parameters of the catalytic degradation of polyolefins ($c_{cat} = 1 \times 10^{-3}$ mol g^{-1}; $\tau = 3.6 \times 10^3$ s).

Polyolefin	Catalyst	T, K	$z \pm 10\%$	$(k_{in} \times 10^7) \pm 5\%$, s^{-1}	E_a, kJ mol^{-1}
Polyisobutylene	$LiAlCl_4$	583	10	0.6	100
		603	8	1.7	
		623	6	4.3	
	$NaAlCl_4$	583	10	0.3	105
		603	7	0.8	
		623	6	2.4	
	$KAlCl_4$	583	4	0.4	140
		603	3	1.1	
		623	3	3.7	
Butyl rubber (copolymer of isobutylene with isoprene)	$NaAlCl_4$	573	40	0.7	54
	$MgCl_2 \cdot AlCl_3$	573	55	1.2	55
	$BaCl_2 \cdot AlCl_3$	573	62	2.0	48
Polyethylene	$LiAlCl_4$	573	8	0.4	118
		603	19	1.2	
		623	26	3.9	
		643	31	5.8	
	$NaAlCl_4$	573	10	0.4	124
		603	12	1.3	
		623	17	3.6	
		643	20	5.0	
	$KAlCl_4$	573	7	0.1	151
		603	9	0.5	
		623	12	1.2	
		643	19	2.7	

With an increase in activity of the catalyst in the series $LiAlCl_4$ > $NaAlCl_4$ > $KAlCl_4$, the value of z and the overall rate of degradation of polymer products increase (Table 4), while with an increase in temperature the length of the kinetic depolymerisation chain of PIB and BR on each of the selected catalysts decreases whereas the rate constant of depolymerisation increases. This is due to an increase in the contribution of the thermal component, which increases the probability of random degradation of the chain as well as chain transfer and termination. In the degradation of PE the yield of monomer is low and the concept of the length of the polymer chain should be applied to the elimination of C_4 hydrocarbons rather than monomer units. However, in contrast to PIB and BR, for PE the adopted value of z increases with an increase in temperature (Table 4), which is evidently due to the increased role of reactions involving decomposition with subsequent chain transfer which assist in increasing the yield of one of the main products of catalytic degradation of PE—isobutane. The overall energy of activation values of the catalytic degradation of polyolefins in all of the cases given are lower than for the thermal decomposition of polymers. This is attributed to a reduction in both the energy of initiation and the energy of decomposition of the polymer chain because of the cationic nature of the active site.

The kinetic scheme presented here represents the overall process of degradation of polyolefins that occurs in the presence of electrophilic catalysts. Therefore it can also be used to represent the overall kinetics of degradation of polyolefins in the presence of active and proton-donating forms of catalysts. However, at the same time it is necessary to take account of the fact that the rate constants of the interaction between catalyst and radical and the radical decomposition of polymer decrease considerably, and the rate of depolymerisation will be determined primarily by ionic processes involving initiation and chain continuation. In this case the kinetic scheme of catalytic thermal degradation of polyolefins can be represented as follows:

a) initiation (valid for initiation by both random and terminal group mechanisms)

$$P + cat \xrightarrow{k_{in}} R^+;$$

b) chain propagation

$$R_i^+ \xrightarrow{k_{dep}} R_{i-z}^+ + zM;$$

c) intermolecular chain transfer

$$R_i^+ + P_m \xrightarrow{k_{ct}} R_i + P_m^+;$$

d) destruction of active sites (chain termination)

$$R_i^+ \xrightarrow{k_t} P.$$

The rate of change in concentration of the polymer carbocations formed by the random mechanism can be given by the equation:

$$d[R^+]/dt = k'_{in}[cat][P] - k_t[R^+].$$

Assuming a steady-state concentration of active sites, we obtain

$$[R^+] = k'_{in}[P][cat]/k_t.$$

In the formation of active sites by the terminal group mechanism the expression for the rate of change in concentration of the active sites is given by the equation:

$$d[R^+]/dt = k''_{in}[cat]C_t - k_t[R^+],$$

where C_t is the concentration of terminal double bonds. Hence under steady-state conditions

$$[R^+] = k''_{in}[cat]C_t/k_t.$$

The equations for the rate of depolymerisation have the form

$$V_1 = k_{dep}[R^+] = k_{dep}k'_{in}[P][cat]/k_t \text{ (random mechanism)},$$

$$V_2 = k_{dep}[R^+] = k_{dep}k''_{in}[cat]C_t/k_t \text{ (terminal group mechanism)}.$$

Assuming that the random and terminal group processes are independent, we obtain an expression for the overall rate of degradation

$$V = k_{dep}[cat](k'_{in}P + k''_{in}C_t)/k_t.$$

Thus, the rate of the overall process of degradation of polyolefins is determined mainly by the initiation reactions, and in particular by the values of the apparent rate constants of initiation by the random and terminal group mechanisms. This makes it necessary to carry out a quantitative determination of the kinetic parameters of the initiation process.

VI. Determination of apparent kinetic parameters

Electrophilic catalytic degradation of polyolefins can be represented by a general equation that takes into account the contribution of both the random and terminal group reactions.

$$-dP/dt = z_t k_{ti} C_t + k_{ri} z_r P. \quad (10)$$

Here P is the decrease in polymer concentration (as a fraction of the original); k_{ri} and k_{ti} are the rate constants of initiation of degradation of polymer by the random and terminal group mechanisms respectively; z_r and z_t are the lengths of the kinetic chain during degradation by the random and terminal group mechanisms: C_t is the concentration of terminal double bonds. Assuming that the terminal groups which can initiate depolymerisation are consumed exponentially during degradation according to $C_t = C_{t0}\exp(-k_{ti}t)$ (C_{t0} is the initial content of terminal double bonds), which is especially typical for PIB, we obtain

$$P = \exp(-k_{ri}z_r t) + \frac{k_{ti}z_t C_{t0}}{k_{ti} - k_{ri}z_r}[\exp(-k_{ti}t) - \exp(-k_{ri}z_r t)]. \quad (11)$$

It is possible to determine the numerical values of k_{ti}, z_t, k_{ri}, and z_r at the initial stages of the process when $P \ll 1$, $t \ll 1/k_{ti}$ and $t \ll 1/k_{ri}z_r$ (experimentally this is possible when the process is carried out under low-temeprature conditions (200–300 °C) when the rates of "burning away" the chains are relatively small). Then

$$P = 1 - k_{ri}z_r t - k_{ti}z_t C_{t0} t. \quad (12)$$

The change in molecular weight of PIB can be determined from the total number of chain scissions. The number of macromolecules is given by $n = n_0 + k_{ri}t$ and their molecular weight is determined from the expression

$$\overline{M}_n = P/n \simeq \frac{1 - k_{ri}z_r t - k_{ti}z_t C_{t0} t}{n_0(1 + k_{ri}t/n_0)} \simeq \overline{M}_n^0(1 - k_{ri}z_r t - k_{ti}z_t C_{t0} t - k_{ri}t/n_0) \quad (13)$$

where $\overline{M}_n^0 = 1/n_0 = 1/C_{t0}$ (the presence of a single terminal double bond in each initial macromolecule of PIB is assumed). The relative degree of polymerisation during degradation will change in accordance with the equation

$$\overline{P}_n/\overline{P}_n^0 = 1 - k_{ri}z_r t - k_{ri}\overline{P}_n^0 t - k_{ti}z_t t/\overline{P}_n^0. \quad (14)$$

Hence it is possible to determine the change in relative degree of polymerisation in relation to the change in degree of conversion $d\alpha = \Delta P$. From Eqn. (12) we obtain

$$\Delta P = (k_{ri}z_r + k_{ti}z_t C_{t0})t.$$

As a result we obtain

$$\frac{d(\overline{P}_n/\overline{P}_n^0)}{d\alpha} = -\frac{k_{ri}z_r + k_{ri}\overline{P}_n^0 + k_{ti}z_t/\overline{P}_n^0}{k_{ri}z_r + k_{ti}z_t/\overline{P}_n^0}. \quad (15)$$

Provided that the length of the kinetic chain z_r is many times less than the degree of polymerisation $\overline{P}_n^0$, namely, $z_r \ll \overline{P}_n^0$, Eqn. (15) can be simplified.

$$\frac{d(\overline{P}_n/\overline{P}_n^0)}{d\alpha} = -\frac{k_{ri}\overline{P}_n^0 + k_{ti}z_t/\overline{P}_n^0}{k_{ri}z_r + k_{ti}z_t/\overline{P}_n^0}. \quad (16)$$

In order to simplify the calculations of the values of the kinetic parameters for each of the competing reactions we shall consider the following limiting cases:

a) when there is a small contribution from reacitons that occur on the terminal groups, i.e., when $k_{ti}z_t/\overline{P}_n^0 \ll k_{ri}z_r \ll k_{ri}\overline{P}_n^0$, the expression for the adjusted relative degree of polymerisation takes the form

$$d(\overline{P}_n/\overline{P}_n^0)/d\alpha = -\overline{P}_n^0/z_r; \quad (17)$$

b) when there is a small contribution from reactions that occur randomly, we obtain $d\alpha/dt \simeq k_{ti}z_t/\overline{P}_n^0$. The value of $\overline{P}_n^0$ in such a process for the most probable initial molecular weight distribution ($\overline{P}_w/\overline{P}_n \simeq 2$) is virtually unchanged, i.e., $d(\overline{P}_n/\overline{P}_n^0)/d\alpha \simeq 0$. This is consistent with the experimental data (Fig. 1, curves *1–3*). There is no point in using Eqn. (16) in this case since complete "burning away" of the macromolecules during depolymerisation of the polymer was not taken into account in its derivation;

c) when the main role in changing the number of chains is played by the random mechanism while the terminal group mechanism plays the main role in depolymerisation, namely when $k_{ri}\overline{P}_n^0 \gg k_{ti}z_t/\overline{P}_n^0 \gg k_{ri}z_r$, we obtain

$$d(\overline{P}_n/\overline{P}_n^0)/d\alpha = -k_{ri}(\overline{P}_n^0)^2/k_{ti}z_t. \quad (18)$$

The three variants a), b), and c) correspond to the three sections on the curve of the dependence of the calculated values of $d(\overline{P}_n/\overline{P}_n^0)/d\alpha$ on $\overline{P}_n^0$ obtained from the gradients of the corresponding experimental curves (Fig. 1). With an increase in the degree of polymerisation each of the three possible variants b), c) and a) occurs successively (Fig. 2).

It is possible to determine z_r and $k_{ri}/k_{ti}z_t$ respectively from the gradients for sections a) and c) of the curve of $d(\overline{P}_n/\overline{P}_n^0)/d\alpha$ against $\overline{P}_n^0$ (Fig. 2). The value of k_{ri} can be calculated by taking into account the fact that the random mechanism provides the main contribution to the decrease in molecular weight of the polymer. This corresponds to the relationship $d(\overline{P}_n/\overline{P}_n^0)/d\alpha = -k_{ri}\overline{P}_n^0$, from which the value of k_{ri} can be determined.

The values of z_r and k_{ri} that are obtained by treatment of the experimental data can be used to determine the numerical values of k_{ti} and z_t from Eqn. (11). The values of the kinetic parameters obtained—the rate constants of initiation and the lengths of the kinetic chain of polymer depolymerisation (given in Table 5 for the degradation of PIB in the presence of $NaAlCl_4$)—suggest that initiation of catalytic degradation by the terminal group mechanism has a predominant role under low-temperature conditions. As the temperature of degradation of the polyolefins is increased, the ratio of k_{ti} to k_{ri} decreases and at 260 °C their values become comparable.

The effect of catalysts on the degradation of polyolefins has been studied using the salts $NaCl{\cdot}AlCl_3$ and $MgCl_2{\cdot}AlCl_3$. The complex salt $MgCl_2{\cdot}AlCl_3$ has a slightly higher acidity than $NaCl{\cdot}AlCl_3$. This gives rise to an increase in activity of the $MgCl_2{\cdot}AlCl_3$ catalyst

during degradation of the polymer. It was shown in the case of the thermocatalytic destruction of PIB that in the presence of $MgCl_2 \cdot AlCl_3$ the total yield of gaseous products and the yield of just isobutylene increase considerably compared to when $NaCl \cdot AlCl_3$ is used. The change in acidity of the catalyst also has an effect on the selectivity of the process with respect to the yield of monomer. The kinetic studies on a determination of the ratio of initiation of degradation of macrochains by the random mechanism to initiation of depolymerisation by the terminal group mechanism suggest that the increase in selectivity of the process is due to an increase in the role of depolymerisation by the terminal group mechanism (Table 5). The ratio of the rate constants of random initiation to that on terminal groups during degradation in the presence of $MgCl_2 \cdot AlCl_3$ is higher than in the presence of $NaCl \cdot AlCl_3$ (Table 5), although the tendency for this ratio to decrease with an increase in temperature also remains.

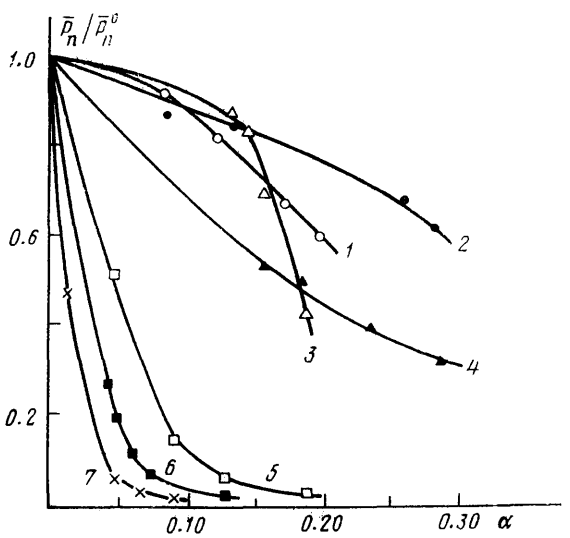


Figure 1. Dependence of relative degree of polymerisation during degradation of polyisobutylene on degree of conversion of samples of polyisobutylene. Initial degree of polymerisation: *1*, 15; *2*, 17; *3*, 20; *4*, 49; *5*, 360; *6*, 1790; *7*, 3570. Catalyst—$NaAlCl_4$, temperature—473 K.

Qualitative proof of the prevailing role of initiaiton by the random mechanism is provided by the nature of the variation in the curves of the dependence of the relative degree of polymerisation on the degree of conversion of the polymer, in particular the marked fall in $\bar{P}_n/\bar{P}_n^0$ at only small degrees of conversion of PE (Fig. 3) and the experimentally determined lack of dependence of the rate of the process on $\bar{P}_n^0$. At the same time similar results obtained using PIB suggest that there is a clearly defined dependence of the degree of conversion of the polymer on the molecular weight of the samples being degraded. Low-molecular weight polyisobutylenes (M = 800–2000) with a high content of terminal double bonds mainly undergo depolymerisation by the terminal group mechanism and the relative degree of polymerisation changes only slowly (Fig. 1, curves *1–3*). An increase in the molecular weight of PIB (Fig. 1, curve *4*) and hence a decrease in the content of C=C double bonds results in a marked increase in the proportion of initiation reactions by the random mechanism and with a very considerable increase in the initial degree of polymerisation ($\overline{M}$ = 1800–16000) (Fig. 1, curves *5–7*), when the content of terminal double bond is small, initiation by the random mechanism plays a decisive role.

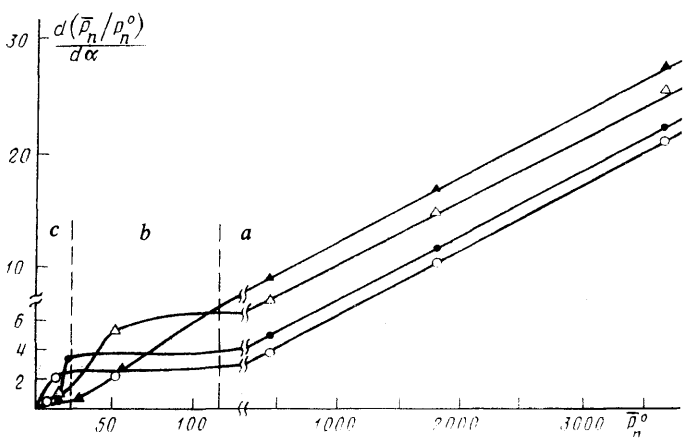


Figure 2. Change in $d(\bar{P}_n/\bar{P}_n^0)/d\alpha$ during degradation of polyisobutylene on an $NaAlCl_4$ catalyst at different temperatures: *1*, 473 K; *2*, 493 K; *3*, 513 K; *4*, 533 K.

VII. Effect of chemical structure of the polymer

For polyolefins that contain internal double bonds as well as terminal double bonds and possibly other defect groups as occurs in PE and BR, the ratio of initiation by the random mechanism to that on terminal groups varies during decomposition of the polymer.

Calculation of the kinetic parameters of catalytic degradation of PE in the presence of $NaCl \cdot AlCl_3$ shows that the values of the rate constants of initiation by the random mechanism are comparable to the rate constants of the overall process of polymer degradation (Table 6). This provides an indication of the predominance of random initiation of PE degradation and the small contribution of reactions that occur by the terminal group mechanism.

Hence, it can be maintained in general that the ratio of the number of internal labile groups (including C=C bonds) to terminal double bonds determines the nature of initiation of catalytic degradation of polyolefins and as a result has a considerable effect on the numerical values of the apparent rate constants of initiation.

VIII. Conclusion

Analysis of the currently available data on the catalytic degradation of polyolefins in the presence of different types of catalysts is able to demonstrate that acidity is one of the deciding factors in the variation in efficiency and selectivity of catalytic

degradation of polymers. However, up to the present time there has been no clear interpretation of the relationship between the acidity of the degradation catalyst and its activity and selectivity values for the majority of catalysts of polyolefin degradation (zeolites, aluminosilicates, superacids).

Table 5. Parameters of the initiation of catalytic degradation of polyisobutylene by random and terminal group mechanisms on different catalysts.

Catalyst	T, K	$k_{ti} \times 10^6$	z_t	$k_{ri} \times 10^6$	z_r	k_{ti}/k_{ri}	E_{ri}, kJ mol^{-1}	E_{ti}, kJ mol^{-1}
$NaAlCl_4$	473	1.6	–	0.2	8.1	8.1	69	47
	493	1.7	–	0.3	6.2	5.7		
	513	1.9	1.3	0.4	4.7	4.8		
	533	2.7	5.7	0.7	3.7	3.8		
$MgCl_2 \cdot AlCl_3$	473	3.35	–	0.3	8.4	10.8	70.7	45.8
	493	3.4	–	0.5	7.1	7.6		
	513	3.8	1.4	0.6	4.9	6.4		
	533	5.4	5.9	1.1	3.7	5.1		

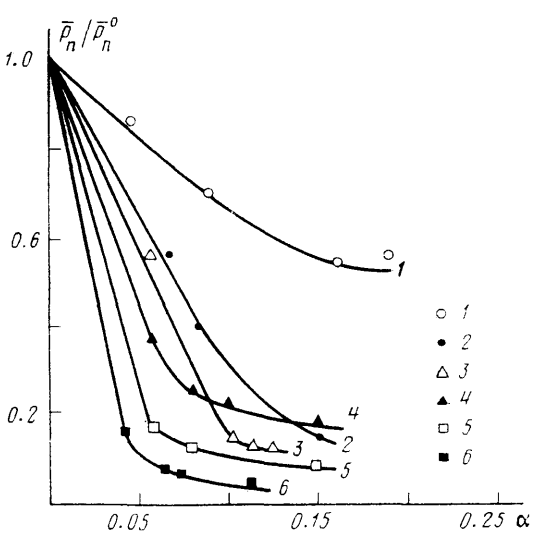


Figure 3. Dependence of change in relative degree of polymerisation on degree of conversion of samples of polyethylene with different initial molecular weights: *1*, 2 × 10^3; *2*, 2 × 10^4; *3*, 6 × 10^4; *4*, 1.45 × 10^5; *5*, 2.5 × 10^5; *6*, 2.7 × 10^5. Catalyst—$NaAlCl_4$; temperature—633 K.

It has been established that by using complex electrophilic catalysts of moderate acidity (considerably lower than the acidity of $AlCl_3$ and $HF{\cdot}SbF_5$) it is possible to increase the selectivity of the process.

The mechanism of the catalytic decomposition of polyolefins on electrophilic catalysts is based on reactions involving the formation of a polymer carbocation and its subsequent selective decomposition to form monomeric and other valuable low-molecular weight products. Initiation of the process is determined by the nature of the catalyst and the chemical structure of the macromolecules and occurs both randomly and on the terminal groups. From kinetic analysis it is possible to determine the ratio of these processes for polyolefins with different macrochain structures.

Table 6. Overall rate constants and rate constants of initiation of catalytic degradation of polyethylene by the random mechanism ($NaAlCl_4$).

T, K	$k_{ri} \times 10^7$, s^{-1}	$k_{rate} \times 10^7$, s^{-1}
573	0.25	0.93
593	0.21	1.50
613	0.95	2.80
633	1.31	6.90
653	1.71	8.70

Note: E_{ri} = 79 kJ mol^{-1}; E_a (overall reaction) = 92 kJ mol^{-1}.

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CHEMISTRY AND ECOLOGY

Proceedings of the Scientific Session of the Division of General Chemistry and Chemical Engineering of the Academy of Sciences of the USSR, Moscow, 27—28 February 1989

During the last decade humanity fully recognised the necessity for thrift as regards all kinds of natural resources and for the reduction of the anthropogenic stress exerted on the environment. This recognition has been reflected in the concept of a steady development of the world community, whose elements are already being realised in countries possessing a strong economic base.

There has been a sharp growth of attention devoted to ecological problems also in our country—both in the community and at the governmental level. Serious attention is being devoted to such problems also in the activity of the Academy of Sciences of the USSR. A "program for the biosphere and ecological research by the Academy of Sciences of the USSR" was adopted in 1989 within the framework of which the "Chemistry and Ecology" section was formulated.

Ecology and its problems are connected by many links to chemistry. These involve the chemical reactions and processes in our environment, the wide variety of chemical industries with an enormous need for resources and energy and a large amount of harmful waste, the chemical pollutants arising from power engineering and transport, and the wide-scale employment in our economy and in the social sphere of a wide variety of chemical substances and products.

However, although chemistry and chemical substances and products constitute one of the principal sources of pollution of the environment, they at the same time open the most universal and effective routes leading to the overcoming of these undesirable phenomena.

The scientific session of the Division of General and Technical Chemistry of the USSR Academy of Sciences was held on 27—28 February, 1989 and the principal aspects and specific results of studies carried out within the framework of the "Chemistry and Ecology" subprogram were discussed. The proceedings of this session are published in the present issue of the journal *Uspekhi Khimii*.

The reports combined under the heading "Chemosphere and Ecology" analyse a series of important aspects of the pollution of the environment by chemicals and describe the present state of the corresponding research. In considering the problems concerning the protection of nature, it is at the same time important not to be content with merely raising the alarm but to become involved as soon as possible in the constructive solution of such problems. In this connection, interesting reports are included in the section "Introduction of Ecological Factors into Chemical Industries" and "Introduction of Ecological Factors into Power Engineering and Transport".

Overall, the proceedings of the scientific session constitute an effective base for the provision of a systematic framework and for speeding up the work of research chemists on acute modern ecological problems.

The preparation and holding in our country of the International Conference on "Chemistry and Steady Development—A Clean Environment, Waste-Free Technologies, Effective Utilisation of Energy" in September of next year should stimulate a new wide-scale employment of the advances in modern chemical science and technology for the solution of complex ecological problems and for improving the quality of the environment.

Academician V A Koptyug
Academician O M Nefedov

I. CHEMOSPHERE AND ECOLOGY

Translated from *Uspekhi Khimii* 3 499–506 (1991)

Protection of the environment and chemical ecology

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A large amount of wide-ranging information on questions of ecology has appeared in the literature in recent years. Ecological problems are being debated not only by scientists pursuing various fields of research but also by journalists, writers, and workers associated with the arts.

Despite the accessibility and array of knowledge on ecology, it would nevertheless be advisable to examine these problems from the chemical standpoint if for no other reason because chemistry and the chemical industry are one of the main sources of disturbance of the equilibrium in the biosphere and because they may provide effective measures and routes for the protection of the environment from so-called anthropogenic activity.

In his studies in the first quarter of this century the eminent Russian scientist, V I Vernadskii, advanced the concept of the biosphere. He perceived the biosphere as the outer membrane of the planet. The Earth, situated within the limits of the atmosphere, hydrosphere, and lithosphere, is covered with living matter. As regards many of their properties the atmosphere, the entire hydrosphere, and a deep layer of the lithosphere are subjected to the same forces as living organisms throughout their life-span and evolution.

The air, soil and water form the totally integrated system of the biosphere, which supports all living matter, generates all energy, and despite its great vitality consists of fragile and vulnerable mechanisms. Vernadskii considered that the combined activity of all organisms on the Earth is the most powerful geochemical factor transforming the Earth's surface and an energy generating factor of planetary proportions. Having developed clear concepts on the role of the biosphere Vernadskii focussed his attention on the fact that the industrial and technological activities of man at the present time is having such a great effect on the change of the face of the Earth that they may be regarded as a "new" geological factor and that human forces have become commensurate with the forces of nature.

The interaction between the biosphere and humankind has proved to be the most important of the modern-day problems of science and technology which are present in abundance and the overall resolution of this problem is a priority for science and technology.

A feature of the modern era is the development of a society which is at variance with the limited life-supporting potential of the biosphere. While the activities of man did not interfere in the affairs of nature, nature herself created the essential conditions for her own development and equilibrium. Processes of self-regulation which balanced human activity have existed in nature. Traditionally this activity, which includes industrial production, has developed on the basis of the concept that nature's resources are unlimited and that the natural environment has limitless ability to undergo self-purification.

On account of compensation mechanisms and huge structural flexibility the biosphere's ecosystem until now has been somehow able to balance the consequences of man's activity. However, increasing human activity, the growth of energy use and technical power of society, and human interference detached from scientific forecasts have led to the contamination and transformation of the biosphere which is becoming an irreversible and frightening process. The resources of dry land and the oceans are becoming depleted, all elements of the environment are becoming contaminated, ecosystems are being degraded, and the biochemical cycles of matter are being impaired.

There are countless ways in which man can pollute the atmosphere, the seas, lakes and rivers. Wash waters from chemical plants, acids, alkalies, dyes and resins, mercury-containing compounds, cadmium, tin, and other metals, wastes from the petroleum, paper, cast-iron, and steel industries, wastes from tanneries, and automobile factories and mines, many tonnes of fertilisers and pesticides washed from the fields, icebergs of detergent foam, and waste products from municipal sewerage. The air, the earth, and the water have been unremittingly diluted and all of these poisonous discharges have been hidden. However the burden has now become inadmissible.

Humankind has finally understood that a strong barrier against the destruction of nature should be erected. A movement in support of the protection of nature is underway, the science of ecology has been created, the government have started to introduce legislation, and state and public organisations have been set up in order to protect the environment in which we live and in which our descendents will live.

The key problems related to ecology are problems of pollution and purification of the atmosphere and the oceans of the world, soil

erosion, depletion of the ozone layer, the global change in the Earth's climate, and the build-up of toxic substances in the biosphere. Most of these problems are associated with a combination of naturally occurring and extraneous chemical substances introduced into the biosphere, and this combination forms the so-called chemosphere. The undesirable changes in the chemosphere mainly on account of anthropogenic activity cause a fall in productivity of natural ecosystems, the death of hydrobionts and forests, and the disappearance of individual species and populations in the plant and animal kingdoms. These factors ultimately have a negative effect on society by retarding its development and they constitute a threat to the survival of humankind.

The increase in variety and quantity of industrial output also leads to an increase in the amount of wastes consequently generated including the so-called xenobiotics, which previously did not exist in nature and which in many ways are foreign to living organisms. Illnesses (allergic, genetic, teratogenic, endocrinal, etc.), which have become more frequent in recent years, are a consequence of such technogenic changes.

According to World Health Organisation (WHO) statistics 40 – 50% of human diseases are presently associated with an increase in ecological stress. Current forecasts indicate that anthropogenic changes in the environment are creating a real threat to the survival of humankind.

Man's interference in natural processes which causes large-scale changes is primarily manifested as the contamination of the atmosphere, the hydrosphere, and the lithosphere, and these are essentially questions of chemistry.

The vast expanse of the ocean of air leads certain people to the conclusion that there is no need to avoid contamination as in the case of water. However statistics on the growing discharge of chemicals into the atmosphere demonstrate that the conservation of pure air is becoming a major problem and that atmospheric pollution has now reached global proportions.

Industrial gases released into the atmosphere present the greatest danger. Huge metallurgical, chemical and oil refinery plants are concentrated in cities and industrial areas. Power plants, thermal power stations, gas-generating plants, and innumerable automobiles and large numbers of people are concentrated in such locations. With population growth and the expansion of industry the loading of the biosphere with gaseous and aerosol discharges has reached global proportions.

All industrial installations utilise a mineral fuel such as oil, coal, oil shale, solar oil, petrol, and kerosene. When the fuel is burned, in addition to carbon dioxide oxidation products of sulphur-containing compounds, oxides of nitrogen, carbon monoxide, and other harmful gases are formed. It has been calculated that industrial installations and chemical and metallurgical plants and other factories and heat and electric power plants release annually into the atmosphere more than 150 million tonnes of sulphur dioxide, 200 million tonnes of ash, and tens of millions of tonnes of aerosols.

By the year 2000 the discharge of sulphur dioxide could reach 450 million tonnes per annum. Sulphur dioxide is known to be harmful to human health even at a concentration of one part per million. The concentration of this gas reaches 5 parts per million or more in industrial areas. Sulphur dioxide is one of the most terrifying enemies of plants. This gas pollutes the air, sours fresh waters and the soil, and is a cause of acid rain, which annihilates entire forest areas. Depending on the moisture content of the air sulphur dioxide is usually converted into a sulphuric acid aerosol. Discharges of hyrogen sulphide, which is also a toxic gas affecting man and animals, are highly dangerous. Top of the league in this regard is the Astrakhan gas condensate factory, which in 1987 released more than one million tonnes of hydrogen sulphide into the atmosphere.

One of the most potent atmospheric pollutants is carbon monoxide, which enters the atmosphere in amounts reaching tens of millions of tonnes during the combustion of all kinds of fuels and especially automobile and engine fuel. It was previously believed that only high concentrations of carbon monoxide were harmful to man. However, studies have shown that the constant presence of even low concentrations of this gas causes cardiovascular diseases, stenocardia, lesions of coronary vessels, and atherosclerosis, and a decrease in the survival rate following infarction.

Factors associated with atmospheric pollution should also include the release of carbon dioxide which is increasing year by year. During the combustion of all kinds of fuels at least 1×10^{10} tonnes of carbon dioxide are released annually into the atmosphere and this gas absorbs a significant proportion of energy emitted by the Earth's surface.

Furthermore carbon dioxide does not impede the penetration of sunlight to the Earth and thereby creates the "greenhouse" effect. It has been suggested that as the concentration of carbon dioxide in the atmosphere increases there will be an increase in the quantity of thermal energy in the surface layers of the atmosphere and on the Earth's surface. By the year 2000 the content of carbon dioxide in the atmosphere may increase from 0.032 to 0.0375 and even to 0.040%. This global increase may cause climatic changes and other deleterious consequences. 1988 was the hottest year this century. The mean temperature in the eighties was found to be 0.34 °C higher than successive decades from 1949 to 1979.

On account of these alarming observations WHO has organised a working group for the study of climatic changes. However it is necessary to investigate and obtain evidence for the "greenhouse" theory, which was initially advanced by Soviet scientists. For example in the last century a similar warming up of the climate was recorded but this was followed by a cooling of the climate. Nevertheless, the danger of ecological changes caused by a cooling of the climate is very serious, since it may lead to a regression of the permafrost, thawing of ice, flooding of the land, and other disasters.

All forms of transport create great ecological losses. Exhaust gases, wash waters, and solid wastes from transport account for more than 30% of total pollution.

During the combustion of chemical fuel in the recovery of metals from ores and electrolysis of salts heavy metals (mercury, lead, vanadium, tin, etc.) are introduced into the environment and constitute dangerous sources of poisoning for humans, animals, and plants. For example with each tonne of caustic 600 grammes of mercury are lost. This metal in itself is a hazard and becomes especially dangerous, when this element is transformed into organomercurial compounds.

Contamination of the atmosphere with oxides of nitrogen and the Freon 11 and 12 type of propellants leads to the depletion of the ozone layer in the atmosphere which being in the upper layers of the atmosphere serves as a defence against the ultraviolet rays of the sun.

In normal operating periods nuclear power stations discharge gaseous aerosol products (krypton-85, xenon-133, radioactive iodine-131, and tritium) into the atmosphere. In addition to gases, solid radioactive fission products (promethium-147, ruthenium-106, cesium-137, strontium-90, zirconium-95, etc.) are also formed, and

the half-life period of these components varies from several months to thirty years. Almost all fission radioactive isotopes apart from the gaseous products undergo transformation into acidic waste solutions during the treatment of fuel elements. These solutions accumulate in nuclear chemical plants and present a difficult problem in regard to reprocessing and safe storage. The quantity of radioactive fission isotopes is increasing together with the increase in nuclear power engineering and burial of these products presents an exceptionally difficult problem. In fact when the Soviet Union constructs nuclear power stations abroad, it regulates the nuclear fuel and fuel elements, and they are returned with the radioactive fission products for reprocessing and burial. Thus there is a requirement to store not only Soviet radioactive wastes but also radioactive wastes from abroad. The safety of operation of the nuclear power stations themselves creates a special ecological problem as is exemplified by the Chernobyl disaster.

The amount of oil being extracted worldwide is in excess of three billion tonnes. Not taking into account accidents and catastrophes the losses of oil during transportation are equivalent to 1% of this figure. This implies that more than 30 million tonnes of oil are transferred largely into the oceans of the world. In the USSR 400 million tonnes of petroleum products are transported per annum by railroad alone. These products pollute the soil and water and other elements of the environment. In the USA petroleum products are conveyed to the consumers by a system of supply lines. A 2200 thousand kilometer network of pipelines enable losses of fuel to be sharply reduced. Of course oil is less harmful to nature than other pollutants but the huge volume produced and the corresponding volume of losses make a significant contribution to the contamination of the natural environment.

Large-scale pollution of water resources is taking place. The total quantity of water in the hydrosphere is 1400 million cubic kilometres, and 97% of this water is present in the oceans and seas, 2.14% exists in the form of ice, while only 0.29% is present in the form of fresh water on the land. In the USSR the amount of freshwater available is extremely small. Furthermore river basins including the Volga basin are being continually polluted. The ecological situation of water basins is deteriorating as a result of the multitude of chemical plants, paper and pulp mills, oil refineries, and textile factories located in areas of water. For example a single chemical plant on the banks of the Volga annually discharges forty five thousand tonnes of wastes from aniline dye manufature into the Volga.

Thousands of establishments situated along river banks in the USSR discharge annually into these rivers more than three million cubic metres of dilute acids, approximately two million cubic metres of liquid wastes including petroleum products, and millions of cubic metres of water contaminated with salts, alkalies, mineral oils, and dyes. Where do these wastes come from? Contaminated water is the result of modern-day industrial technology. The production of one tonne of synthetic fibre generates 500 cubic metres of sewage water, and this volume is increased several-fold when one takes into account the dilution of the sewage.

Present-day industrial manufacturing processes create enormous irreversible losses of fresh water leading to an increase in shortages of fresh water.

Water is also polluted at farms in which plant protection measures are adopted. We live in an age in which chemicals are extensively used in agriculture and forestry. In addition to artificial fertilisers large quantities of chemical agents are used for pest and weed control. They are of great benefit by helping to preserve the harvests of agricultural crops. For the Soviet Union alone they preserve 18–20% of the harvest.

However on account of the large-scale and at times incorrect methods of application these substances have become a serious factor in regard to the increase in ecological stress. The use of chemical products in agriculture and forestry has become the target of acute and well-founded criticism. Many negative aspects of the use of pesticides are associated with the fact that scientifically based use recommendations are abused in practice. Rates of application, use periods, and instructions for use are disregarded. However, there is another side to this problem.

In the USSR large miscalculations have been made in the elaboration of chemical systems for plant protection and the justification of their use. This situation has led to the extensive development of the production of several kinds of chemicals harmful to man and to the concentration of large quantities of dangerous chemicals and chemical plants in certain areas of the country. Underestimation of the danger of excessive production of organochlorine compounds has left its mark.

The danger of chlorine production is determined not only by the acute and chronic toxicity associated with the production of large tonnages of compounds such as hexachloran, DDT, polychlorocyclodienes and other compounds but also by polychloropolycyclic compounds (PCPC)†, which are formed as impurities in many processes involving the use of elemental chlorine and chlorine-containing substances together with aromatic organic compounds (dioxin, dibenzofuran, chlorazobenzene, and similar substances) and which are responsible for significantly more harmful and distant effects. These substances are particularly dangerous on account of their high biological activity, high chemical stability in the environment and in living organisms and their ability to be transferred from one living organism to another in nature. Even when present in negligible concentrations PCPC compounds suppress the immune system of organisms and reduce their ability to become adapted to the changing conditions of the outside world.

This type of action is accompanied by an increase in the sensitivity of the organisms to infection, particularly viral diseases, and by a decline in mental and physical working capacities. At higher concentrations (several tens of parts per trillion) PCPC compounds are found to exert a mutagenic, carcinogenic, teratogenic, and embryotoxic effect, and these compounds adversely affect the central and peripheral nervous sytem, the alimentary canal, and other organs.

Polychloropolycyclic compounds primarily 2,3,7,8-tetrachlorodibenzo-*p*-dioxin or simply dioxin inhibit all aerobic microorganisms in ecosystems, the organisms known to be responsible for the accumulation of organic substances and for the conservation and growth of the organic potential. In the human body these compounds inhibit genetically encoded mechanisms of adaptation to the natural environment, i.e. the immune system.

Intensive accumulation of PCPC compounds in nature commenced in the period in which DDT and hexachloran production unfolded. Especially large quantities of these agents began to be produced after plants were created for the production of polychlorophenols and polychlorinated biphenyls. However the manufacture and use of chlorine-containing pesticides is not the only source of PCPC compounds.

† For more detailed information see the paper by A F Kolomiitsa "Polychloropolycyclic xenobiotics" in the present issue.

These compounds are also formed in paper and pulp mills, when the paper pulp is bleached with chlorine or chlorinating agents. One cannot rule out the possibility that these xenobiotics will appear in water during chlorine disinfection procedures.

Dioxin and dienzofuran may appear in exhaust gases in non-optimised regimes for burning rubbish and wastes containing organochlorine materials. Burning articles made from polyvinyl chloride has proved to be particularly dangerous.

Exacerbation of the medical and ecological situation in cotton-growing regions of central Asia and Moldavia and the rice-growing areas in the Sea of Azov region, and the stressed state of ecosystems in the Sea of Azov and the Caspian Sea in may ways is the result of the underestimation of the effects of chlorine production and plants from which PCPC compounds are introduced into the natural environment. For example on the territory of Uzbekistan alone over the last decade approximately six thousand tonnes of chlorine-containing pesticides (in terms of active ingredient) have been used each year, despite the fact that the use of these compounds has been banned abroad.

The herbicide, propanil, which contains harmful polychlorazo-benzenes and the use of which is prohibited abroad, has been introduced and is extensively used in this country. In the USSR production of hexachloran and DDT continues. Hexachlorophene and dichloraniline, which contain harmful xenobiotics or their precursors, are also produced.

Certain pesticides which have been banned abroad have until recently been imported (for example keltan, tophos, diuron). In this country the large-scale production of polyvinyl chloride, and articles manufactured from this compound is carried out and the use and destruction of the latter are not controlled. A large number of outmoded pulp and paper mills are still in operation and in these establishments there are no facilities for the effective purification of sewage waters, and treatment of drinking water with chlorine has still not been replaced by ozonisation. It is possible to list more examples of this type.

These inconsistencies primarily arise as a result of a lack of any understanding of ecological problems and a low level of ecological awareness. Thus, so far no scientific strategies for the assessment of the ecological hazards of chemical reagents have been elaborated in the USSR. There is a lack of methodology for the prediction of ecologically acceptable routes for the advancement of chemical sciences and industry. Fully developed chemical ecology does not yet exist in this country.

Resolutions of questions concerning the control of chemical pollution reflect outdated approaches to the evaluation of the ecological hazard of chemical agents, since these approaches are based on the study of the properties of individual chemicals. Such a strategy does not take into account many associated factors. Under real life conditions a living organism in nature is exposed to the action not of a single substance but a combination of all naturally occurring and man-made chemical compounds present in the biosphere. In this case it is essential to take into acocunt the possible additive, antagonistic, and synergistic effects of the compounds in the chemosphere. For example in the presence of dioxins there is an abrupt increase in the hazard associated with the action of mycotoxins (aflatoxins and nivalenols) and carcinogen precursors (arylamines) and neurotoxic poisons on the body.

It should be emphasised that it is not the susbtances themselves but the impurities, decomposition products, and products of metabolism which may affect man and nature. One should also take into consideration the fact that, with the appearance of foreign substances in natural environments and their associated harmful effect on ecosystems, a change in the composition of the chemosphere occurs and the direction and consequences of this type of change can not yet be predicted.

The examples and facts presented indicate the importance and significance of the action of chemicals on the stressed state of the biosphere and the need to thoroughly investigate questions of chemical ecology.

It is evident from the experience gained in ecological studies carried out in the industrially developed countries that comprehensive characterisations of the ecotoxicity of chemical agents may be obtained on the basis of a fundamental knowledge of the chemosphere and its effect on ecosystems. Moreover it is surprising that the "Project of Concepts in the Programme of Biosphere and Ecology Studies by the Academy of Sciences of the USSR in the Period up to the Year 2015", which was assessed in the general assembly of the Academy of Sciences of the USSR devoted to ecology, does not include a unit concerned with the chemistry of the biosphere and chemical anthropogenic effects on nature as one of the main directions of research. Questions concerning the chemistry of the environment included in separate units of the project do not span the complete range of problems of chemical ecology but reflect an outmoded utilitarian approach to the evaluation of the ecological hazards of chemical agents.

It would be expedient to include "The Study of the Chemosphere" as a separate priority direction in this project. Fundamental studies within the framework of this unit should provide for the following sections:

—The establishment of the fundamentals of ecotoxicology as a science concerned with the effect of chemical agents on the biosphere and the development of methods of ecological normalisation. In this case it would be necessary to start from the position that, when chemical agents are used for intensive farming practices, efforts to achieve maximum bioproductivity are incompatible with the conservation of the natural environment. Thus from the ecological standpoint it is necessary to approach so-called intensive agricultural technology with great caution.

—The elaboration of scientific bases for the prediction of ecologically safe routes for advancement in the chemical industry, the creation of ecologically balanced industrial technologies and use of chemical agents. In this case the potential hazards presented by the chemical plants themselves should be assessed. Mathematical modelling of the spread of all kinds of pollution is also a necessity. At this stage it would probably be necessary to include a study of the problem of alternative fuels and studies on the sharp reduction in water consumption by industry, as for example in the "close-up" of water systems.

—The creation and organisation of essentially novel resource-saving technologies in which no wastes or very small quantities of wastes are generated.

—The elaboration of effective techniques for the purification of gaseous, liquid and solid wastes based on sorption, membrane, catalytic, and other technological processes.

—The development of pathways for the prevention of chemical and microbiological contamination of agricultural products and the environment.

—The elaboration of scientific strategies for improving the sanitation of ecosystems adversely affected by chemical agents.

—The creation of non-persistent pesticides and other chemical agents which are readily degraded and rapidly assimilated into the

natural environment and which have no harmful effect on the environment.

Information on the state of natural systems especially in regard to chemical and other kinds of contamination is of enormous importance for the protection of the environment. Most of the operative information on the biosphere is currently provided by the Earth's artificial satellites which have a resolving power of better than 10 m. However such information is suitable for "the monitoring of areas" but is inadequate for "the monitoring of the state" of natural systems. The elaboration of convenient techniques, equipment, and instruments for obtaining quantitative measurements of environmental parameters is of great importance for attaining progress in terrestrial monitoring. In this regard the design of instruments and the development of techniques which employ chemical or physicochemical principles will play an important role. The design of novel and readily obtainable instruments and techniques will improve the accuracy, validity, and range of measurable parameters in natural systems.

These are merely a few of the directions for research into the field of chemical ecology and they will undoubtedly be supplemented by new directions in the elaboration of a chemical ecology programme.

On account of the sharp increase in potential hazards to man and nature posed by the accumulation of xenobiotics in the environment, special national programmes have been organised on this aspect of chemical ecology by the industrially developed countries and through international collaboration. For example since 1980 international conferences on dioxin have been held. Of the major producers and users of chlorine products only the Soviet Union is not participating in the international collaboration on this problem and so far has no kind of programme for engaging in research into this problem. Extension of international collaboration on questions of chemical and other aspects of ecology is also an urgent necessity and should constitute a significant part of the programmes being prepared and projects targetted towards the protection of the environment.

The main objective of chemical ecology is the conservation of the vital qualities of the biosphere and the prevention of progressive pollution of the natural environment by reorganisation of anthropogenic activity which would promote the growth of industrial and agricultural output and which would exclude any unfavourable effect on nature. Ultimately the problem concerns the elaboration of conditions and measures which would promote the further development of human civilisation and the survival of humankind.

Translated from *Uspekhi Khimii* **60** 507–513 (1991)

The chemical physics of the ozone layer

V L Tal'rose, I K Larin
Institute of Energy Problems of Chemical Physics,
Academy of Sciences of the USSR

The ozone layer exerts a significant effect on the properties of the middle atmosphere and creates the conditions under which the flora and fauna can exist on the Earth's surface. These features of the ozonosphere are in a sense caused by the unique physicochemical properties of ozone. The ozone molecule absorbs solar radiation intensely in the wavelength region below 290 nm, which is harmful to biological matter, and also (although less intensely) the "terrestrial" infrared radiation at a wavelength of 9–10 μm thereby enhancing by 10% the greenhouse effect caused by carbon dioxide and other radiatively-active components of the atmosphere. On the other hand ozone molecules are highly reactive on account of the low value of the energy bond between the "third" oxygen atom and the oxygen molecule. It is correct to say that the chemistry of the atmosphere and the troposphere and particularly the chemical processes associated with anthropogenic contaminants and their destruction in the atmosphere are controlled by ozone, albeit with the loss of the molecule itself.

As regards the effect of atmospheric ozone on global ecology it can be ascertained that the ozone layer is important as a factor providing a biologically safe level of ultraviolet radiation close to the Earth's surface and is involved in the conservation of the Earth's overall climate and controls the content of certain anthropogenic and natural contaminants in the atmosphere. It is noteworthy that the latter usually is under the shadow of the opposite problem, the effect of anthropogenic impurities on the ozone content. However these problems are evidently closely associated.

The stratification of the middle atmosphere caused by the change in temperature and distribution of ozone with altitude is shown in Fig. 1. The stratosphere contains the main reserves of ozone. The maximum concentration is found at an altitude of 20–25 km. At these altitudes the relative content of ozone in the atmosphere is about 1 ppm, and the total quantity of ozone in the atmosphere is equivalent to 3.3 billion tonnes. This quantity would correspond to a gas layer 3 mm in depth at normal temperature, and pressure. It should also be mentioned that ozone is not uniformly distributed over the Earth. On average there is less ozone in the tropics and more at the poles. In addition at all latitudes the total content of ozone changes with the seasons.

The above-mentioned aspects of the ecological significance of ozone will now be discussed.

I. The role of the ozone layer as a filter for biologically harmful ultraviolet radiation

This effect is caused by the fact that short-wave radiation at $\lambda < 300$ nm is harmful to many biological molecules, especially for DNA. The ozone layer which exists at present successfully fulfils a radiation protective function which may be judged according to the change in the intensity of sunlight in the 210–290 nm wavelength range with altitude. There is a distinct dip in the intensity of

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sunlight in the above-mentioned wavelength range. However, in the 300 nm wavelength region ozone does not so effectively absorb light and the light intensity rapidly increases with increase in wavelength.

It is generally agreed that the increase in skin cancer diseases in people living at low latitudes and other biologically unfavourable consequences for the fauna and flora which have not been fully investigated is the result of a decrease in the ozone content of the atmosphere (possible also as a result of the influence of anthropogenic factors).

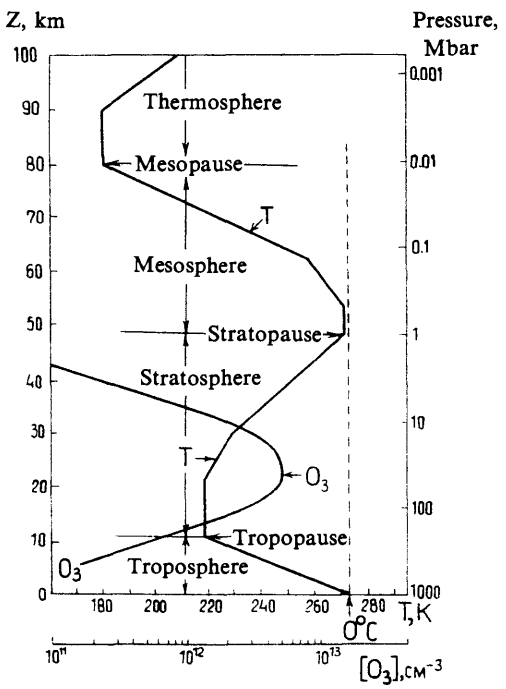


Figure 1. Stratification of the Earth's atmosphere.

II. The ozone layer as a climate-forming factor

The effect of the ozone layer on the climate is also associated with the absorption of light not only in the ultraviolet but also in the infrared region. It has already been mentioned that in absorbing infrared radiation emerging from the Earth's surface the ozone layer intensifies the greenhouse effect. However the question of the link between ozone and the climate is much more complex, because of the significantly larger number of physical and chemical factors which may affect the content of ozone in the atmosphere, since the effect of ozone on the temperature of the Earth's surface and climate is dependent on the altitude at which a change in the content of ozone occurs.

When the ozone content changes, the overall temperature effect is dependent on the absorption of short-wave and long-wave radiation. The plot in Fig. 2 illustrates how the temperature of the Earth's surface will change if the ozone content increases at different altitudes within a narrow range of altitudes when there is 3% change in temperature throughout the entire column. It is evident that up to an altitude of 30 km an increase in the content of ozone will lead to a warming of the Earth's surface and at altitudes above 30 km there will be a cooling of the Earth's surface. In this case the maximal effect will occur, when the ozone content changes in the tropopause region. At these altitudes the effect may be attributed to absorption and over-irradiation by the "terrestrial" infrared radiation at a wavelength of 9–10 μm.

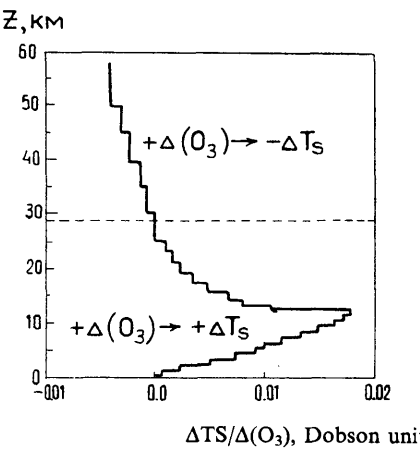


Figure 2. "Radiation" change in the temperature at the Earth's surface when the total content of ozone changes by 3% on account of the local change in ozone content at different altitudes[1] (D. U. = Dobson units).

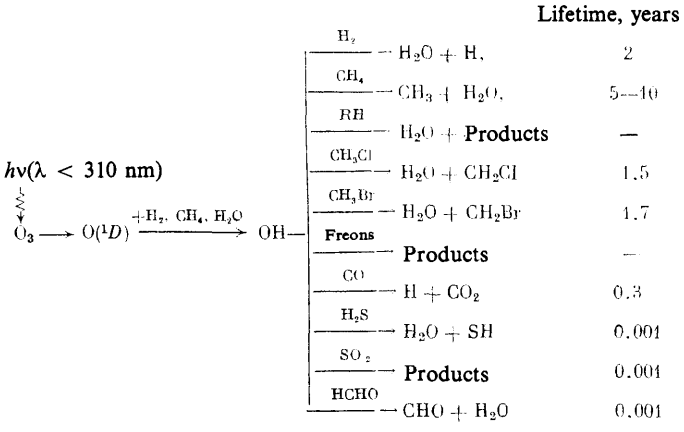
It is known that the greenhouse effect reaches a maximum at the maximal temperature contrast between absorbed and emitted radiation and that the temperature reaches the lowest values in the tropopause region.

"Cooling" as a result of the increase in content of ozone at altitudes greater than 30 km is associated with the absorption of solar radiation.

The possible change (according to data issued by the World Meteorological Organisation) in temperature of the Earth's surface within 50 years as a result of a change in the composition of microcontaminants in the atmosphere including ozone during expansion of industrial and agricultural production is shown in Fig. 3. It is apparent from assessment models that the ozone content will increase in troposphere and decrease in the stratosphere. This leads to effects acting in one direction and being additive. In this regard one should emphasise that these evaluations are not highly accurate, since it is difficult to take into account all feedbacks which arise in the system. The temperature change range for the various microcontaminants corresponds to the potential range of changes of their content within fifty years. It is evident that the maximum possible climatic effect of ozone may be even greater than that of carbon dioxide.

III. Atmospheric ozone as a factor in the chemical degradation of contaminants entering the atmosphere

It has been mentioned above that chemically active solar radiation with a wavelength shorter than 300 nm does not penetrate the troposphere and in the photochemical sense one might say that eternal night reigns. However various chemical processes occur in this short-wave "darkness" which are caused by the absorption of longer wavelength ultraviolet radiation by ozone. The mode of action of ozone towards anthropogenic and natural atmospheric components in the troposphere is presented below. The lifetimes of the atmospheric components governed by their reactions with the hydroxyl radical are also presented below. The basis of this mechanism is that photolysis



of ozone by light with a wavelength of 300—310 nm leads to the creation of metastable excited oxygen atoms in state ^1D with an energy of 1.97 eV and a radiative lifetime of 110 sec (i.e. very great in comparison with the time between collisions under tropospheric conditions). By reacting with water vapour, hydrogen and methane the $O(^1D)$ radicals form the hydroxyl radical, which in turn interacts with many anthropogenic and natural contaminants, thereby determining their lifetime in the atmosphere.

The mechanism described is an important component of the overall mechanism for the removal of contaminants from the troposphere and, as can be seen below, its actual existence may lead to the protection of the ozonosphere from certain Freons.

One should mention that similar processes also occur in the stratsophere, although in this case short-wave radiation is the main factor acting upon the Freons, and furthermore from the ecological standpoint these processes are not of such key importance as in the troposphere.

The ecological importance of the ozone layer and therefore the reason why it is essential to conserve this layer unchanged has already been mentioned.

Of all the anthropogenic factors which are potentially damaging to the ozone layer the present authors are only focussing on those Freons, which are generally considered to present the greatest hazard to the ozonosphere. This conclusion is based on results obtained by many authors over the past fifteen years from numerical modelling and from laboratory data and full-scale measurements.

An example of a model prediction of the change in content of ozone in the presence of Freons and other anthropogenic and natural contaminants is presented in Fig. 4. It is apparent from these data that the ozone content may significantly decrease with increase in the production of Freons (one has in mind mainly Freons 11 and 12).

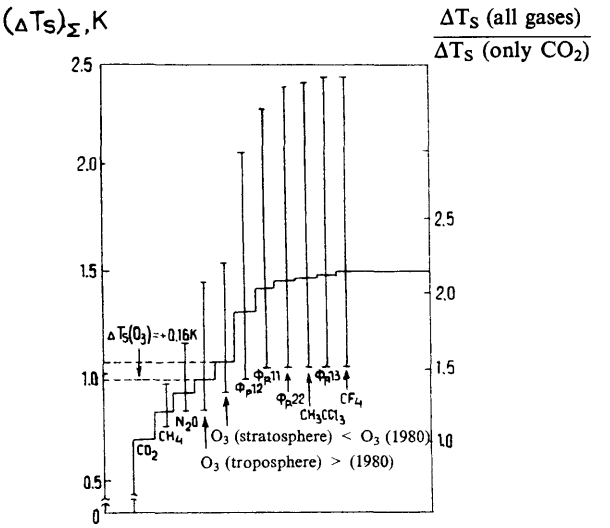


Figure 3. Change in temperature of the Earth's surface within fifty years as a result of the increase in various minor components in the atmosphere.

As regards the experimentally determined ozone trend, according to data obtained with the aid of the American satellite Nimbus-7 between 1978 and 1985 there was a 2.6 to 10% decrease in the ozone content in different latitudinal zones and an increase in the content of chlorine, and the anthropogenic proportion of the latter is nowadays one third of the total number of chlorine particles in the atmosphere.

Finally the observation in 1985 of the so-called Antarctic ozone "hole", which is characterised by a decrease of tens percent of the total content of ozone in this region in spring, supports the argument that the Freons pose a real threat to the ozonosphere.

These findings have led to the adoption of international agreements on refrigeration and the subsequent phaseout of the production of ozone-destroying Freons, which are the main source of supply of anthropogenic chloride to the stratosphere. One has in mind the Vienna convention on the protection of the ozone layer (23 May 1988) and the Montreal Protocol of the convention adopted in September 1987 and ratified by the Soviet Union in September 1988. Essentially the question concerns the prospects of renouncing the production of ozone-destroying Freons and replacing them by ozone-friendly compounds, ideally by Freons which possess the same physicochemical and biological properties but which do not destroy the ozone layer.

As a result the need arose to compare the extent of the hazard which different Freons presented to the ozonosphere and to select the less active so-called alternative compounds.

In order to meet this objective it was at first necessary to answer the question why are certain Freons harmful while others present no

hazards for the ozonosphere. In order to answer this question it was necessary to understand the mode of action of the Freons on stratosphere ozone. The mode of action is relatively well understood and in general terms all Freons, which enter the stratosphere, undergo photodissociation in the presence of solar ultraviolet radiation with emission of chlorine atoms or atoms of other halogens which destroy ozone in the following chain of reactions:

$$Cl + O_3 \rightarrow ClO + O_2,$$
$$ClO + O \rightarrow Cl + O_2.$$

In each pair of reactions of this type two particles of so-called odd oxygen, O and O_3, disappear while the chlorine atom is conserved, thereby enabling one chlorine atom to enter the stratosphere to destroy up to 100 000 ozone molecules. This "chemical amplification" is the reason for the potential hazard of Freons for the ozone layer.

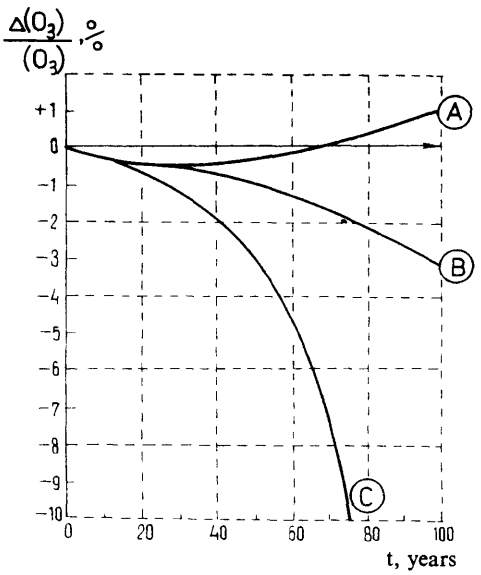


Figure 4. Change in the total content of ozone for different scenarios of increase in anthropogenic contaminants in the atmosphere[1]: A, an increase in content of CH_4 by 1% per annum; N_2O, a 0.25% increase per annum; CO_2, a 0.5% increase per annum in comparison with the level of 1980 (without any increase in content of Freons); B is A + a 1.5% increase in the content of Freons per annum in comparison with 1980; C is A + a 3% increase in the content of Freons per annum in comparison with 1980.

Thus if Freons undergo photodissociation or by some other route supply halogen atoms to the stratosphere, the ozone will be destroyed.

If the Freons underwent photodissociation or were destroyed in the troposphere, ozone-destroying particles would not appear in the stratosphere, since they may normally be rapidly washed on to the Earth's surface.

Thus a search for compounds which present no hazard for ozone would involve the identification of compounds which are destroyed in the troposphere.

It can be demonstrated that of all possible processes for the destruction of Freons in the troposphere the most important are those reactions with a hydroxyl radical and reactions involving photodissociation in the presence of light with a wavelength of more than 300 nm entering the troposphere.

The relative hazard of chlorine-containing Freons may be quantified according to the following formula:

$$\xi = W_{str}/(W_{str} + W_{trop}),$$

where W_{str} and W_{trop} is the rate of destruction of the Freon in the stratosphere and troposphere respectively. According to this formula the hazard rating of Freons 11 ($CFCl_3$) and 12 (CF_2Cl_2), which are extensively used nowadays and which are not destroyed in the troposphere, is equal to unity, while for the required ideal Freons, which undergo total degradation in the troposphere, a hazard value of zero will be obtained.

Knowing the concentration of hydroxyl radicals in the troposphere it is possible to find the minimal value of the rate constant for the reaction between the Freon and OH so that this process could have competed with the photodissociation process of Freons 11 and 12 in the stratosphere giving a lifetime of 100 years, a value typical of ozone-destroying Freons. Setting the characteristic reaction time of the Freons with OH to 100 years it is found that the required value of the rate constant should be equal to or in excess of the value of 3×10^{-16} cm^3 s^{-1}.

In fact there is a larger group of Freons with a rate constant value for the reaction with OH significantly higher than this minimal value, and the lifetime is less than 100 years. These compounds include Freons containing hydrogen atoms which can be detached by the hydroxyl radical. Freons which contain no hydrogen atoms, do not react with OH, and hence they are not degraded via this route in the troposphere. This group of compounds includes Freons 11 ($CFCl_3$), 12 (CF_2Cl_2), 113 ($C_2F_3Cl_3$), 114 ($C_2F_4Cl_2$), and 115 (C_2F_5Cl) which are extensively used in refrigeration technology and other branches of the economy and which are considered to be ozone-destroying compounds. It also follows that it could have been possible to find a substitute for these ozone-destroying compounds. However, this is not such a simple objective, because in a decomposition in which a hydrogen atom is detached from the molecule while the remaining radical can still travel around the troposphere the halogen (chlorine or bromine) remains a hazard for the ozonosphere. This reduces the problem to the chemical (with respect to the subsequent collision of the radical) or photochemical "troposphere" fate of this radical, a problem which still requires investigation.

For this reason the prediction of the extent of the hazard for ozone based on the photo-detachment of the dangerous halogen by troposphere ultraviolet radiation would be a more realistic approach.

Of those Freons which are being developed in the MGO Tekhnokhim in Leningrad as alternative compounds, three Freons are currently under investigation in the Institute of Energy Problems of Chemical Physics, Academy of Sciences of the USSR, i.e. Freons 123 ($C_2HCl_2F_3$), 134 ($C_2H_2F_4$) and 114B2 ($C_2F_4Br_2$). It has been found that with all of these compounds the rate constants of the reactions with free hydroxyl are such that for at least two of them (if these reactions would be adequate) degradation would primarily occur in the troposphere. Unfortunately the extent of

photodissociation of these two compounds by troposphere ultraviolet radiation was found to be extremely low.

The prediction in relation to the third compound, $C_2F_4Br_2$, is more realistic. The extent of light absorption in the 300 nm region was found to be low (10^{-22} cm^2) but adequate, so that $C_2F_4Br_2$ underwent photodissociation primarily in the troposphere. Nevertheless on account of the significantly greater efficiency of bromine particles in comparison with chorine particles the hazard of $C_2F_4Br_2$ was found to be greater than that of for example Freons 11 and 12.

Thus the problem of the assessment of the hazard of alternative compounds can be considered to be correctly set up but further studies are necessary in order to resolve this problem.

References

1. *NASA Reference Publication, No. 1162,* Acad. Press, New York, etc., 1986

Translated from *Uspekhi Khimii* **60** 514–520 (1991)

Mathematical modelling of the distribution of atmospheric contaminants taking account of chemical transformations

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The troposphere is the layer of the atmosphere adjacent to the surface of the Earth. Although the altitude of this layer is small, no more than 11 km, it plays a dominant role in the chemical processes which take place in the atmosphere. Various chemical impurities enter the troposphere, originating both from the Earth's surface as a result of natural geological, biological, chemical and physical processes, and from the upper layers of the atmosphere. In recent years, a considerable proportion of substances entering the troposphere have stemmed from anthropogenic influences, their strength being in some instances comparable to that of natural sources. A very important outcome of the anthropogenic influences is the emission into the atmosphere of substances which either do not occur in the natural state, or have until now been present in very small concentrations as, for example, freons. This may have completely unexpected and hardly foreseeable consequences.

On entering the atmosphere, the impurities become immediately involved in processes of two types:
(a) physical dilution and transport caused by different processes of diffusion and motion of air masses;
(b) chemical transformations.

The aim of the present work is to describe secondary mechanisms of atmospheric pollution, associated with the chemical transformation of impurities in the troposphere, and modelling of these mechanisms combined with hydrometeorological processes.

1. Chemical transformation of substances in the troposphere

Let us consider the possible ways of chemical transformation of substances in the troposphere. The following can be regarded as the main impurities in the troposphere: O_3, CO_2, CO, NO, NO_2, NH_3, CH_4, H_2, SO_2, CH_2O, H_2S, etc.[1] Under typical conditions (at a temperature of 25 °C) all these substances are stable enough. With few exceptions, they do not react with each other or with the main components of the atmosphere. A typical exception is apparently nitric oxide, capable of entering the reaction

$$2NO + O_2 \rightarrow 2NO_2,$$

However, the rate of this reaction, too, is insignificant as long as the NO concentration is low. Nevertheless, chemical transformations in the atmosphere do occur.

The main reason for these chemical reactions is the effect of solar radiation on constituents of the atmosphere.[2] The spectrum of solar radiation measured at the Earth's surface and in the stratosphere, is shown in Fig. 1. It is clear from it that only photons with wavelengths in excess of 300 nm reach the surface of the Earth. Thus in the troposphere photochemical dissociation of oxygen, and even to a greater extent that of nitrogen, into atoms is impossible, although some impurities may undergo photolysis. Table 1 presents some information on these components.[3]

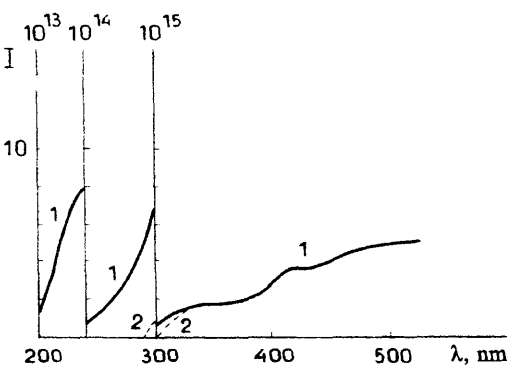


Figure 1. Spectrum of solar radiation.[3] *I* is the number of photons per second reaching an area normal to their propagation: *1*, in the stratosphere; *2*, at the Earth's surface.

It can be seen from the table that the number of substances undergoing photochemical dissociation in the atmosphere is small. Yet some of these substances, for example, HNO_2, H_2CO, NO_2, and O_3, may exhibit very high dissociation rates, their lifetimes in the troposphere being as short as a few hours. However, not all these processes play an important part in the elimination and transformation of tropospheric substances, since the path a particular substance has entered the atmosphere is also important. For example, the photolysis of nitrous acid HONO, which proceeds at a high rate, leads to the formation of OH and NO radicals, but then nitrous acid itself is formed in the atmosphere (if one excludes its anthropogenic origin) as a result of the reaction between OH and NO particles:

$$OH + NO \rightarrow HONO.$$

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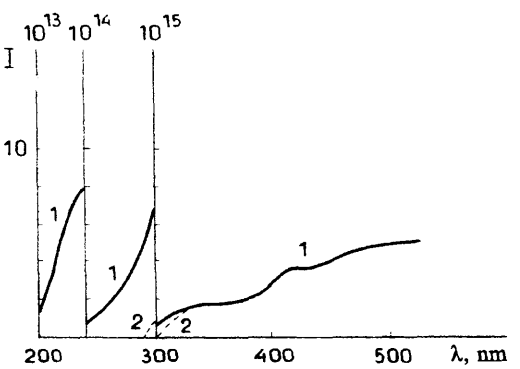


Figure 1. Spectrum of solar radiation.[3] *I* is the number of photons per second reaching an area normal to their propagation: *1*, in the stratosphere; *2*, at the Earth's surface.

It can be seen from the table that the number of substances undergoing photochemical dissociation in the atmosphere is small. Yet some of these substances, for example, HNO_2, H_2CO, NO_2, and O_3, may exhibit very high dissociation rates, their lifetimes in the troposphere being as short as a few hours. However, not all these processes play an important part in the elimination and transformation of tropospheric substances, since the path a particular substance has entered the atmosphere is also important. For example, the photolysis of nitrous acid HONO, which proceeds at a high rate, leads to the formation of OH and NO radicals, but then nitrous acid itself is formed in the atmosphere (if one excludes its anthropogenic origin) as a result of the reaction between OH and NO particles:

$$OH + NO \rightarrow HONO.$$

Therefore, the formation of HONO represents more of a sink of OH radicals than a source of them, so that a physically maintained equilibrium should exist in the troposphere

$$OH + NO \underset{h\nu}{\rightleftarrows} HONO.$$

Table 1. Chemical transformations of substances in the troposphere.

Substance	λ, nm	Photochemical reactions	Quantum yield
O_3	440÷850	$O_3 \rightarrow O(^3P) + O_2(^3\Sigma)$	~1
	300÷360	$O_3 \rightarrow O(^3P) + O_2(^1\Sigma \text{ or } ^1\Delta)$	~1
	200÷320	$O_3 \rightarrow O(^1D) + O_2(^1\Delta)$	~1
H_2CO	300÷365	$H_2CO \rightarrow H_2 + CO$	0.5÷0.6 [4]
	300÷330	$H_2CO \rightarrow H + HCO$	0.3÷0.5 [4]
NO_2	368	$NO_2 \rightarrow NO + O(^3P)$	~1 (λ = 313 nm)
HONO	370	$HONO \rightarrow OH + NO$	~1
HNO_3	300	$HNO_3 \rightarrow OH + NO_2$	~1
H_2O_2	254	$H_2O_2 \rightarrow 2OH$	~1

The situation is similar with nitric acid, hydrogen peroxide, and formaldehyde. The photodissociation of NO_2 cannot likewise result in a rapid transformation of impurities, since the former process involves the formation of an oxygen atom in the ground state $O(^3P)$. In the atmospheric conditions with a high content of oxygen, this atom reacts almost immediately with O_2 to form ozone.

The photolysis of ozone occurs in two ways. In the long-wavelength region ($\lambda > 320$ nm), photolysis brings about the formation of an oxygen atom in the ground state, $O(^3P)$, whereas at shorter wavelengths an oxygen atom in the excited state, $O(^1D)$, is formed. A feature of this atom is that it can react with water molecules, yielding two OH radicals:

$$O(^1D) + H_2O \rightarrow 2OH.$$

It is these reactions, resulting in the formation of OH radicals, that are responsible for nearly all the variety of chemical processes in the troposphere. It is worth noting that ozone enters the troposphere from the stratosphere,[1] although in the event of a high level of atmospheric pollution, one should take account of ozone sources within the troposphere.

Fig. 2 presents a scheme illustrating the general character of the chemical reactions involved. Its most characteristic feature is the occurrence of chain reactions of the type $OH \rightarrow HO_2 \rightarrow OH$. However, the chain lengths are short, being no more than several units in the layer adjacent to the surface of the Earth. Another peculiarity resides in the fact that the initial transformations of stable impurity components begin with reactions involving the OH radical. For example, the transformation of methane in the atmosphere begins with the reaction

$$OH + CH_4 \rightarrow CH_3 + H_2O,$$

followed by the reactions

$$CH_3 + O_2 \rightarrow CH_3O_2,$$

$$CH_3O_2 + NO \rightarrow NO_2 + CH_3O,$$

$$CH_3O + O_2 \rightarrow HO_2 + CH_2O,$$

$$NO_2 \xrightarrow{h\nu} NO + O,$$

$$O + O_2 \rightarrow O_3 \text{ etc.}$$

This means that substances incapable of reacting with the OH radical will have very long lifetimes, as found in the case of freons.

To describe the scheme presented in Fig. 2, one should consider approximately 40 reactions. The question is therefore often asked whether the number of reactions that need to be considered could be made smaller. As previously mentioned, the key species responsible for the transformations in the troposphere is the OH radical. The above question may be therefore worded as follows: let us assume that a reaction is important if a change in its rate by a factor of 2 results in a change in the hydroxyl concentration of 10% or more. In this case we would need to consider only 10 reactions. If the same assumption is made also to apply to all the intermediate radical species, one should consider 24 reactions.

Hence it is impossible to reduce substantially the number of reactions that need to be taken into account without a loss in the accuracy of description. It is worth noting that the validity of the kinetic description is supported by the fact that calculated concentrations of different substances agree fairly well with those obtained experimentally.[5] This allows us to formulate and solve the more complicated problem, namely simultaneous description of the processes of the transport and transformation of impurities.

2. Mathematical model of the transport and transformation of impurities

To describe the processes of the transport of impurities that would take account of chemical reactions we need mathematical models that will adequately reproduce from the physical viewpoint the motion of the atmosphere over the Earth's nonuniform surface, redistribution of various pollutants in the lower layers of the atmosphere, their transport to the upper levels, and incorporation into the system of atmospheric circulation.

One of the main 'blocks' of mathematical models developed for the solution of environmental problems is that describing the processes of the transformation of impurities. The design of such a block is governed by the fact that the atmosphere of each industrial region or city is characterised by a specific assortment of substances of natural and anthropogenic origin which may interact with each other and undergo transformations. Therefore the block describing the transformation of impurities should be specially adapted to fit the environmental conditions of the sites under investigation.

Atmospheric impurities form a multicomponent medium. The different components interact with the atmosphere and with each other. Depending on the specific physical formulation of a problem and the objectives pursued, one may describe the transformation of substances with different degrees of detail. In doing so, the 'lifetime' of each substance may be regarded as its prime characteristic. However, prior to incorporating the model of reactions into the equation of the transport of impurities, this model should be adjusted so that it does not disturb the main equilibrium conditions with respect to the mass yield of substances.

Simulation of chemical processes in the atmosphere has special features of its own. Systems of differential equations describing

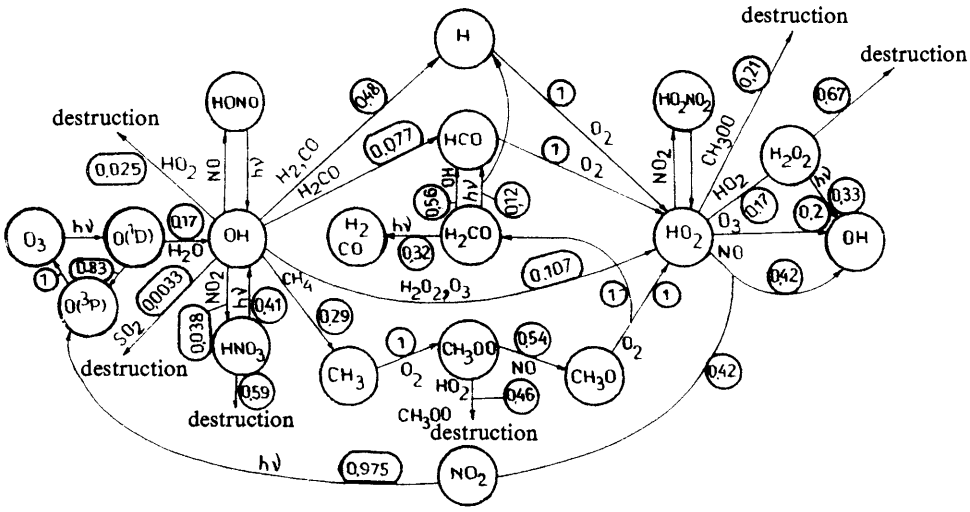


Figure 2. Scheme of chemical processes in the atmospheric layer close to the surface of the Earth; the numbers give the probability of the occurrence of particular reactions.

these processes are nonlinear. In actual problems, the number of reactions may be as great as several hundred, these reactions occurring throughout a three-dimensional domain comparatively large in size, since a typical size of an industrial region is about 100 km. Reaction rate constants differ from one another by orders of magnitude, their true values being not always precisely known. On the basis of their properties, the systems of differential equations which define the impurity transformation block may be classed as 'rigid' ones, characterised by a wide range of points within a spectrum of matrices of linearised equations. At each point of the three-dimensional space there may exist specific rigidity constraints, imposed on the system of equations, while the characteristic time scales involved in the description of chemical reactions should fit those of hydrometeorological processes. All this defines the main requirements that must be satisfied by mathematical models of the processes under study and methods of their computer-aided implementation.

The general structure of models and methods for the solution of a given class of problems, as well as examples of how to use them under specific conditions, are presented in Warneek's monograph.[6] In this paper we have therefore restricted ourselves to a brief account of the main stages of modelling.

As an example, let us consider the model of the transport and diffusion of an impurity in the atmosphere of an industrial region, these processes occurring against the background of local atmospheric events. We shall assume that all the required parameters of meteorological fields and their turbulence characteristics are given. These parameters are determined either through the use of hydrodynamic models or by measuring them in a real atmospheric environment.

Let us designate the domain as $D_t = D[0, \bar{t}]$, where D is the range of variation of spatial coordinates (x, y, z); $[0, \bar{t}]$ is the interval of time t, x and y are the coordinates in the horizontal plane and z is the altitude.

Let there be n gaseous impurities with concentrations

$$c_i = c_i(\vec{x}, t), \quad \vec{x} = (x, y, z), \quad (i = \overline{1, n}).$$

Let us designate the vector composed from these concentrations as

$$\vec{c} = \{c_i\} \quad (i = \overline{1, n})$$

and use the following system of equations to describe the processes of the transport and transformation of impurities:

$$\frac{\partial c_i}{\partial t} + \operatorname{div} \vec{u} c_i - \frac{\partial}{\partial x} \mu_x \frac{\partial c_i}{\partial x} - \frac{\partial}{\partial y} \mu_y \frac{\partial c_i}{\partial y} - \frac{\partial}{\partial z} \nu_z \frac{\partial c_i}{\partial z} +$$

$$+ B_i(\vec{c}, \theta) = F_i \quad (i = \overline{1, n}) \tag{1}$$

where

$$\operatorname{div} \vec{u} c_i \equiv \frac{\partial u c_i}{\partial x} + \frac{\partial v c_i}{\partial y} + \frac{\partial w c_i}{\partial z}; \quad \vec{F} \equiv \{F_i\} \quad (i = \overline{1, n})$$

are the sources of the impurities; $\vec{u} = (u, v, w)$ is the velocity vector; μ_x, μ_y and ν_z are respectively the coefficients of turbulent exchange of impurities in the directions x, y, and z, and θ is the air temperature. Judging by their structure, these coefficients are diagonal matrices of an order n, defined throughout the domain D_t. The coefficients of molecular diffusion are incorporated in ν_x, μ_y, and ν_z In principle, the effect of molecular diffusion may be neglected everywhere outside the lowest atmospheric layers adjacent to surface roughness. The rates of gravitational sinking or rise of impurities $w_g = \{w_i\}$ $(i = \overline{1, n})$ are incorporated in the vertical component w of the velocity vector $\boldsymbol{u}$. A matrix operator

$$B_i(\vec{c}, \theta) \equiv \{B_{ij}(\vec{x}, t, \vec{c}, \theta)\} \quad (i, j = \overline{1, n}) \tag{2}$$

defines the rates of change of the concentrations of impurities due to their transformation. Chemical reactions are nonlinear, i.e. the elements of an operator depend not only on the spatial coordinates and time, but also on the concentrations of the impurities themselves and the temperature.

A mathematical model deals with averaged fields of hydrometeorological parameters and concentrations of impurities. The scale of averaging depends on the procedure for the sampling of a model; in finite difference models this scale is characterised by the sizes of space–time cells of the lattice domain $D_t^n c D_t$. This should be taken into consideration when calculating the rates of transformation of impurities. It may be formally done through determining the average transformation rates from the average concentrations, using the same scale of averaging as that adopted in the sampling of the model. Such parametrisation procedure follows from the basic correlations of the balance of substances. Naturally, when this procedure is used, additional requirements are imposed on the choice of steps for the sampling of the model.

For the sake of simplicity, assume that contaminants do not directly influence the dynamics of the atmosphere. This assumption enables the transport and transformation processes to be considered against the background of motion of the atmosphere, the feedback from hydrothermodynamic processes being effected only through the flows of heat and moisture, and the radiation characteristics of the atmosphere.

The boundary conditions at the upper and lateral boundaries of a domain are set in such a way that the concentrations of impurities fit their background values. At the lower boundary, this condition is written in a parametric form, starting with the equation of the balance of impurities at the surface roughness level. Assuming that each impurity interacts independently with the surface of the Earth, we get

$$v_z \frac{\partial c_i}{\partial z} + \tilde{w}_i c_i = \beta_i c_i + f_{si} \quad (i = \overline{1, n}), \tag{3}$$

where β_i describes the interaction of an impurity i with the underlying surface, and f_{si} is the source of this impurity at the Earth's surface.

Different ways of parametrisation of the boundary conditions at the lower boundary of the air mass are used,[6] depending on the specific formulation of the problem.

At the initial moment, $t = 0$, the concentrations of impurities in the domain D are assumed to be known. The algorithm adopted for the solution of problems (1)–(3), is based on the splitting method. This leads to an effective and simple implementation of the model on a computer.

One usually distinguishes two stages of splitting of the equation system. The first describes the transport of impurities along the trajectories of air masses defined by the field of wind velocity $\vec{u}$, and their exchange through turbulence; the second describes the local conversions of impurities through transformation processes and takes account of their sources.

The computing algorithm is organised in such a way that, in the first stage, the equations of transport and turbulent diffusion are solved with respect to the concentrations c_i ($i = \overline{1, n}$) of each substance and independently of the others within the domain D^n and time interval $t_j \leqslant t \leqslant t_{j+1}$ with duration Δt. In the second stage, the mutual adaptation and interaction of all substances are accomplished at every point within the domain D^n independently from other points.

In practical calculations, the equation system describing the transformation of impurities need not be solved at every lattice point of the domain D^n, but only at those points where impurity concentrations reach certain threshold values, at which it becomes worthwhile to consider transformation processes. Confinement of the transformation of impurities to particular cells of the lattice domain D^n, which is a characteristic feature of the splitting method, is quite consistent with the short characteristic times of chemical reactions. Hence taking account of the transformation of impurities at an individual stage of splitting is one way of its parametrisation in numerical models. In this approach it is essential that changes in the description of particular reactions or of the mechanism of the transport of impurities as a whole are introduced at the level of separate blocks and do not affect the overall structure of the mathematical model.

The main principles of the design and implementation of models of the chemical transformation of impurities, were developed by simulating emissions which are most typical of the atmosphere of industrial cities: the emissions of sulphur-containing substances, nitrogen oxides and methane (as an illustration of the possible mechanisms of photochemical oxidiation of hydrocarbons). These individual types of transformations may occur in different combinations, depending on specific chemical conditions in the atmosphere of an industrial region. They have been incorporated in mathematical models of hydrometeorological processes and atmospheric pollution. Altogether up to 200 chemical reactions, involving 32 chemical species with different lifetimes, were included. These models were used to carry out a series of numerical trials covering a fairly wide range of possible emissions. Examples of these calculations have been reported earlier.[6–8] A model of the transport of impurities that took no account of transformation processes was also used in evaluating the impact of different anthropogenic sources of pollution on the Baikal lake area. From the analysis of results of the calculations conclusions were made as to the relative hazard to Baikal of sources located both in the lake area itself, and at greater distances in the Northern hemisphere.

Numerical trials performed with the aid of the models have demonstrated the advantages of a combined study of the conditions leading to the setting up of a hydrometeorological regime and the transport and transformation of impurities; this basic procedure makes it easier to take account of direct relations and feedbacks when estimating the influence of various natural and anthropogenic factors on the environment.

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Translated from *Uspekhi Khimii* **60** 521–529 (1991)

Transformation of nitrogen- and sulphur-containing compounds in the atmosphere and procedures for reducing the amounts of nitrogen and sulphur oxides in industrial waste

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Various nitrogen- and sulphur-containing compounds of both natural and anthropogenic origin enter the atmosphere of our planet. Examples of compounds of natural origin are reduced sulphur compounds [H_2S, CS_2, $(CH_3)_2S$, COS] and nitrogen-containing compounds (NH_3, N_2O). The principal sources of nitrogen- and sulphur-containing compounds of anthropogenic origin are nitrogen and sulphur oxides.

Various aspects of the protection of the air on our planet and in the first place the problem of "acid rain" require the knowledge of the mechanisms of the chemical transformations of nitrogen- and sulphur-containing compounds in the atmosphere. It is known that the appearance of "acid" rain may be caused by the increased content in the troposphere of the oxides NO_x and SO_2. The knowledge of the mechanisms of the formation and removal of NO_x and SO_2 from the troposphere is therefore essential. The understanding of the principles governing the self-purification of the tropsphere makes it possible to employ them for the creation of technological processes leading to a decrease in the anthropogenic NO_x and SO_2 waste ejected into the atmosphere.

The gas-phase processes relevant to the problem under consideration have been investigated for several years at the Institute of Chemical Physics of the USSR Academy of Sciences. Problems of practical importance are solved jointly with other organisations. For example, the solution of the problem of the influence of photochemical sources of sulphur and nitrogen compounds on the background level of air pollution on a regional and global scale is being sought jointly with the Laboratory for Atmospheric Monitoring. The development of methods for the purification of industrial gaseous waste is being prosecuted together with the Dzerzhinskii All-Union Thermotechnical Institute (VTI), the Southern Branch of the VTI (YuzhVTI), and the Krzhizhanovskii Energy Institute (ENIN).

Consistent study of the elementary reactions, on the basis of which the mechanisms of the chemical transformation of particular compounds in the atmosphere were devised, served as the starting point for the research being prosecuted. These studies have made a definite contribution to the understanding of the mechanisms of the oxidation of hydrogen sulphide, carbon disulphide, and ammonia in the atmosphere which has been achieved and have made it possible to propose physicochemical models for the technological developments designed to reduce the nitrogen and sulphur oxide waste ejected into the atmosphere.

Table 1. Examples of the elementary processes investigated.

(a) Reactions of radicals with components of the atmosphere (R + M → products)

R	M	Refs.
NH_2	O_2, NO, NO_2, O_3, SO_2	[1–5]
HNO	NO, HNO	[6]
OH	NH_3, CS_2	[7, 8]
HS	O_2, NO_2	[9]
HSO	NO_2, NO	[9, 10]
HO_2	NO, H_2S, HO_2, NH_2, HNO	[11, 12]

(b) Heterogeneous radical destruction processes (R + surface → destruction)

R	Surface	Refs.
HO_2	Teflon, quartz, boric acid, metal oxides, NaCl, etc.	[13, 14]
OH	Quartz, sulphuric acid, Teflon, boric acid, ice, etc.	[15]
NH_2	Quartz, quartz coated by adsorbed NH_3	[16]

(c) Elementary processes with participation of excited species ($A^* + M \rightarrow$ products, $A^* + M \rightarrow A + M$)

A*	M	Refs.
$O(^1D)$	NH_3, H_2, CH_4, O_3	[17, 18]
$NH_2(v)$	O_2, N_2, O_3, CH_4	[19]
$NO_2(v)$	NO_2, CO	[20]
$OH(v)$	N_2, O_2, O_3, CH_4, H_2	[18, 21]
$O_3(v)$	O	[22]

The majority of the gas-phase reactions in the atmosphere involve the participation of radicals. For this reason, three types of elementary processes were investigated: the reactions of radicals with the components of the atmosphere; the radical-destruction reactions on surfaces close in chemical composition to that of aerosols; elementary processes with participation of excited species (Table 1). The present day requirements are such that virtually only studies of elementary processes by direct spectroscopic methods are of practical value. For this reason, we developed new effective methods for the investigation of elementary processes based on advances in laser and computer techniques.[23]

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It is possible to differentiate three types of methods. Intracavity laser spectroscopic (IRLS) methods[24] were developed jointly with members of the Lebedev Physical Institute. Priority on a worldwide scale has been achieved in these methods. The laser magnetic resonance (LMR) method in the IR range combined with EPR spectroscopy is the second procedure. An apparatus of this kind was first devised by Gershenzon and co-workers to investigate elementary processes.[25] The third procedure is the laser-induced fluorescence method combined with laser photolysis.[26]

These methods are highly sensitive ($\sim 10^7$ particles cm^{-2}), possess high time (10^{-7} s) and spectral (10^{-2} cm) resolutions, and make it possible to investigate various types of elementary processes.

With the aid of the above methods, we investigated the elementary reactions of the NH_2, HS, HSO, OH, HO_2, and HNO radicals with the components of the atmosphere (Table 1). On the basis of the results obtained in these studies and the available literature data, the mechanisms of the oxidation of ammonia, hydrogen sulphide, and carbon disulphide in the atmosphere were established.

It was assumed previously that minor components of the atmosphere are oxidised via the mechanism

$$M \xrightarrow{+OH} R \xrightarrow{+O_2} \ldots,$$

where M is a minor component of the atmosphere and R a radical. This mechanism involves two postulates. Firstly, as a rule the primary reaction of the minor component M is with a hydroxyl radical. Secondly, the main reaction of the R radical formed is with molecular oxygen. However, studies in recent years have shown that each minor component M can exhibit its specific features in its chemical transformation in the atmosphere and the above postulates are not general.

As suggested earlier, the mechanism of the oxidation of ammonia corresponds to the traditional mechanism

$$NH_3 \xrightarrow{+OH} NH_2 \xrightarrow{+O_2} NH_2O_2 + \ldots .$$

It has been shown[1,2] that the radical NH_2 hardly reacts with molecular oxygen at room temperature. The theoretical explanation of this finding is that the adduct NH_2O_2 has a weak N–O bond and rapidly decomposes in the reverse direction with formation of an NH_2 radical. The reactions of the NH_2 radical with the minor components of the atmosphere NO_2, NO,[3] and O_3[4] were investigated and it was shown that these reactions are fairly effective. The mechanism of the oxidation of ammonia in the atmosphere can be represented as follows:

$$NH_3 + OH \rightarrow NH_2 + H_2O, \quad (1)$$

$$NH_2 + NO_2 \rightarrow N_2O + H_2O, \quad (2)$$

$$NH_2 + NO \rightarrow N_2 + H_2O, \quad (3a)$$

$$NH_2 + NO \rightarrow N_2 + H + OH, \quad (3b)$$

$$NH_2 + O_3 \rightarrow NH_2O + O_2. \quad (4)$$

Reactions (2) and (3a) lead to the removal of nitrogen oxides, since the stable products NO_2 and N_2 are formed. A product of reaction (4) is the NH_2O radical whose reactions have not so far been investigated because of the lack of spectroscopic data for this radical. Nevertheless, our experimental data demonstrate qualitatively that the chemical transformation of this radical can lead to the formation of HNO and then NO_x, i.e.

$$NH_2O \rightarrow HNO \rightarrow NO_x.$$

There are two opposed views in the literature concerning the role of ammonia in the formation of nitrogen oxides in the atmosphere: some workers believe that the oxidation of ammonia is a major source of NO_x in the troposphere, while others believe that ammonia hardly contributes to the formation of NO_x in the troposphere. Within the framework of the mechanism established one may introduce the parameter α defined as the ratio of the rates of removal and formation of NO_x:

$$\alpha = \frac{k_2[NO_2] + k_3[NO]}{k_4[O_3]},$$

where k_2, k_3, and k_4 are the reaction rate constants and $[NO_2]$, [NO], and $[O_3]$ are the concentrations of the corresponding compounds in the troposphere.

Since the temperature dependences of the rate constants have been determined, it follows that, knowing the profiles of nitrogen oxides and ozone with respect to altitude and humidity, it is easy to calculate the influence of ammonia on the formation and elimination of NO_x. Estimates have shown that there may be regions in the lower troposphere for which α may be both greater and less than unity. However, if ammonia enters the stratosphere, then it undoubtedly removes nitrogen oxides, i.e. promotes the conservation of the ozone layer.[27]

As examples of the oxidation of reduced sulphur compounds, we shall consider the mechanisms of the oxidation of carbon disulphide and hydrogen sulphide. The mechanism of the oxidation of carbon disulphide in the troposphere can be represented as follows:

$$CS_2 + OH \longrightarrow CS_2OH \xrightarrow{O_2} COS + HSO_2.$$

According to this mechanism, the primary reaction is the association of CS_2 with the hydroxyl radical to form the adduct CS_2OH.[7] The adduct can decompose in the reverse reaction or can react with molecular oxygen.[28] It is then that further reactions of CS_2OH in the presence of oxygen lead to the formation of carbonyl sulphide and sulphur dioxide.[29] One can therefore postulate that the primary products are COS and HSO_2. The reactions of the radicals will be discussed below, but it is clear that it is in fact the reactions of HSO_2 with the components of the atmosphere which lead to the formation of sulphur dioxide.

The classical mechanism proposed previously for the oxidation of hydrogen sulphide was the reaction of hydrogen sulphide with the hydroxyl radical which affords the HS radical, which then reacts with molecular oxygen. However, it was found that the HS radicals react effectively with minor components of the atmosphere (nitrogen dioxide, ozone),[9,30] whereas the reaction with molecular oxygen is fairly slow. Although the existing estimate of the rate constant for the reaction of the HS radical with oxygen[31] still does not permit its complete exclusion, nevertheless one can assume at the present time the following sequence of principal reactions:

$$H_2S \xrightarrow{+OH} HS \xrightarrow{+NO_2,\ O_3} HSO \xrightarrow{+O_3,\ NO_2} HSO_2 \xrightarrow{O_2} SO_2.$$

In this chain of elementary reactions,[7,9,10,30,31] virtually all the rate constants are known. We investigated the reactions of the HS and HSO radicals.[7,9]

As already stated, in the majority of the mechanisms considered, the primary oxidation reaction was assumed to be the reaction with the hydroxyl radical. This seemingly natural hypothesis was based on the fact that this radical is very reactive and its concentration in the atmosphere is adequate. However, data have been obtained recently[32] showing that the reaction of H_2S with the relatively unreactive HO_2 radical proceeds effectively:

$$HO_2 + H_2S \rightarrow HSO + H_2O. \quad (5)$$

This finding was checked both as regards the kinetics of the decrease in the HO_2 concentration and as regards the accumulation of HSO. The rate constant for this reaction is virtually the same as for the reaction of the hydroxyl radical with hydrogen sulphide. Since the concentration of the HO_2 radicals is approximately 100 times greater than the concentration of the OH radicals, we postulated a new mechanism for the oxidation of hydrogen sulphide:

$$H_2S + HO_2 \rightarrow HSO + H_2O,$$
$$HSO + NO_2 \rightarrow HSO_2 + NO,$$
$$HSO + O_3 \rightarrow HSO_2 + O_2,$$
$$HSO_2 + O_2 \rightarrow HO_2 + SO_2.$$

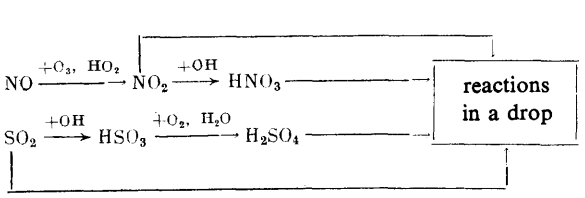
This is a chain mechanism of the oxidation of H_2S. The chain carriers are only two radicals—HO_2 and HSO. The rate constants for these reactions are known. The formation of HSO_2 in the reaction of HSO with ozone is tentative.

If our data for reaction (5) are correct, then the mechanism of the oxidation of carbon disulphide should also be revised. In this case, one can postulate the following mechanism:

$$HO_2 + CS_2 \rightarrow CS_2HO_2 + O_2 \rightarrow COS + HSO.$$

As regards other reduced compounds, the mechanism of their oxidation in the air has been less well investigated and therefore will not be discussed. One can only note that the principal product of the oxidation of these compounds is sulphur dioxide.

Nitrogen and sulphur oxides are removed from the atmosphere in two ways:[33] as a result of the dry deposition of SO_2 and NO_x and as a result of washing out by rain. There are in the latter case two ways in which nitrogen and sulphur oxide enter a rain drop, which can be illustrated by the following scheme:



The nitrogen dioxide and sulphur dioxide molecules can dissolve in water drops. The rate of their removal can then depend significantly on the concentrations in the drops of other substances, because if the latter react chemically with nitrogen dioxide and sulphur dioxide, then the ability of drops to absorb these gases will increase significantly compared with the level determined by Henry's law. The second channel leading to their removal involves gas-phase reactions with the formation of nitric and sulphuric acid molecules which enter the water drops.

Water drops containing nitrogen and sulphur oxides fall on the surface of our planet as rain. In certain regions, where there is much ammonia in the sinks for nitrogen oxides, the NH_2 radical can play a role analogous to that of hydroxyl radicals (its gas-phase reactions with nitrogen and sulphur dioxide):

$$NH_2 \xrightarrow{+NO_2} N_2O + H_2O,$$

$$NH_2 \xrightarrow{+SO_2} NH_2SO_2.$$

The latter reaction has been recently investigated.[34]

It follows from the foregoing that the OH and HO_2 radicals play an important role in the gas-phase atmospheric chemistry. It is therefore important to understand how the heterogeneous processes involving the destruction of these radicals on aerosols influence the nitrogen and sulphur formation and elimination processes. Processes leading to the destruction of the OH and HO_2 radicals on different surfaces, presented in Table 1, have been investigated.[13–15] The experiments were performed using surfaces whose chemical composition was close to that of the aerosols.

By generalising the experimental data obtained, the authors were able to conclude that the accommodation coefficients, i.e. the probability of the destruction of the radicals (γ) per collision with the surface, are within the following ranges for the OH and HO_2 radicals:

$$\gamma_{OH} \approx 10^{-2}—1; \quad \gamma_{HO_2} = 10^{-3}—10^{-2}.$$

Mathematical modelling based on the standard model of the atmosphere at aerosol concentrations typical for urbanised regions has shown that it is necessary to take into account the heterogeneous processes involving the destruction of both OH and HO_2 radicals.[35] The heterogeneous radical destruction reactions lead to an increase in the concentration of pollutants (for example, sulphur dioxide) in the lower atmosphere, which means that the self-purification of the troposphere is impaired with increase in the concentration of aerosols.

The calculations have also shown[36] that the heterogeneous OH radical destruction processes must be taken into account in the chemistry of the stratosphere as well. After volcanic eruptions, droplets of sulphuric acid, on which the heterogeneous destruction of OH radicals takes place very effectively, appear in the stratosphere. Allowance for the destruction of OH radicals leads to an increase in the concentration of nitrogen oxides, which leads in its turn to a decrease in the concentration of nitrogen in the ozone layer.

The third type of elementary processes investigated includes processes involving excited species, which are presented in Table 1. These studies were designed to elucidate the role of vibrationally excited species in the photochemistry of the stratosphere. As was to be expected, vibrationally excited species do not play a significant role in the troposphere.

As already stated, an appreciable amount of N_2O molecules travel from the surface of our planet to the atmosphere. These molecules are chemically inert and therefore readily reach the stratosphere, where they can participate in the formation of nitrogen oxides either under the influence of sunlight or as a result of their reaction with electronically excited oxygen atoms. The movement of NO_x to the troposphere naturally depends on the mechanism of the photochemical reactions in the stratosphere. The experimental data obtained for the deactivation processes and the reactions of excited species have made it possible to analyse the important role of the vibrationally excited species in the photochemistry of the stratosphere. Such species may be the vibrationally excited molecules of ozone $O_3(v)$ and the hydroxyl $OH(v = 9)$ (v is the

vibrational quantum number). The OH(v = 9) molecules are formed in the reaction

$$H + O_3 \rightarrow OH(v = 9) + O_2.$$

The interaction of OH(v = 9) with oxygen can lead either to the deactivation of OH(v = 9) or to the reaction

$$OH\ (v = 9) \xrightarrow{+O_2} H + O_3,$$
$$OH\ (v = 9) \xrightarrow{+O_3} OH\ (v = 8) + O_2.$$

Data obtained recently by Cheskis[37] for elementary processes involving OH(v) have shown that the rate constants for these two processes are comparable and they should therefore be taken into account in the photochemistry of the stratosphere. Allowance for these processes leads to an increase in the calculated ozone concentration in the ozone layer.

The interaction of OH(v = 9) with molecular nitrogen could also occur via two pathways:

$$OH\ (v = 9) \xrightarrow{+N_2} N_2O + H,$$
$$OH\ (v = 9) \xrightarrow{+N_2} OH\ (v = 8) + N_2.$$

Unfortunately there are no data concerning the pathway followed in the reaction of OH(v = 9) with nitrogen. However, estimates have shown that, if the rate constant for this pathway exceeds 3×10^{-15} cm^3 s^{-1}, then, when account is taken of OH(v = 9), the rate of formation of N_2O is comparable to the rate of arrival of N_2O from anthropogenic sources in the atmosphere. Ideas of this kind show that such high effectiveness of the vibrational energy in such reactions is possible.

At high altitudes (80 km), the concentration of oxygen atoms is high and vibrationally excited ozone molecules $O_3(v)$ are formed very effectively by the reaction

$$O + O_2 + M \rightarrow O_3(v) + M.$$

The $O_3(v)$ molecules can be either deactivated or they can enter into a chemical reaction with an oxygen atom:

$$O_3(v) \xrightarrow{+O} 2O_2,$$
$$O_3(v) \xrightarrow{M} O_3.$$

Experimental studies on the elementary processes with participation of $O_3(v)$ have shown[22] that the vibrational form of energy is effective in the reaction pathway. Estimates demonstrated[38] that processes with participation of $O_3(v)$ should also be taken into account in the mechanisms operating in the chemistry of the stratosphere. This process diminishes the calculated ozone concentration.

The development of methods for reducing the anthropogenic nitrogen and sulphur oxide waste ejected into the atmosphere constitutes an independent and important problem associated with the protection of the atmosphere. The understanding of the natural mechanisms of the elimination of nitrogen and sulphur oxides from the atmosphere and the study of elementary reactions made it possible to put forward chemical models for the reduction of nitrogen and sulphur oxide waste. Table 2 presents three methods for the removal of nitrogen and sulphur oxides from industrial gases. These methods are based to some extent on the principles governing natural sinks for the removal of nitrogen and sulphur oxides from the atmosphere.

The gas-phase ammoniacal purification method is based on the reactions which also occur in the atmosphere:

$$OH \xrightarrow{+NH_3} NH_2,$$
$$NH_2 \xrightarrow{+NO} N_2 + H_2O,$$
$$NH_2 \xrightarrow{+NO} N_2 + H + OH,$$
$$NH_2 \xrightarrow{+NO_2} N_2O + H_2O. \qquad (6)$$

The difference is that in the atmosphere there is a sufficiently high concentration of OH radicals (ultimately due to the effect of sunlight) and these processes can occur at room temperature. In the purification method considered, ammonia must be introduced at a fairly high temperature ($\sim$1000 K) of the effluent gases, where the branching route (6), capable of maintaining the required concentration of OH and NH_2 radicals, is significant. Studies by this method are conducted jointly with the VTI, where the technological version of this method has been applied. The method has been tested on the experimental industrial plant at the Kirovakan heat and power generating plant. However, an earthquake precluded the completion of these experiments. It has to be said that the method has not found a wide-scale development abroad hitherto, but ways of applying it at lower temperatures are being sought continuously. It is seen from the example of this method that the dry methods for the removal of nitrogen oxides must be based on the preparation of OH and NH_2 radicals at sufficiently high concentrations and low temperatures. These can be chemical, radiation, or photolytic methods.

Table 2. Methods for the removal of NO_x and SO_2 from effluent industrial gases.

Method	Reagent	Gas	Degree of purification, %	Products
Gaseous ammoniacal	NH_3	SO_2 NO_x	– 80	N_2, H_2O
Radiation-chemical	without reagents NH_3	SO_2 NO_x	90 90	HNO_3, H_2SO_4 $(NH_4)_2SO_4$, NH_4NO_3
Ozone-ammoniacal	O_3, NH_3	SO_2 NO_x	95 80	 $(NH_4)_2SO_4$, N_2, N_2O

In the radiation-chemical purification methods, the required NH_2 and OH concentrations are established by the reaction of the effluent gas with electrons. Studies conducted recently at the Institute of Chemical Physics of the USSR Academy of Sciences under the supervision of A P Shvedchikov jointly with the State Institute of Non-Ferrous Metals showed that the radiation-chemical method is promising for the purification of not only the effluent gases from heat and power generating plants containing $<0.1\%$ of carbon dioxide but also of the waste gases from industrial non-ferrous metallurgical undertakings, where the carbon dioxide content is higher. This leads to the possibility of using industrial electron accelerators not only for reducing the amount of ecologically harmful impurities (SO_2, NO_x) in waste gases but also possibly for

the creation of a new technology for the synthesis of sulphuric acid as a result of the radiation-chemical oxidation of sulphur dioxide.

The ozone-ammoniacal method is based on the principle used by nature to remove NO_x and SO_2 from the atmosphere in which a significant role is attributed to the reactions in the water drops. Ozone is needed only to convert NO into NO_2 in the gas phase:[39]

$$NO \xrightarrow{+O_3} NO_2 + O_2.$$

Next NO_2 and SO_2 enter the water drops where chemical reactions take place and the rate of removal of NO_2 and SO_2 is determined. Studies by V A Lozovskii, Yu N Kozlov, and A N Petrov (Institute of Chemical Physics of the USSR Academy of Sciences) have shown that under optimum conditions the purification process depends significantly on the interaction of NO_2 with SO_2 dissolved in the drops, which can be illustrated schematically as follows:

$$(NO_2)_{gas} \rightarrow (NO_2)_{aq} \rightarrow NO_2^- \xrightarrow{+HSO_3^-} NH_4^+,\ SO_4^{2-},\ N_2,\ N_2O.$$

This method is being developed jointly with VTI, YuzhVTI, and ENIN. It has been tested on the experimental industrial plant of the Moldavian Hydroelectric Power Station. The design of a full-scale plant for the purification of the flue gases from the heat and power generating plant in Dushanbe is now being completed.

It is noteworthy that this method has been designed in the USSR and has many advantages over foreign methods.

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Translated from *Uspkhi Khimii* **60** 530–535 (1991)

Systematic treatment and assessment of the risks due to superecotoxicants

A D Kuntsevich

At the dawn of his appearance 30 000–40 000 years ago, *Homo sapiens*, being a product of the overall evolution of the geosphere, depended on nature, but he soon (against the background of the 4 billion years of the existence of the planet) disturbed the essential balance of nature.

The scientific-technical revolution in the 20th century gave rise to the "explosive character" of the development of anthropogenic energy and mass exchange. As a result of the extremely rapid functioning of this process, in essence via a "chain mechanism", qualitative and quantitative changes have taken place in the geosphere of a kind such that their accumulation has been responsible for the conversion of the anthropogenic factor into a significant factor on not only a regional but also a global scale.

The long neglect of this objective consideration, the euphoria associated with gaining control of powerful types of energy, the synthesis and introduction of new substances and materials, and the "victories" over nature have in general suddenly and in an acute form faced humanity with the ecological problem as a problem of its survival.

Indeed the global climate, the ozone layer, the oceans, the forests, the biological species, and the natural resources are being increasingly considered with alarm.

A reliable answer to the question whether or not the equilibrium between the interactions in the geosphere has now been disturbed can be given on the basis of the solution of a fairly complete global model. Its main components are the dynamics of the processes, the establishment of the permissible limits to the structural, phase, and functional changes, and the estimation of the relationship between fact and norm. The development of such a model will apparently make it possible to find a satisfactory solution to the problem of the preservation of the global equilibrium. However, this requires international efforts by scientists for a long time.

At the same time, together with the development of a global model and large-scale studies within the framework of the biosphere and biological research at governmental and international levels under the auspices of the United Nations Organisation, UNESCO, and other organs, rapid assessments of signal systems in various fields, which might reveal negative trends requiring immediate action by the community, are needed without delay. One of the most important objects of such assessments should be man himself (and, by analogy, all the components of the flora, fauna, and the environment as a whole).

In the outcome of the evolution of man against the background of the manifestation of negative factors one may note undoubted positive aspects: the growth of population, the increased lifespan, development, etc. However, during the past 30 years an appreciable (severalfold) increase in congenital deformities, allergies, and other negative phenomena has been noted throughout various countries of the world. If these figures are objective, and there are no grounds for disbelieving them, then they may in fact serve as the signal indicator system indicating the exhaustion of not only the capacity for adaptation to changes in the environment inherent in man but also of the capacity of the compensating mechanisms underlying the basis of modern medicine with its system of total monitoring of persons, diagnosis, and prophylactic and therapeutic measures.

A relaxed approach to this situation is not permissible. Firstly, it is essential to estimate urgently and repeatedly the reliability of the occurrence and the growing incidence of persons with congenital deformities. The point is that, if only the growth of human lifespan is adopted as a factor measuring man's well-being and the changes in the gene stock are not analysed, then one is faced with the objective problem of the risk of the appearance after a short time of a new "destructive" population of persons, the development of which, after the attainment of a certain "critical mass", would acquire the character of a chain reaction.

It is entirely clear that it is essential and a matter of extreme urgency to alter fundamentally the general trend towards an increase in congenital deformities. After all, if even now decisive measures are adopted, the alteration of the general trend will require time and hence will involve new victims.

The solution requires the discovery of the new factor or several factors responsible for this jump in the degradation index of human gene stock. Naturally, it would be most correct to carry out research in numerous directions: the influence of the external background electromagnetic radiation, the growth of the consumption (provided that this has occurred objectively) of alcohol and drugs, as well as other negative factors.

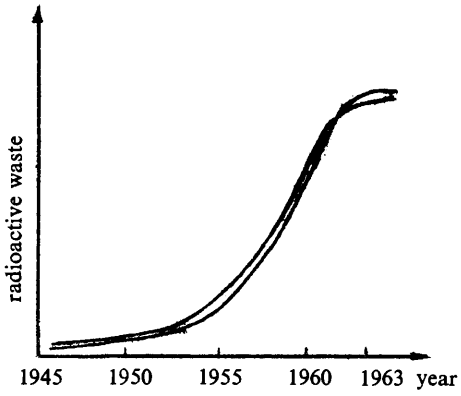


Figure 1. Approximate scale of the pollution forming the "dirty" background and exhibiting a polyfunctional biological activity. Fall-out Σ(^{90}Sr and ^{137}Cs) $\simeq 10^{18}$ Bq; amount in the stratospheric reservoir (fall-out continues) $\sim 10^{16}$ Bq.

Greenhouse effect: $\leftarrow CO_2 \rightarrow$ > 500 million tonnes (increment 0.3–0.5% annually), SO_x ~ 300 million tonnes, petroleum and petroleum products ~70 million tonnes, pesticides ~2 million tonnes, surfactants 10 million tonnes, solid waste ~4 billion tonnes, domestic waste (Moscow—2 million tonnes) ~50 million tonnes, liquid waste from animal husbandry (> 100 thousand tonnes ha^{-1}) ~13 billion m^3.

An attempt at a comparative analysis of the radiation and chemical factors has been made. Fig. 1 illustrates the approximate scale of pollution, which, in terms of its regional and global

distribution, gives rise to a kind of constant qualitative and quantitative "dirty" background which exhibits objectively, by virtue of its nature, a polyfunctional biological activity. Hence arise the anomalies in the diseases of individual regions and, as the global "dirty" background grows, the biological response to it is manifested on a planetary scale.

The understanding of this approach makes it possible to formulate at the present time the fundamentally new problem of drawing maps of the planet, state, region, town, or village based on the index of the biologically harmful activity of samples of air, soil, water, and food in terms of an integral indicator of the activity of pollutants against a very small but chronic background.

Unfortunately world practice is directed at the present time to the investigation of biological activities of individual specific substances, involving the determination of the limiting permissible concentrations (LPC) of the latter. We believe that there are at present sufficient data to transfer the estimation of the biological activity of daily air, water, and food samples also to a new polyfunctional level.

Returning to the problem of the determination of the factors responsible for the increase in the number of persons with altered heredity, one cannot fail to pay attention to the chemical factor. Among the widely distributed "chemical pollutants", mention should be made of the mutagenic polyaromatic hydrocarbons (PAH), polychlorophenols (PCP), heavy metals, and other compounds. The present author has given the term superecotoxicants (SET) to substances small doses of which exhibit a powerful activity inducing or inhibiting enzymes (Fig. 2).

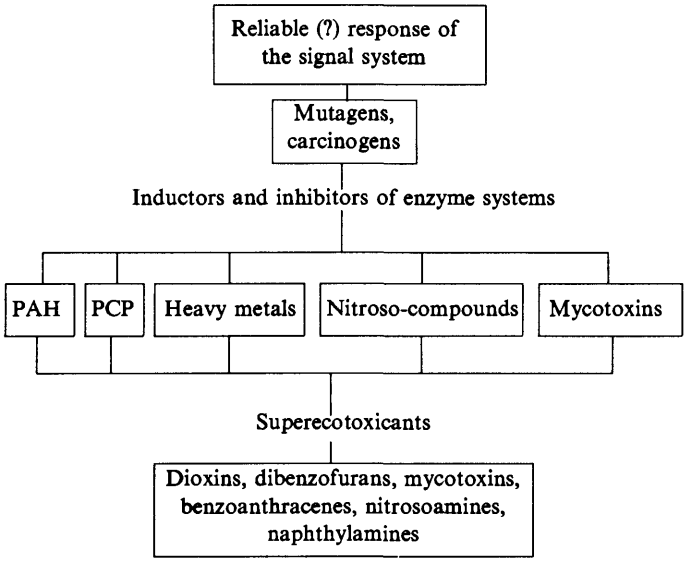


Figure 2. Chemical factors responsible for the increase in the number of persons with altered heredity.

Together with their inducing and inhibiting activities, superecotoxicants can also induce in man and animals a sharp increase in sensitivity to xenobiotics and other natural agents in the environment. It is essential to note also their natural stability and the absence of a toxicity limit (superaccumulative effect). The concept of the limiting permissible concentrations loses significance for virtually all superecotoxicants. The superecotoxicants circulate in all media and exhibit their activity through the components of the medium. Man is subject to their activity both via the aerobic pathway and perorally together with food products of plant and animal origin and water in which they accumulate from the soil and the hydrosphere. Thus yet another property is characteristic of superecotoxicants—an extremely high mobility in the ecosphere. These properties are in fact responsible for the complex toxic activity of various superecotoxicants, which can induce mutagenic, teratogenic, carcinogenic and porphyrogenic effects and can also suppress cell immunity, damage internal organs, and waste the organism.

The enormous experience gained in past toxicological studies made it possible to discover the normal logarithmic law governing the distribution of living organisms with respect to sensitivity to the action of harmful factors, including toxic substances. According to this law, the "dose–effect" relation can be in most cases fitted by monotonically increasing S-shaped curves, which are converted into straight lines when plotted on a logarithmic or a logarithmic probit grid. .

At the same time, in a number of instances experimenters have encountered significant deviations of the experimental data from the fitted S-shaped curves. The extreme case of such deviations are the so called paradoxical bimodal or two-phase effects where within a certain range an increase of dose leads not to an increase but to a decrease in the effect. The paradoxical dose relations have now been differentiated as a separate group, since they cannot be fitted by the known methods.

In our view, this shows that the methodology adopted fully takes into account all the features of the response of the organism as a complex system with numerous compensating and adaptive functions.

Theoretical treatment of the essential features of the response by living organisms to the effect of harmful factors suggests that toxic substances (superecotoxicants) act simultaneously or successively to a greater or lesser extent on virtually all the biotargets and systems of the organism, exerting their toxic action simultaneously via different mechanisms. The overall effect is then equivalent to the effect of the combined action of two or more substances involving summation (additivity), internal potentiation (synergism), and even autoantagonism.

On the basis of these features, a series of chemical substances inducing such two-phase effects have been specifically synthesised and investigated.

Analysis of experimental data on the dose relations for these compounds and of certain literature data made it possible to discover the rule governing the occurrence of "dose–effect" curves and to find a logical explanation in terms of which they can be fitted:

$$P = \frac{(D/X)^n \frac{1}{1+(D/Z)^k} + (D/Y)^m}{1 + (D/X)^n \frac{1}{1+(D/Z)^k} + (D/Y)^m},$$

where D is the dose of the substance, X and Y are the average lethal doses in the first and second phases, Z is the average effective

autoantagonistic ("antidote") dose, and n, m, and k are the corresponding coefficients for the intensity of the increase in the effect.

It has also been established that Z is a dependent quantity and can be expressed by the formula

$$\lg Z = \lg X + \frac{3.1}{m/n + k} \lg (Y/X).$$

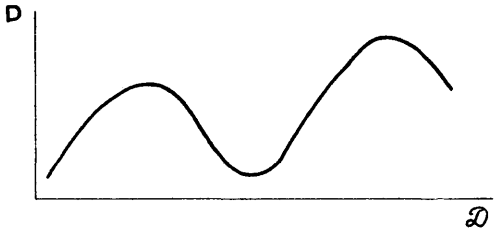


Figure 3. Two-phase dose relation.

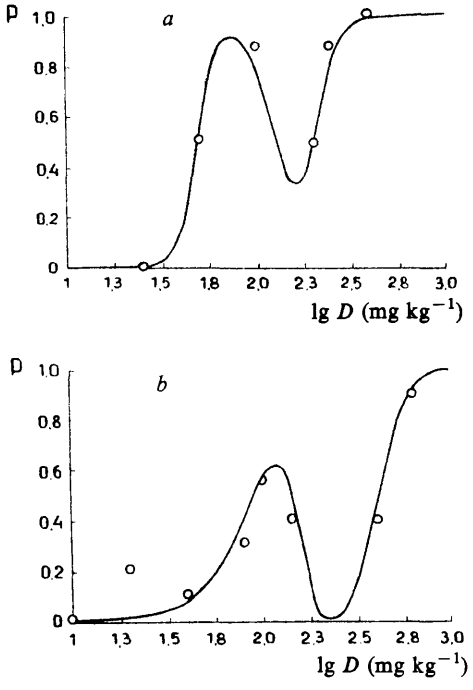


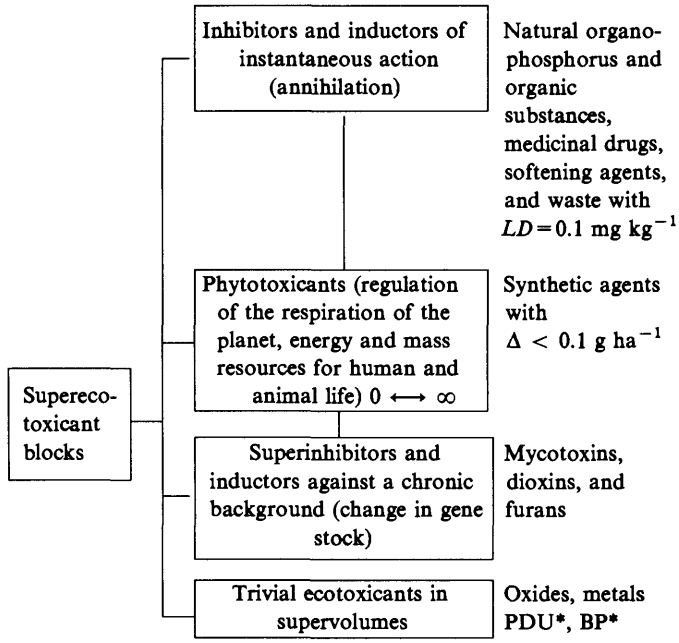
Figure 4. Experimental curves for the two-phase dose relation (composition based on dimethylbenzoanthracene) on the 45th day for white rats (*a*) and white mice (*b*).

A typical two-phase relation is presented in Fig. 3. The coefficients n, m, k, X, and Y as well as the standard deviation were determined by the multiple regression method on a computer.

An experimental confirmation of the validity of the relation is presented in Fig. 4 for dimethylbenzoanthracene (DMBA).

On the basis of the analysis carried out, it is suggested that for practical applications the superecotoxicants be treated systematically on the basis of four main blocks (they can be expanded in terms of substructures).

SCHEME



*Unidentified Russian abbreviation (Ed. of Translation).

It is striking that controls in relation to the first block have been adopted in a number of international conventions and agreements and in registers of medicinal drugs.

Controls in relation to the second block have not yet been organised although one cannot rule out the possibility that they will be included in the convention on chemical weapons.

As regards the third block, the methods of registration and control of submicro-amounts of the relevant substances and experimental estimation of their biological activity in combination with accompanying "pollutants" and "ordinary" substances require urgent tests and development on national and international levels.

The fourth block requires a more clear-cut formulation and control. Overall, the following problems come to the fore:

1. Detection, screening, systematic treatment, registration, and international control (Soviet and international systems).

2. Monitoring and local and remote control methods for chemical and express biological detection with a high sensitivity. Mapping of the planet, regions, and populated areas. Dynamics. Characteristic features. Predictions. Solutions. Practice.

3. Methods for the estimation of the integral "response" to multifactorial influences.

4. Detection, location, isolation, and abolition of sources of pollution.

5. Development of controlled cycles (waste-free technology, closed cycle manufacturing processes, absorption of absorbable gases, and the supercycle).

It is very important to note that overall, within the framework of the earlier estimate of the degree of risk associated with chemical factors, a systematic treatment and control of superecotoxicants and

the development of a methodology for their estimation should be prosecuted on a universal, international scale, since this would make it possible to obtain maps of the probable biological effects of various media (air, water, soil, food) for populated areas, regions, and the planet as a whole. This would in fact serve as a guide in the adoption of solutions.

It is necessary to go over to a new philosophy of the organisation of the life cycle of any article, any material, and any substance. This cycle must include in a unique whole the extraction of the raw material, transport, conversion of the raw material into the product, the utilisation of waste, ecologically clean employment of the product, and methods for its complete utilisation after the article has fulfilled its function (purpose). This in fact constitutes a closed "supercycle".

Translated from *Uspekhi Khimii* **60** 536–544 (1991)

Polychloropolycyclic xenobiotics

A F Kolomiets
A N Nesmeyanov Institute of Heteroorganic Compounds,
Academy of Sciences of the USSR, Moscow

Xenobiotics from a number of polychloropolycyclic compounds (PCPC) of the dioxin type such as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD), 2,3,7,8-tetrachlorodibenzofuran (2,3,7,8-TCDF), their more highly chlorinated derivatives and also 3,3',4,4'-tetra-3,3',4,4',5-penta- and 3,3',4,4',5,5'-hexachlorobiphenyls (Table 1) are some of the most dangerous ecotoxicants passed into nature from the production of the chloro-compounds and from technologies based on the use of chlorine and its compounds.

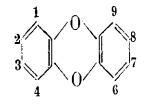
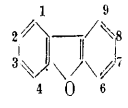
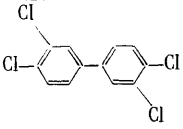
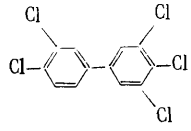
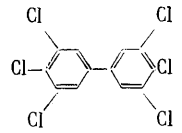
Some general properties of these xenobiotics (compiled in 1984) are given in a short review.[1] However, during the past five years the number of scientific publications on PCPC has more than doubled. Among the more than 1600 studies there are monographs, handbooks, and large reviews of the various aspects of the PCPC problem, summarising results on national and international programmes, results of national and international scientific meetings and conferences. New information, a significant part of which is presented in the proceedings of international symposia on 'Dioxin and Related Compounds',[2–5] has enabled a more ordered concept to be created of PCPC as poisons, ecotoxicants, on their influence on contemporary medicine and on the ecological situation. The most important conclusions are given below.

I. Toxic effects

Acute toxicity for warm-blooded animals is not now considered to be a criterion of the danger of PCPC for man. The primary and secondary effects of PCPC on an organism and their consequences, which depend substantially on the habitat and conditions of existence of the organism, have proved to be more important in this regard.

The primary effects of 2,3,7,8-TCDD and its analogues are linked with the high specificity of these xenobiotics towards the cytosolic A*h* receptor controlling primarily the activation of genes A1 and A2 (on the 15th human chromosome) and the set of non-specific monooxygenases, viz. cytochromes P-4501A1 and P-4501A2.[6] Recently a third locus activating the A*h* receptor has become apparent and has been investigated.[7] Participation of the complex of 2,3,7,8-TCDD with the receptor has also been shown in the suppression of a gene on the 16th human chromosome producing menadioneoxidoreductase.[8] A high affinity has been established for dioxin-type PCPC towards the nuclear thyroxine receptor and an increase in thyroxine receptor concentration has been shown in the nuclei of cells of animals poisoned with 2,3,7,8-TCDD.[9] These data suggest that the action of PCPC is directed towards a series of regulatory mechanisms of the living cell, selected in the course of evolution, started by receptor proteins with a single type of active centre. Haem, which is sterically accessible for planar PCPC, emerges as the most probable target, since of natural substances only the iron-porphyrins are capable because of their geometric and electronic parameters of interaction with all the known inducers of the dioxin type.[10]

Table 1. List and relative danger of polychloropolycyclic compounds.

Compound*	Relative danger	Compound*	Relative danger
			
2,3,7,8-TCDD	1.0	2,3,7,8-TCDF	0.1
1,2,3,7,8-PCDD	0.5	1,2,3,7,8-PCDF	0.01
1,2,3,6,7,8-HxCDD	0.1	2,3,4,7,8-PCDF	0.5
1,2,3,7,8,9-HxCDD	0.1	1,2,3,6,7,8-HxCDF	0.1
1,2,3,4,7,8-HxCDD	0.1	1,2,3,4,7,8-HxCDF	0.1
1,2,3,4,6,7,8-HpCDD	0.01	1,2,3,7,8,9-HxCDF	0.1
octa-CDD	0.01–0.001	1,2,3,4,7,8,9-HpCDF	0,1
		octa-CDF	0.01–0.001
	0.001		0.3
	0.01		

Footnote. Relative danger is given for carcinogenic risk.
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On passing into an organism PCPC act as inducers of extended false responses enabling the accumulation of a series of biocatalysts-haemoproteides in quantities dangerous for cell and organism function. Essentially, the regulatory mechanisms affected by these xenobiotics lead to a disturbance of the protective mechanisms of the

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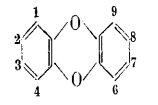
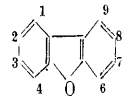
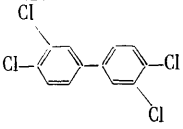
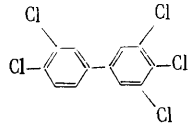
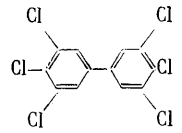
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1,2,3,7,8,9-HxCDD	0.1	1,2,3,6,7,8-HxCDF	0.1
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1,2,3,4,6,7,8-HpCDD	0.01	1,2,3,7,8,9-HxCDF	0.1
octa-CDD	0.01–0.001	1,2,3,4,7,8,9-HpCDF	0,1
		octa-CDF	0.01–0.001
	0.001		0.3
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On passing into an organism PCPC act as inducers of extended false responses enabling the accumulation of a series of biocatalysts-haemoproteides in quantities dangerous for cell and organism function. Essentially, the regulatory mechanisms affected by these xenobiotics lead to a disturbance of the protective mechanisms of the

organism towards xenobiotic and toxic products of metabolism, to disturbance of hormonal metabolism and suppression of the immune system. Consequently the primary effects of PCPC are linked mainly with disturbance of the genetically controlled adaptation mechanisms of the organism to its surroundings. Thus even weak PCPC affections, manifesting as a constant discomfiture of the organism, high fatigue, reduced physical and mental ability and increased susceptibility to infection, may lead to dramatic consequences under conditions of additional, normally readily endurable, physical, chemical, biological and psychological stress.

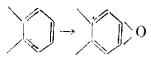
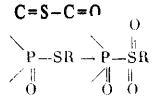
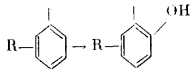
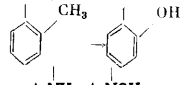
Secondary effects of PCPC on the organism are initiated by the biocatalyst-haemoproteides induced by them, of which only cytochromes P-4501A1 and P-4501A2 have been adequately studied. Accumulation of the latter is dangerous for two reasons. In the first place complexed with PCPC they trigger the mechanism for transforming the energy resources of the cell to the conversion of O_2 into $O_2^{\cdot}$, H_2O_2 and $HO^{\cdot}$, which leads to a mutagenic effect, the biodegradation of hormones, vitamins and lipids which are sensitive to oxidation, disruption of biomembranes and disturbance of the functions of membrane-bound complexes. Immune cells are particularly susceptible to similar actions. Secondly these biocatalysts participate in the biotransformation of a great number of xenobiotics and normal metabolites by converting them into hydroxylation and epoxidation products (Table 2). As a result there is increased biodegradation of several low molecular hormones, neuromediators, vitamins, aromatic aminoacids, drugs and bioactivation of foreign substances of which precursors of aflatoxin B_1, nivalenol, carcinogens, neurotoxic substances and strong nerve poisons are particularly dangerous. All these secondary effects of PCPC aid suppression of the primary effects and, in the presence of certain xenobiotics, to the appearance of ecological illnesses.

The effect of the accumulation of nuclear thyroxine receptors stimulated by PCPC has not yet been studied. It is only possible to suppose that it is equivalent to the known effect of hyperthyroidism (activation of oxidation processes, uncoupling of oxidative phosphorylation, general emaciation of the organism), appearing at an excess of hormones of the thyroid gland. In reality the symptoms of heavy PCPC poisoning coincide with the features of hyperthyroidism.

The ecotoxicity of PCPC is caused not only by their negative action of fauna but also by the particular sensitivity to them of aerobic microorganisms, the protective mechanisms and flexible metabolism of which are controlled by a system of haem-containing monooxygenases. Anaerobes and photosynthesising organisms are significantly less sensitive to them. Consequently the accumulation of PCPC in nature and their inevitable concentration in the organic phase converts the latter into an unfavourable habitat primarily for aerobic organisms which determine the ability of ecosystems for self-restoration. The inevitable consequence of this in soil ecosystems is an expansion of habitats of anaerobes and, linked with this, biodegradation of humus and impoverishment of soils. In aqueous ecosystems PCPC extend the habitats of various algae, the accumulation of which leads to deoxygenation of the medium and acceleration of the degradation of the system.

Thus both at the level of organisms and at the level of communities of organisms PCPC destroy the most vulnerable regulatory mechanisms of living matter which determine their capability for autorestoration under aerobic conditions. A viability regulatory link weakened by PCPC endures further destruction by any other stresses. Consequently the assertion is correct that after appearing and accumulating in the biosphere PCPC of the dioxin type remain an important factor determining the increased sensitivity of man and nature to any anthropogenic influence.

Table 2. Known effects of cytochromes P-4501A1 and P-4501A2.

Biochemical effect	Reaction type	Consequence
Epoxidation of ethylenic bond, inhibition of epoxyhydrolases	C=C→C–C (O)	Bioactivation and stabilisation of mycotoxins, terpenoids, etc.
Epoxidation of arenes		Bioactivation of procarcinogens, promutagens, biodegradation of drugs
Epoxidation of thionephosphates	P=S–P=O	Bioactivation of pesticides
Epoxidation of dithiocarbamates	C=S–C=O	Biodegradation of disinfectants
Oxidation of thiol ethers		Bioactivation of neurotoxicity
ortho-Hydroxylation of substituted arenes		Bioactivation of neurotoxicity
Hydroxylation of CH_3 group		Bioactivation of neurotoxicity
N-Hydroxylation of arylamines and their derivatives	ArNH→ArNOH	Bioactivation of procarcinogens
Dealkylation of alkylaryl ethers	$ArOCH_3$→ArOH	Accumulation of phenols

II. Danger of 2,3,7,8-TCDD and its analogues to man

The danger of PCPC of the dioxin type to man is no longer the subject of discussion. It is no secret that pregnant women and children comprise a special group at risk of PCPC poisoning among people,[5] and that in regions of increased PCPC content in the environment the population and animals are characterised by increased deficiency of the immune system,[11] which may reach dramatic levels when other poisoning factors are superimposed. All the accumulated information leaves no doubt that PCPC are one of the decisive factors determining the currently observed process of reducing the geno-background of the human population in individual regions of the globe.

The subject of scientific investigations and discussions is now the problem of determining the degree of danger for man of these poisons, which is extremely important for the regulation of an effective complex of measures for health in the medical and ecological fields. Regretably there are no significant achievements in this area since mankind has proved to be unprepared to solve so important a problem.

The particular complexity of the PCPC problem is that these xenobiotics, which possess extraordinary biological activity, pass into nature as complex mixtures. The 17 main substances of this type are shown in Table 1. If one considers that many bromo-, nitro- and some methyl-substituted analogues possess a similar action their quantity grows severalfold. However even for the mixtures of

substances shown in Table 1 determination of the degree of danger is extremely complex. For this it is necessary to have reliable methods of determining the compositions of such complex mixtures qualitatively and quantitatively, to know the complete toxicological characteristics of each component and to make apparent the character of the mutual influence of substances after intake by the organism.

Up to the present time the US Environmental Protection Agency and a group of experts from the Scandinavian countries have developed the first methodology for assessing the degree of danger of PCPC to man.[12,13] It is based on the assumption that the danger of PCPC may be assessed according to carcinogenic risk, that the character of PCPC action on man and animal species is like the action of 2,3,7,8-TCDD and that the total effect of a PCPC mixture on the organism is equal to the sum of the effects of its components. Proceeding from these assumptions the dose of 2,3,7,8-TCDD considered safe on chronic administration proved to be 1 pg per kg body weight of man per day and indices of relative danger were found for all isomers relative to 2,3,7,8-TCDD (Table 1). This enabled a definite concentration of an isomer mixture to be represented by the equivalent concentration of 2,3,7,8-TCDD and its admissible quantity in various parts of the environment, in drinking water and in food to be regulated.

Results obtained using such methodology proved to be optimistic since it assumes consumption by adult man of water and food containing PCPC at concentrations up to 20–35 parts per trillion in 2,3,7,8-TCDD equivalents. Fish products and undefatted meat products are foods in which PCPC accumulates up to such concentrations. However, human milk must be considered to be dangerous for children in industrial countries since the concentration of PCPC in it exceeds that permissible by 2–10 times. In addition a mass of other information refers to such a conclusion optimistically.

In the first place on examining populations of persons, including volunteers, subjected to the action of PCPC, it was shown that these xenobiotics are retained significantly longer in man than in experimental animals. The time for the half-elimination of dioxin is 7 years from human lipid tissue, 1 year from monkeys and from several days to several weeks from other animal species. The absorption of dioxin is also appreciably greater in the human gastro-intenstinal tract (85% and more) compared with animals. It also turns out that highly chlorinated PCPC are retained longer than TCDD and TCDF. In animals, as in soil, they are subject to reductive dechlorination to more toxic compounds, which causes their unusual toxokinetics. Thus in animals poisoned with octa-CDD, symptoms typical of dioxin poisoning are displayed only after 13 weeks.[14] All these data cast doubt on the reliability of the methodology considered above for assessing the danger of PCPC to man. It does not consider the enhanced ability of these xenobiotics towards bioconcentration and retention by man, the inevitable result of which must be a strengthening of the long term after-effects of poisoning.

Secondly material appearing in recent years indicates the significantly higher danger of PCPC poisoning of the immune system than the carcinogenic risk. Thus in experiments on primates using food containing 5 parts dioxin per trillion for a year a strong and extended (up to 4 years) reduction was shown in the number of immune cells and in the T_4/T_8 ratio which indicates the extremely strong suppression of cellular immunity by these poisons and primarily of lymphocyte-helpers. This needs watching over since contemporary illnesses such as AIDS, T_4-leukaemia, Legionnaires' disease, etc. are linked precisely with T_4 cell activity. The extemely strong dose-dependent influence of dioxin on the immune system after oral administration (from the suppression of interleukin-1 synthesis and the sensitivity of T-lymphocytes to it, suppression of antibody formation, viability of B-lymphocytes and their bone marrow precursors to atrophy of the thymus and depletion of lymphoid tissue) is linked with the direct inflow of this xenobiotic from the gastrointestinal tract to bone marrow and subsequent migration to the thymus with poisoned cells. This must explain the excessive distribution, in regions of PCPC accumulation, of illnesses such as viral hepatitis and various intestinal infections in people and intestinal infections, viral distemper and other illnesses in animals. In such regions the status of babies and children, whose immune systems are just being formed, is particularly dramatic, the treatment of infections is greatly hindered since PCPC increase the biodegration of drugs in man and induce resistance of microorganisms to them.

The sensitivity of the immune system to substances related to dioxin is only beginning to be investigated. First results show that the danger of polychlorodibenzofurans and biphenyls for animals linked with the risk of affecting the immune system is incomparably greater than the carcinogenic risk and in this respect they are probably more dangerous than polychlorodibenzo-*p*-dioxins.[15] This correlates with the special features of their interaction with iron-porphyrin as a result of which furans and biphenyls possess high substrate specificity to a wider collection of haemoproteides than dioxins.[16]

The study of the influence of PCPC on the immune system begun in recent years is a new, significantly more difficult step in the understanding of the secrets of the actions of these xenobiotics on living matter. Chemically the main difficulty of the investigations at this step is the need to develop uniquely sensitive methods for the qantitative determination of PCPC, since the information already existing enables their danger to be considered according to the risk of affecting the immune system at concentrations of the order of tens of parts per quadrillion. Not by chance evidently, the US national programme on dioxin even in 1985 provided for the development of a method for the analysis of 2,3,7,8-TCDD with a sensitivity greater than 10^{-15} g g^{-1}.

III. Sources of dioxin-type PCPC

Investigations in recent years have led to the uncontrolled development by man of technology based on the use of chlorine and its compounds. This development has forced planning of such problems as the possibility of creating ecologically harmless chloro-compound manufacture, an ecological foundation for further large scale chlorine manufacture, the use of inorganic chlorides, in electrochemical, pyrometallurgical processes, the use of chlorine-containing oxidising agents in processes for treating material of natural origin, etc. The investigiations have stimulated searches for the rapid development of technology unconnected with the formation or use of chlorine for obtaining caustic soda, potash, oxides of alkaline earth and transition metals, etc., since PCPC are formed in dangerous quantities in a vast number of the technologies using chlorine, its organic and inorganic derivatives, in the presence of carbon and its compounds.

It has been shown in several countries that in the industrial synthesis of organochlorine compounds, the processing and use of the products introduces the maximal quantity of PCPC into the environment. Particularly dangerous are the majority of high

temperature processes for chlorinating organic substances, pyrolytic processing, combustion of organochlorine compounds and the synthesis and use of so-called PCPC precursors in nature, which include tri-, tetra-, pentachlorophenols, polychloropyrocatechols and their derivatives, 3,4-dichloroaniline and its derivatives, polychlorobenzenes and other polychloroaromatic compounds, isomeric hexachlorocyclohexanes, including Lindane, etc. All these compounds are converted into PCPC not only on pyrolysis or combustion but also on metabolism *in vivo* and on oxidation in the presence of haemoproteides. The content of PCPC in dangerous organochlorine products varies within wide limits, from fractions of a gram to tens of grams per ton. On average it may be considered that the manufacture and use of a million tons of a chloro product introduces no less than a ton of PCPC into nature.

The cellulose–paper industry is the second dangerous source of PCPC. When bleaching cellulose pulp with chlorine, oxidation and chlorination of the lignins present in the pulp occur which is accompanied by the formation of PCPC and its precursors. Replacement of chlorine by its oxide, by hypochlorites, chlorites and chlorates do not prevent the appearance of PCPC, concentrations of which reach 400 parts per trillion in waste water and up to 40 parts per trillion in bleached cellulose. The preparation of one ton of bleached cellulose by this means introduces up to 1 g PCPC and hundreds of grams of their precursors into nature. PCPC are formed by a similar route on disinfecting water containing phenolic substances and lignins with chlorine.

Significant quantities of PCPC are formed on combustion of solid domestic waste. According to existing data, operating one incinerator for a year put from 1 to 100 g PCPC into the atmosphere, the main quantity of which is evolved with the effluent gases. The quantity of PCPC formed depends on the combustion regimen and the composition of the waste burned. Their content is increased by the presence in the waste of polychlorovinyl and other polymers, and of organic and inorganic compounds of chlorine.

Sources of PCPC which are still insufficiently clarified are electrochemical processes for the manufacture of oxides of magnesium, nickel and possibly other metals from their corresponding chlorides. It is considered that these processes are comparable with the cellulose–paper industry in quantity of PCPC discharged into nature.

The smelting or initial heating of metals in electric arc furnaces is accompanied by the formation of PCPC. They are found on smelting copper and in the preparation of intermediate products for steel alloy objects. Large quantities of PCPC are emitted by motor transport using organochlorine or organobromine additives in motor fuel or in lubricants.

The list already presented indicates the extremely wide scale of poisoning of the biosphere with PCPC which has taken place in the past 30–40 years all the more so since their high stability in nature enables their constant accumulation. It may be considered roughly that during the period the manufacture and use of tens of millions of tons of organochlorine substances have introduced into the biosphere tens of tons of PCPC and several million tons of their precursors which are also partially converted into PCPC in nature. The cellulose–paper industry, metallurgy and processing of domestic refuse introduce into nature no less a quantity of PCPC than the manufacture of chlorine compounds. The total volume of PCPC fed into nature may seemingly be estimated at several hundred tons. This vast quantity of such strong poisons is sufficient to induce global disturbance of the functions of the animal life of the planet. That is why it is not remarkable that all the industrially developed nations have allotted huge resources to the exposing and elimination of technological practices emitting into the biosphere PCPC in quantities even of the order of tens of grams per year.

IV. Protection of man and nature from PCPC

Protection from PCPC is an unusual problem which is impossible to solve by traditional methods. This is due to the unusual properties of the xenobiotics considered[1] and their remarkable persistence.[17] PCPC may be destroyed in the gas phase or in solution by UV irradiation or even by sunlight. However on passing into the environment they are absorbed by inorganic materials and become insensitive to radiation. Their stability increases on passing into an organic phase and especially in living organisms where they accumulate. Only aerobic cells detoxify PCPC at a low rate. However on trying to degrade PCPC by such powerful oxidising agents as superoxide anion radicals and hydroxyl radicals, the latter destroy themselves. This guarantees the extended preservation of PCPC in nature (time for half-destruction is from 10 to 30 years or more), their ability to migrate along food chains or with water streams and transfer across borders into complexation with organic substances.

Several approaches have been studied in the search for methods of protection of man and animals from PCPC. The influence of natural antimutagens (vitamins A, B_1, E, C, etc.) on the toxic effects of dioxin has been studied in animal experiments. Competitive inhibitors of PCPC binding to bioreceptors have been studied as possible therapeutic agents. Only some reduction of dioxin effects on animals has been obtained in these cases. Evidently the formulation of a solution to the problem as the creation of a single cardinal method of protecting man from PCPC is not valid. In addition our investigations have enabled consideration of methods of prophylaxis and therapy of a series of ecological disorders arising as the fault of PCPC, primarily for groups at enhanced risk (pregnant women, babies, children).

With the aim of cleaning up the medical and ecological situation in regions of PCPC accumulation there is particular interest in the complex of programmes which, judging by available data, are being carried out in the industrially developed nations. The aim of one of them is to obtain a sharp fall in the technological burden on man and nature in affected regions. This provides:

elimination of the flow of PCPC to nature;

ecologisation of pesticides and of methods of applying them, optimisation of preparations and medicinal chemicals for living conditions and industry;

ecological standardisation of the manufacturing and agricultural industries.

Simultaneously a programme for protecting the population is being put into practice which is directed towards the partial disconnection of man from the PCPC biotransfer chain (cutting down of the consumption of dangerous food products, creation of new food sources from safe production) and the increase of man's resistance to PCPC (vitaminisation of drinks and food products, optimisation of food sources for amino acid composition, phospholipid content, etc.). Apparently the development of a complex of drugs intended for the treatment of ecological illnesses is also included.

Much attention is being paid to the ecologisation of landscapes around populated localities, in recreation zones and in plant growing areas. The aim of this programme is the creation of optimal

conditions for the development of aerobic microflora and the maintenance of constantly high activity for them. In the complex of agrotechnical and agrochemical measures developed a major role is played by a wide application of organic and microbiological fertilisers and also to growth stimulators and the development of lower and higher plants.

Significant results, obtained from putting into practice a complex of programmes in Japan, USA, Canada, FRG, and other countries in which huge quantities of PCPC have passed into the environment, indicate that mankind cannot now disregard the presence of these poisons in the biosphere and is obliged for many future decades to build up specially new conditions for his poison-free existence and cleaning of the environment. An unsafe medical situation and a multitude of regional ecological outbursts in our country are undoubtedly connected with underestimation of world-wide practice on the route and scale of using chlorine and its compounds and also of attempts to protect man and nature from the technological activity under conditions of enhanced PCPC content in the environment.

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Translated from *Uspekhi Khimii* **60** 545–551 (1990)

Main directions for reducing the ecological burden when using pesticides

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The influence of human society on the environment began in the period when people moved from gatherings in dense forests to farming and animal husbandry. The process developed particularly intensively in the period of scientific-technical revolution and the creation of various branches of industry. Each branch of modern industry makes its 'contribution' to the action on the environment. Thus combustion of coal and lignite mined at the present time leads to contamination of the environment by powerful carcinogens such as benzopyrene and benzanthracene.[1,2] Combustion of coal alone leads to the discharge of about 3000 tons of mercury into the environment[3] and a significant quantity of sulphur dioxide and other harmful products. It is sufficient to say that in the USA alone about 200 000 000 tons of various chemical compounds pass into the environment each year. Contaminants such as polychlorobiphenyls (used in the electrical industry), polychlorodibenzofurans and polychlorodibenzo-*p*-dioxins formed on combustion of municipal refuse, or when bleaching paper with chlorine and in many other cases are a serious danger. It is possible to form an opinion on the danger of this group of substances only from their acute toxicity for mammals. Thus the LD_{50} of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin for guinea pigs is 0.6–2 μg kg^{-1}, and for monkeys 70 μg kg^{-1}.[4] In addition these compounds possess carcinogenic, teratogenic and immunotoxic actions. The safe concentration of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in drinking water is considered to be 0.000035 μg $litre^{-1}$.[5] Pesticides as contaminants of the environment amount to less than 1% of total contamination, however since they are physiologically active compounds serious attention is paid to them and there is discussion in print on the expediency of their practical use. In addition it is impossible to obtain high and consistent harvests without the application of pesticides for the protection of plants against vermin, diseases and weeds.[6,7] The application of pesticides is spreading without interruption. In 1986 a total of US$17.4 billion worth were used, in 1987 $20 billion, and according to a forecast their consumption in 1990 will rise to $21 billion.[8]

The consumption of pesticides in various countries in 1987 was as follows (in $ millions): USA 4450, Japan 3450, France 3400, USSR 1075, Brazil 875, Italy 860, FRG 855, Great Britain 760, Canada 545, India 510, Spain 485, Chinese People's Republic 465, Australia 399, Hungary 320, South Korea 280, Denmark 240, Netherlands 210, Argentina 205, Indonesia 170 and Mexico 155. The consumption of pesticides in 1987 according to preparation types was (in $ millions): herbicides 8600, insecticides 6100, fungicides 4100 and others 1200. It should be noted that the data given cover only 20 countries, the largest consumers of pesticides.[8]

The influence of pesticides and other xenobiotics depends on the following main properties: persistence, acute and chronic toxicity for various forms of living organisms, decomposability under the action of various forms of living organisms (biodecomposition) and the presence of various negative effects from small doses of preparation over an extended time. Pesticides are subdivided into six

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groups according to persistence: 1) preparations with a retention time in the environment of more than 18 months, preparations with a retention time of 2) 18 months, 3) 12 months, 4) 6 months, 5) 3 months and 6) less than 3 months. It is quite evident that depending on climatic conditions the retention time of any xenobiotic in the environment may vary within fairly wide limits. However it is possible to use the following formula to compare individual preparations for persistence and overall ecological burden on the environment:

$$EB = \frac{C}{LD_{50}} P,$$

where EB is the ecological burden per hectare, C the standard consumption of the preparation per hectare in g, P the persistence of the preparation in weeks (half life) and LD_{50} is the standard acute toxicity in mg kg^{-1}.[9] Finally, the formula shown does not give absolute values but enables comparison of the relative danger from one preparation to another.

Table 1. Persistence, acute toxicity and standard consumption of pesticides of various generations.

Pesticide generation	Persistence group	LD_{50}, mg kg^{-1}	Standard consumption, kg $hectare^{-1}$
Insecticides			
First generation:			
arsenic compounds	1	1.8–5	4–10
Second generation:			
organochlorine	1–2	25–1000	0.1–2
organophosphorus	5–6	1–3000	0.5–5
carbamates	5–6	25–1000	0.5–2
Third generation:			
pyrethroids	5–6	40–2000	0.006–0.1
hormonal	5–6	1000–2000	0.05–0.3
Fungicides			
First generation	1–3	5–450	5–9
Second generation (disinfectants)	5–6	18–200	0.003–0.2
Third generation (dithiocarbamates)	5–6	400–6000	1.8–3
Fourth generation (azoles)	5–6	400–4000	0.025–0.15
Herbicides for monocotyledonous weeds			
First generation (TCAN, Dalapon)	4–5	3000–4000	4–20
Second generation (thiocarbamates)	5–6	400–1400	1–2
Third generation (hydroquinone derivatives)	5–6	800–3000	0.25–1
Herbicides for dicotyledonous weeds			
First generation:			
dinitrophenols	5	40–100	2–4
ammonium sulphate, chlorates	4–5	100–500	200–600
Second generation (aryloxyalkanecarboxylic acids, benzoic acid derivatives)	2–4	300–1000	0.2–2
Third generation (sulphonylureas)	1–6	1000–5000	0.01–0.05

It should be noted that in the last decade pesticides have undergone profound changes both in persistence and in ecological burden on the environment and in danger to animals and man. Data are shown in Table 1 on some properties of pesticides of various generations. As is evident from Table 1 a sharp change has occurred in the persistence, toxicity and standard consumption per hectare of the preparations under consideration. For example the standard consumption of insecticides has been reduced from several kilograms to several grams per hectare, the acute toxicity has also changed. Preparations may be selected with different duration of action and the same toxicity for mammals. Earlier compounds, chiefly of arsenic, were used which had a practically absolute persistence but at the present time there are preparations which are decomposed into the simplest substances during one or two days, weeks or months. Such preparations may not damage the environment.

There is a completely analogous picture for fungicides the standard consumption of which is up to 25–100 g $hectare^{-1}$. At such standards of consumption it is difficult to visualise contamination of the environment, since two tons of soil will carry 2.5–10 mg preparation. Results on the design of new herbicides are particularly prominent both for control of monocotyledonous and dicotyledonous weeds.

Regarding persistence it is also possible to select herbicides the rate of decomposition of which does not exceed one vegetation cycle.

It should also be noted that fairly weakly toxic preparations may be selected according to their mammalian toxicity, in many cases not exceeding the acute toxicity of sodium chloride. It is pertinent here to recall the hypothesis of Paracelsus, that all substances are poisonous but only the dose makes them a poison. This hypothesis is also true for establishing maximum tolerated levels (MTL) for such effects as teratogenic and carcinogenic action. For example on feeding animals with food containing more than 120 g kg^{-1} ethylenethiourea, the appearance of malignant tumours is observed while at a lower content of this substance in food no carcinogenic action was recorded. Furthermore it is necessary to study the possible remote consequences of the action of small doses of preparations over an extended time in certain animal species and in three generations of experimental animal. Adequate guarantees of the safety of a preparation will emerge in such a study.

An important problem in the study of new preparations is their biodegradation by various species. With this aim the metabolism of pesticides has been studied in mammals, plants and microorganisms with isolation and identification of all the pesticide decomposition products and also with determination of the rate of metabolism and the dynamics of residues at harvest. Determination of the dynamics of decomposition of pesticides in plants enabled establishment of the expected time after treatment necessary to obtain products free of pesticide. In many countries the expected time is the chief criterion for the quality of products treated with pesticides (in addition to analytical determination of residues of them at harvest). Finally the expected time, which is determined for each region separately, may not be the same under different climatic conditions and in different cultures. The expected time is linked to a significant extent with temperature, residues and the metabolic rate in a given culture. For example chlorosulphone metabolises rapidly in wheat and is practically not decomposed at all in sugar beet.

Prior to permitting a new preparation for practical use in agriculture it is carefully studied in all the aspects enumerated above including the mutagenic, carcinogenic action and the teratogenic effect in animals. However data obtained in one animal species may not always be transferable to another animal species or man. Consequently a 'safety margin' is taken which in the majority of cases is two orders of magnitude less than the safe level for animals.

Pesticides intended for the treatment of animals and their food are studied in a given species of animal. Not only is their content determined in animal husbandry products going into human food but also the dynamics of their elimination from animals and the character and content of the metabolic products. Such a study guarantees to a fair degree the safety of using animal husbandry products in human food. It is noted that preparations which give residues in animal husbandry products, are not used at the present time in the majority of countries. However it is necessary to note that after use fairly significant quantities of DDT, toxafen and other similar substances were retained in the environment, hence residues of the substances indicated are frequently found in water although in insignificant quantities.[10] It is noted that significant quantities of polychlorobiphenyls are found in many living organisms as is seen from Table 2.

Table 2. Content of polychlorobiphenyls in various forms of animal.

Organism	Year	PCB content mg kg^{-1}*	Region
Pike	1980	2.4	Baltic
Guillemot	1981	100	Sweden
Cormorant	1975	130	Sweden
Eider	1980	2.6	Spitzbergen
Osprey, eggs	1978	200	North Sweden
Marsh harrier, eggs	1977	150	North Sweden
White tailed eagle	1982	340	Lapland
Grey seal	1976–1978	38	Baltic
Ringed seal	1981	85	—
Greenland seal	1982	4.5	—
Caspian seal	1977	1.5	Caspian

*Calculated in lipids.

As is known polychlorobiphenyls are not used as pesticides but are extremely stable compounds being metabolised slowly by various living organisms. Even more stable is 2,3,7,8-tetrachlorodibenzo-*p*-dioxin which may be retained in Californian soil for more than 14 years.

It is noted that extremely poisonous compounds, products of the metabolism of phytopathogenic fungi, such as mycotoxins, may accumulate in the environment. The toxicity of some of them is given in Table 3. The use of pesticides enables elimination of mycotoxins which possess carcinogenic and mutagenic action as well as high toxicity.

Analysis of grain cereals for nivalenol content (500 samples from 19 countries) showed that mycotoxins may be contained in grain in extremely significant quantities.[11] Results are shown in Table 4 on the determination of nivalenol in several grain crops from 19 countries. It shows that the nivalenol content of same samples reached fractions of one percent. Fungi of the fusarium, verticillium and some other genera are producers of many toxins.

In addition to the toxins produced by microorganisms there are a large number of poisonous plants in nature by which people used to be poisoned with lethal outcome. In Central Asia over 30 years there was a large number of poisonings by trichodesma seeds which contaminated wheat and entered flour, as a result of which many cases of poisoning were recorded. After the application of herbicides of the aryloxyalkanecarboxylic acid type this weed was successfully eliminated and poisoning of people ceased. Toxicities for mice of certain peptides isolated from plants are given in Table 5.[12] As is seen such peptides are extremely toxic and are close in potency to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, which is the most poisonous xenobiotic.

Table 3. Acute toxicity of some mycotoxins in rats.

Mycotoxin	LD_{50}, mg kg^{-1}
Aflatoxin B_1	7.2
Toxin T	3.6
Nivalenol	7.4
Fusarenone X	4.4
Maloformin	4.0
Strychnine (for comparison)	7.5

Table 4. Content of the mycotoxin nivalenol in various cultures.

Culture	Nivalenol content, mg kg^{-1}
Wheat	127
Barley	101
Maize	766
Rye	47
Oats	438
Rice	22
Sorghum	90

Table 5. Acute toxicity of some peptides of vegetable origin.

Name	Plant	LD_{50}, mg kg^{-1}
Abrin	*Abrus precatorius*	0.6
Viscotoxin	*Viscum album*	2.4
Volkensine	*Adenia volkensii*	1.4
Modecin	*Adenia degitata*	2.1
Ricin	*Ricinuscommunis*	2.6

The 17-year experiment of Polish investigators on the influence of pesticides in crop rotation on the environment is of interest.[13] It was carried out from 1963 to 1980 in an area of more than 500 hectares. In all of this period 11 846.3 kg pesticides were applied to the area mentioned. This included 804.2 kg DDT, 376.26 kg Lindane, 170.28 kg Methoxychlor, 476.626 kg organophosphorus and carbamate insecticides, 697.975 kg fungicides (including 9.02 kg mercury compounds) and 9315.302 kg herbicides. All products grown on the area mentioned were analysed each year as well as the wild animals, birds, water and soil. As a result of the work the

authors concluded that contamination of plants by pesticides, Lindane, DDT, or organophosphorus compounds was not observed. They were not detected in the parts of plants near the ground nor in roots. It is particularly interesting that they were not detected in potato tubers or in sugar beet in spite of their presence in the soil. The best test object for determining soil contamination by organochlorine preparations is the earthworm, in which bioconcentration of DDT and Lindane occurs, and is linked with their constant living in soil and feeding specifically on organic residues. Ground beetles and field mice are also capable of accumulating organochlorine preparations and carbamates but do not accumulate organophosphorus compounds.

The observations of the Polish investigators correlate to a definite extent with results of the work of scientists of other countries, including the Soviet Union.

The dynamics of growth of the numbers of wild animals and birds are of interest. In Hungary in 1967 roe deer, boar, deer, grey partridges, pheasants and hares were recorded at 107.8, 12.2, 21.8, 588, 889.0 and 101.76 thousands respectively at a pesticide consumption of less than 3 kg hectare^{-1}. In 1974 when the consumption of pesticides per hectare of seeding and planting land had grown to 4.6 kg the numbers of animals indicated above increased to 173.0 17.0, 38.0, 860.0, 2360.0 and 1100.0 thousands respectively.[14] A similar picture was observed in North Rhine Westphalia.

The influence of pesticides on aquatic flora and fauna has great significance and in this connection their toxicity for water organisms, including various fish species, has been studied in an extremely detailed manner. It was established that organochlorine compounds are capable of accumulating in fish, from which they are eliminated comparatively slowly and as a result they may pass with the fish into the human food chain. However, the use of such a type of compound has either been sharply reduced or stopped completely in the majority of countries, including the Soviet Union. Organophosphorus pesticides themselves do not as a rule accumulate in fish and are rapidly eliminated. For example Carbofos is eliminated from fish in one day and other phosphorus pesticides in a week.

It is necessary to record that the use of insecticides in agriculture may be reduced by 30–50% by using sex pheromones for determining numbers of the most dangerous pests and determining thresholds for their noxiousness. Pheromones are ecologically clean and may not damage the environment or useful insects. It is expedient to use insect pheromones as widely as possible. Pheromones may replace insecticides to a significant extent in the disorientation of insects.

Cutting down the consumption of fungicides may occur only through the removal of stable sorts of plants, which however lose their resistance to a given form of disease after 2–3 years. In this connection it is doubtful whether it will be possible to give up fungicides in the next decade. There is no reasonable alternative to herbicides. In addition, in the majority of cases residues of herbicides are not found in the harvest. However in all cases it is most expedient to use a combined system of plant protection with intensive farming technologies. An integrated system of plant protection when considering harm thresholds and a well tuned monitoring of harmful organisms helps appreciably to reduce the ecological burden arising from the use of pesticides.

It is necessary to set up a state plant protection service of the type of the veterinary service which will secure correct and intelligent use of pesticides and the observance of a standard plant health situation. Special self-supporting teams must be set up for plant protection for tenants, which should use pesticides in a skilled manner and guarantee purity of the resulting products.

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Brief communications

Translated from *Uspekhi Khimii* **60** 552 (1991)

Possible approaches to ecologically sparing insecticides

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The main danger of using synthetic insecticides is their toxic action on warm-blooded animals and man, linked with the fact that the preparations used until now act on the life-guaranteeing systems common to the living world. There are two possible ways to reduce this danger, either to reduce the stability of preparations or to increase the selectivity of their action. The first is a palliative since it, in the final consideration, leads to accumulation in nature of only secondary conversion products of the labile preparation. Solution of the selectivity of action problem may in our view be found in diverting interest to that region of insect physiology which is most removed from the physiology of vertebrates, viz. the insect endocrine system, the functional principles of which differ markedly from those of vertebrates. Thus compounds replacing or blocking juvenile hormones or shedding (ecdysteroids) and capable of causing sudden or irreversible changes in insect activity may prove to be completely neutral or even useful for all remaining living beings.

The possibility of such an approach has been verified in our laboratory using synthesised compounds of the polyhydroxysteroid series as examples.

These compounds were represented by derivatives of 20-keto-21,24-dinorcholane with an open side chain or tetrahydropyran ring E and with Δ^5,5αH,5αOH-6-keto grouping in rings A/B, with derivatives of 20-acetoxy-21,24-dinorcholane with increasing number of oxygen-containing substituents in ring E and with the same substituents in rings A/B, with derivatives of Δ^5,5αH,5αOH-6-keto-steroids with a δ-lactone ring E, with analogues of the natural chiogralactone with various degrees of saturation and oxidation state of ring E or derivatives of 21,24-dinorcholan-23-oic acids.

It was shown that compounds of the types investigated may actually intrude in the process of metamorphosis of insects, inhibiting it. At the same time, as was established in other experiments, compounds of the same type are synergists of the binding of glucocorticoids with cytosol receptors in the heart of warm-blooded animals, i.e. they display adaptogenic properties. Such a combination of actions on insects and warm-blooded animals is at least extremely promising. Naturally the direct use of complex steroidal preparations as insecticides is unsuitable because of their low availability, however determination of the parameters of groups strengthening their interaction with those and other receptors, may lead to simpler analogues.

Translated from *Uspekhi Khimii* **60** 553–554 (1991)

New trends in the creation of pesticides with a low ecological stress

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Modern farming cannot do without effective protecting agents against pests, disease, and weeds. The use of pesticides makes it possible to reduce the labour expended in agriculture on the care of seedlings and makes it possible to proceed to the growing of the most important cultures by an industrial technology which ensures high and stable crops.

At the same time the use of pesticides poses a series of most important ecological problems because of their negative side effects on the ecosphere, accumulation in objects within the environment, etc. World science—chemical, biological, and ecological—is therefore faced by the important and urgent problem of creating a new generation of ecologically safe chemical plant protecting agents.

The use of the ideas suggested by nature appears the most promising, in particular the creation of compounds analogous to natural chemical plant protecting agents, as well as their chemical modification. Such compounds act as a rule at low and ultralow concentrations, are highly selective, and do not persist for a long time. They include, for example, phytoalexins (substances of endogenic origin synthesised in plants in response to the action of various factors, including pathogenic microorganisms, in order to combat them), allelopathic agents (minor metabolites of higher plants which suppress the development of other plant species, i.e. which exhibit herbicidal properties), phytocides, cytokinins, and auxins of natural origin, etc.

The procedures for the chemical modification of natural biologically active compounds are similar to the approaches used in the modification of natural chrysanthemic acid (secondary metabolite of camomile), which led to a whole new branch in the field of synthetic metabolites—pyrethroids.

Ecologically clean biotechnological processes for the preparation of pesticides have been developed vigorously in recent years, for example, the advances by Japanese investigators in the biotechnological synthesis of avermectins—ionoform antibiotics exceptionally active against a number of vicious pests (ticks, phytophages, and nematodes). These studies were noted in 1986 as the greatest worldwide achievement in the field of pesticides.

A series of other aspects of the creation of highly selective and relatively ecologically safe pesticides are also noteworthy. These include photodecomposable pesticides, herbicides with photodynamic activity (PDH), and propesticides.

The photodecomposable pesticides include compounds which exhibit fungicidal and herbicidal effects in the dark and which are converted into inactive and non-toxic compounds in the light. The first representatives of these compounds have been synthesised in the

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The activity of the PDH is based on the use of natural regulators of intracellular biochemical processes. This suggests a comparatively high ecological cleanliness of preparations with photodynamic activity. Among the advantages of the PDH, one may include the high selectivity of their toxic activity based on the photodependent biological effect, achieved in plant organisms, and the impossibility of their photoactivation in the organisms of warm-blooded animals. In addition, one should note that the outcome of the effect of the PDH on the cell is the activation of radical oxidation reactions of various intercellular components and in the first place membrane components. The quantum yield of these processes can significantly exceed unity. By virtue of this feature of photodynamic processes, one may hope that it will be possible to reduce sharply the active concentrations of the preparations, which is important from the ecological and economical points of view. Furthermore, one should postulate that the non-specificity of the activity in the photodependent stage rules out the possibility of the development of plant species resistant to the PDH.

The action of propesticides (compounds which do not exhibit a pesticidal activity from the beginning) is based on the biochemical activation of the molecules by the enzyme systems of plants, as a result of which the pesticide molecules are generated in the plant cells. The species specificity of such preparations is based on the differences in the activities of enzymes in cultivated plants and weeds. For example, the difference between the activities of alcohol dehydrogenase in various plants served as a basis for the creation of selective propesticides of the chlorophenoxyethanol series (phenteracol — Hungary).

The study designed to create herbicides of this type as well as PDH necessitates the development of a biochemical base for the investigation of the principles governing the species specificity and selective toxicity. Here it is possible to distinguish three most important problems:

The study of the characteristic features of the transport of pesticides through biological membranes, the establishment of relations between their transport characteristics and their structure, and the determination of the characteristic features of the interaction of pesticides with biological membranes, including the molecular mechanisms of the influence of pesticides on the structure and function of membranes.

The study of the differences in the biochemical homeostasis of cells of useful and harmful organisms and in pathological states. The determination of the molecular mechanisms of the response reactions to the action of xenobiotics.

The study of the characteristic features and pathways in the metabolism of pesticides in the cells of living beings and in objects within the environment in order to elucidate the mechanisms of the pesticide effect and also the routes to their metabolic activation and the characteristics of the latter.

Translated from *Uspekhi Khimii* **60** 554–555 (1991)

Biologically active substances of ecological importance and methodological aspects of the estimation of the biological activity of pollutants

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The study of natural ecological chemoregulators and chemomediators is important for the development of new ecologically safe pesticides and chemical plant and crop protecting agents.

Substances of this kind include phytoalexins and other antifungal substances in plants, phage repellants, antifeedants, toxins, antiovipositants, phytoecdysones, juvenile hormone substances, and various attractants and pheromones. One of the problems associated with the chemical pollution of the biosphere is that of the estimation of the biological activity of pollutants. In order to discover the optimum methods of estimating pollutants and xenobiotics, to investigate the possibility of a correspondence between data obtained by various methods and for various objects, and also with the aim of securing new information about the biological activity of anthropogenic substances, the author carried out biotests on certain pesticides and surfactants as well as certain industrial preparations on various biological objects. The substances investigated included pesticides (DNOK and lontrel), surfactants (sulphonol, sodium dodecanesulphonate [sodium dodecyl sulphate?], Triton X-100, ethonium, and TDTMA), and surfactant-containing preparations "Kashtan" (chestnut), "Verbena" (vervain), "Vil'va" [?], and others. The seedlings of a number of plants, including macrophytes, were used as the test objects. It has been shown in the latest experiments that sulphonol (0.5 ml litre^{-1}) almost completely suppresses the growth of the roots of *Oryza sativa*. It is proposed that the adopted modifications of biotesting methods be used on a wider scale for the estimation of the biological activity and ecological danger of substances.

Translated from *Uspekhi Khimii* **60** 555–557 (1991)

Social-ecological aspects of the use of plant protecting agents in Uzbekistan

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Since the 1970s, the problem of dangerous xenobiotics among polyhalogenated polycyclic compounds capable of exhibiting mutagenic, carcinogenic, teratogenic, and embryotoxic activities and of damaging the liver and the immune and central nervous systems as well as the blood forming organs at very low concentrations has been widely discussed in the world press. One of such compounds is dioxin, which forms part of the composition of copper

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trichlorophenoxide and other numerous plant protecting agents. This communication deals with the problem of dangerous xenobiotics in relation to Uzbekistan and an attempt is made to develop a strategy for the replacement of copper trichlorophenoxide by non-trivial preparations, which make plants resistant to bacterial diseases.

In order to solve the problem of the replacement of copper trichlorophenoxide by non-toxic preparations, it is essential in our view to develop the following measures: to eliminate the use of waste from cotton fields as fuel; to rethink the solution to problems concerning the preparation of the soil in regions where subterranean water is in close proximity; to eliminate the ploughing in of the stems, branches, and other parts of the cotton plant after raw cotton has been harvested; to develop measures for the stabilisation of light soils; to develop methods for the attachment of preparations to the surfaces of seeds during their treatment, which will make it possible to reduce the dispersion of the preparations and their accumulation within the preserving areas in cotton cleaning workshops; to go over to an improved automated technology for the pre-sowing preparation of seeds; to replace phenthiurams and copper trichlorophenoxide by highly effective preserving agents which are non-toxic to warm-blooded animals; to carry out preserving only under stationary conditions, during periods which do not coincide with the flowering of fruit trees; to abandon procedures involving the enzymic treatment of the waste from cotton fields (cotton stems and branches after harvesting raw cotton) in order to obtain additives to the main diet of cattle.

All this can be achieved with the aid of polymer systems for the stabilisation of sand and soil, which makes it possible to prevent the migration of sand and light soils and this in turn will tend to reduce the horizontal migration of preparations incorporating dioxin and other toxic admixtures, with the aid of polymer compositions for the encapsulation of cotton seeds whereby one can eliminate the friability of the preserving agent in the treatment of seeds, storage, transport, and sowing, and by discovering the physicochemical properties of polymer systems and the biological principles on the basis of which it is possible to achieve the specific synthesis of fungicides and bactericides and to create polymer compositions with a high adhesive strength.

In order to solve the social problem, it is desirable to reconstruct the technological process of the presowing preparation of seeds by the following measures: to devise systems for the remote control of the preserving-encapsulation process which would eliminate contact between man and toxic preparations; to develop machines for the encapsulation of cotton seeds and the seeds of other agricultural cultures, which would differ from the existing analogous devices by social advantages combined with a comparatively high productivity; to develop measures for the replacement of traditional preserving agents by compounds of both chemical and biological origin which are non-toxic to warm-blooded animals.

For the solution of the problems formulated, an experimental-industrial specimen of an ecologically closed device "Kapsula-1" was created. It rules out, on the one hand, contact between man and preserving agents and, on the other hand, their tendency to slide off the surfaces of seeds after the additional introduction of water-soluble polymers into the suspension of preserving agents. A satisfactory social effect is achieved by constructing a device for the high-quality coating of seeds by virtue of the high strength of the adhesion of polymer coatings to the surfaces of seeds.

We have now developed together with the VNIIKhSZR polymeric forms of a series of seed preserving agents based on polyvinylpyrrolidinone, the sodium salt of carboxymethylcellulose, methylcellulose, and their mixtures manufactured both in the Soviet Union and abroad. The choice of the polymer matrices is dictated by the characteristic features of the dissolution in the temperature range coinciding with the temperatures at which the seeds of various agricultural cultures germinate. Familiar preparations with systemic and contact activities are used as preserving agents—bronocot, sandopan, alett, tigan, ridomil, and their combinations. However, the majority of these preparations exhibit a definite toxicity to warm-blooded animals and we shall therefore consider in greater detail the alett + polymer binder system.

The treatment of cotton seeds by this system does not exert a significant influence on the capacity of the seeds to germinate in the field compared with the control (phenthiuram) and does not affect the crop of raw cotton. Bearing in mind that alett is based on aluminium and the aluminium compound of triethyl phosphate, whose toxicity is low, and that the toxicity indices are not comparable with those of copper trichlorophenoxide, the data obtained in the field experiments can satisfy the high requirements of the agroindustrial complex of the region. However, the high norms for the consumption of the preparation undoubtedly cannot fail to influence the ecological system in the case of its universal use for a long time. This is why we have devoted much attention to the search for alternative plant protecting agents, which fully rule out a negative effect on the environment and which subsequently determine the ecological strategy concerning the important problem of the protection of agricultural cultures against pathogens and pests.

The complex preparation biopolan, consisting of green microalgae, an antibiotic of the polyene series, and polyvinylpyrrolidinone and systems based on chitin-chitosan derivatives are in our view most promising. Without exerting a negative influence on the capacity of the cotton plant to germinate in the field, grow, and develop as well as the cotton crop, biopolan restores the balance between various species of microorganisms in the soil, creating ultimately highly fertile ecological areas. The introduction of the antibiotic into the composition of biopolan significantly expands the methods for combating the pathogenic fungal species inducing root rot in agricultural plants. The mechanism of the action of systems of this kind has been fairly thoroughly investigated. The role of the chitin-chitosan derivatives in the plant protecting system and in the disinfection of soils has not been investigated thoroughly enough to be able to infer with a high degree of probability their effectiveness let alone recommend their introduction into agriculture. In the study of these systems, it is necessary to investigate the mechanisms of the action of such preparations and to carry out screening and field tests against different backgrounds of infection of soils by pathogenic forms of microorganisms and of pollution by dioxin and its decomposition products.

Thus the solution of problems associated with the use of plant protecting agents at the present time and in the future should follow the route involving the creation and application of a very precise and ecologically closed technology, careful selection of plant protecting agents, and the selection of the method of application, taking into account the ecological crisis situation in the region.

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The activity of the PDH is based on the use of natural regulators of intracellular biochemical processes. This suggests a comparatively high ecological cleanliness of preparations with photodynamic activity. Among the advantages of the PDH, one may include the high selectivity of their toxic activity based on the photodependent biological effect, achieved in plant organisms, and the impossibility of their photoactivation in the organisms of warm-blooded animals. In addition, one should note that the outcome of the effect of the PDH on the cell is the activation of radical oxidation reactions of various intercellular components and in the first place membrane components. The quantum yield of these processes can significantly exceed unity. By virtue of this feature of photodynamic processes, one may hope that it will be possible to reduce sharply the active concentrations of the preparations, which is important from the ecological and economical points of view. Furthermore, one should postulate that the non-specificity of the activity in the photodependent stage rules out the possibility of the development of plant species resistant to the PDH.

The action of propesticides (compounds which do not exhibit a pesticidal activity from the beginning) is based on the biochemical activation of the molecules by the enzyme systems of plants, as a result of which the pesticide molecules are generated in the plant cells. The species specificity of such preparations is based on the differences in the activities of enzymes in cultivated plants and weeds. For example, the difference between the activities of alcohol dehydrogenase in various plants served as a basis for the creation of selective propesticides of the chlorophenoxyethanol series (phenteracol — Hungary).

The study designed to create herbicides of this type as well as PDH necessitates the development of a biochemical base for the investigation of the principles governing the species specificity and selective toxicity. Here it is possible to distinguish three most important problems:

The study of the characteristic features of the transport of pesticides through biological membranes, the establishment of relations between their transport characteristics and their structure, and the determination of the characteristic features of the interaction of pesticides with biological membranes, including the molecular mechanisms of the influence of pesticides on the structure and function of membranes.

The study of the differences in the biochemical homeostasis of cells of useful and harmful organisms and in pathological states. The determination of the molecular mechanisms of the response reactions to the action of xenobiotics.

The study of the characteristic features and pathways in the metabolism of pesticides in the cells of living beings and in objects within the environment in order to elucidate the mechanisms of the pesticide effect and also the routes to their metabolic activation and the characteristics of the latter.

Translated from *Uspekhi Khimii* **60** 554–555 (1991)

Biologically active substances of ecological importance and methodological aspects of the estimation of the biological activity of pollutants

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The study of natural ecological chemoregulators and chemomediators is important for the development of new ecologically safe pesticides and chemical plant and crop protecting agents.

Substances of this kind include phytoalexins and other antifungal substances in plants, phage repellants, antifeedants, toxins, antiovipositants, phytoecdysones, juvenile hormone substances, and various attractants and pheromones. One of the problems associated with the chemical pollution of the biosphere is that of the estimation of the biological activity of pollutants. In order to discover the optimum methods of estimating pollutants and xenobiotics, to investigate the possibility of a correspondence between data obtained by various methods and for various objects, and also with the aim of securing new information about the biological activity of anthropogenic substances, the author carried out biotests on certain pesticides and surfactants as well as certain industrial preparations on various biological objects. The substances investigated included pesticides (DNOK and lontrel), surfactants (sulphonol, sodium dodecanesulphonate [sodium dodecyl sulphate?], Triton X-100, ethonium, and TDTMA), and surfactant-containing preparations "Kashtan" (chestnut), "Verbena" (vervain), "Vil'va" [?], and others. The seedlings of a number of plants, including macrophytes, were used as the test objects. It has been shown in the latest experiments that sulphonol (0.5 ml litre^{-1}) almost completely suppresses the growth of the roots of *Oryza sativa*. It is proposed that the adopted modifications of biotesting methods be used on a wider scale for the estimation of the biological activity and ecological danger of substances.

Translated from *Uspekhi Khimii* **60** 555–557 (1991)

Social-ecological aspects of the use of plant protecting agents in Uzbekistan

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Since the 1970s, the problem of dangerous xenobiotics among polyhalogenated polycyclic compounds capable of exhibiting mutagenic, carcinogenic, teratogenic, and embryotoxic activities and of damaging the liver and the immune and central nervous systems as well as the blood forming organs at very low concentrations has been widely discussed in the world press. One of such compounds is dioxin, which forms part of the composition of copper

trichlorophenoxide and other numerous plant protecting agents. This communication deals with the problem of dangerous xenobiotics in relation to Uzbekistan and an attempt is made to develop a strategy for the replacement of copper trichlorophenoxide by non-trivial preparations, which make plants resistant to bacterial diseases.

In order to solve the problem of the replacement of copper trichlorophenoxide by non-toxic preparations, it is essential in our view to develop the following measures: to eliminate the use of waste from cotton fields as fuel; to rethink the solution to problems concerning the preparation of the soil in regions where subterranean water is in close proximity; to eliminate the ploughing in of the stems, branches, and other parts of the cotton plant after raw cotton has been harvested; to develop measures for the stabilisation of light soils; to develop methods for the attachment of preparations to the surfaces of seeds during their treatment, which will make it possible to reduce the dispersion of the preparations and their accumulation within the preserving areas in cotton cleaning workshops; to go over to an improved automated technology for the pre-sowing preparation of seeds; to replace phenthiurams and copper trichlorophenoxide by highly effective preserving agents which are non-toxic to warm-blooded animals; to carry out preserving only under stationary conditions, during periods which do not coincide with the flowering of fruit trees; to abandon procedures involving the enzymic treatment of the waste from cotton fields (cotton stems and branches after harvesting raw cotton) in order to obtain additives to the main diet of cattle.

All this can be achieved with the aid of polymer systems for the stabilisation of sand and soil, which makes it possible to prevent the migration of sand and light soils and this in turn will tend to reduce the horizontal migration of preparations incorporating dioxin and other toxic admixtures, with the aid of polymer compositions for the encapsulation of cotton seeds whereby one can eliminate the friability of the preserving agent in the treatment of seeds, storage, transport, and sowing, and by discovering the physicochemical properties of polymer systems and the biological principles on the basis of which it is possible to achieve the specific synthesis of fungicides and bactericides and to create polymer compositions with a high adhesive strength.

In order to solve the social problem, it is desirable to reconstruct the technological process of the presowing preparation of seeds by the following measures: to devise systems for the remote control of the preserving-encapsulation process which would eliminate contact between man and toxic preparations; to develop machines for the encapsulation of cotton seeds and the seeds of other agricultural cultures, which would differ from the existing analogous devices by social advantages combined with a comparatively high productivity; to develop measures for the replacement of traditional preserving agents by compounds of both chemical and biological origin which are non-toxic to warm-blooded animals.

For the solution of the problems formulated, an experimental-industrial specimen of an ecologically closed device "Kapsula-1" was created. It rules out, on the one hand, contact between man and preserving agents and, on the other hand, their tendency to slide off the surfaces of seeds after the additional introduction of water-soluble polymers into the suspension of preserving agents. A satisfactory social effect is achieved by constructing a device for the high-quality coating of seeds by virtue of the high strength of the adhesion of polymer coatings to the surfaces of seeds.

We have now developed together with the VNIIKhSZR polymeric forms of a series of seed preserving agents based on polyvinylpyrrolidinone, the sodium salt of carboxymethylcellulose, methylcellulose, and their mixtures manufactured both in the Soviet Union and abroad. The choice of the polymer matrices is dictated by the characteristic features of the dissolution in the temperature range coinciding with the temperatures at which the seeds of various agricultural cultures germinate. Familiar preparations with systemic and contact activities are used as preserving agents—bronocot, sandopan, alett, tigan, ridomil, and their combinations. However, the majority of these preparations exhibit a definite toxicity to warm-blooded animals and we shall therefore consider in greater detail the alett + polymer binder system.

The treatment of cotton seeds by this system does not exert a significant influence on the capacity of the seeds to germinate in the field compared with the control (phenthiuram) and does not affect the crop of raw cotton. Bearing in mind that alett is based on aluminium and the aluminium compound of triethyl phosphate, whose toxicity is low, and that the toxicity indices are not comparable with those of copper trichlorophenoxide, the data obtained in the field experiments can satisfy the high requirements of the agroindustrial complex of the region. However, the high norms for the consumption of the preparation undoubtedly cannot fail to influence the ecological system in the case of its universal use for a long time. This is why we have devoted much attention to the search for alternative plant protecting agents, which fully rule out a negative effect on the environment and which subsequently determine the ecological strategy concerning the important problem of the protection of agricultural cultures against pathogens and pests.

The complex preparation biopolan, consisting of green microalgae, an antibiotic of the polyene series, and polyvinylpyrrolidinone and systems based on chitin-chitosan derivatives are in our view most promising. Without exerting a negative influence on the capacity of the cotton plant to germinate in the field, grow, and develop as well as the cotton crop, biopolan restores the balance between various species of microorganisms in the soil, creating ultimately highly fertile ecological areas. The introduction of the antibiotic into the composition of biopolan significantly expands the methods for combating the pathogenic fungal species inducing root rot in agricultural plants. The mechanism of the action of systems of this kind has been fairly thoroughly investigated. The role of the chitin-chitosan derivatives in the plant protecting system and in the disinfection of soils has not been investigated thoroughly enough to be able to infer with a high degree of probability their effectiveness let alone recommend their introduction into agriculture. In the study of these systems, it is necessary to investigate the mechanisms of the action of such preparations and to carry out screening and field tests against different backgrounds of infection of soils by pathogenic forms of microorganisms and of pollution by dioxin and its decomposition products.

Thus the solution of problems associated with the use of plant protecting agents at the present time and in the future should follow the route involving the creation and application of a very precise and ecologically closed technology, careful selection of plant protecting agents, and the selection of the method of application, taking into account the ecological crisis situation in the region.

Translated from *Uspekhi Khimii* **60** 557–558 (1991)

Ecological aspects of the technology for the application of pesticides

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Studies on the problem of reducing the amount of pesticides in order to diminish the pesticide stress on the environment have been prosecuted for many years at the Institute of Chemical Kinetics and Combustion of the Siberian Division of the USSR Academy of Sciences.

It is believed that, for the effective use of pesticides, it is essential to achieve a certain density of the pesticide deposit and to distribute uniformly its particles on the surfaces of plants with which insects come into contact. If this postulate is always valid, then estimates show that in this case the amounts used are minimal. However, our investigations showed that this is not always true. We demonstrated that the size of the particles influences significantly the efficiency of the pesticide and that there is an optimum particle size for which the consumption of the pesticide is minimal. This size depends on the type of plant, the insect species, the meteorological conditions, and the height of the source (depending on the technology of the application). Together with the Computer Centre of the Siberian Division of the USSR Academy of Sciences, theoretical models have now been developed, which, when executed on a computer, make it possible to determine the optimum particle size. Using this generator, experimental-industrial tests have been carried out in various regions of the country, on different cultures, and with different classes of pesticides. Overall, the experimental-industrial treatment was performed on an area in excess of 200 000 hectares. It was confirmed that the application of the optimum aerosol technology makes it possible to reduce the consumption of the pesticide by a factor of 2 to 10 compared with the traditional technologies. The levels of pollution of the vegetation are reduced by a factor of 10 and more and those of the soil by a factor amounting to tens and hundreds. Aerosol treatments exert a milder influence on biocenoses. The harmful consequences to animals and man are diminished. Labour productivity becomes tens of times higher, while the expanditure of labour and materials diminishes severalfold. Six self-financing enterprises have already been organised in various regions of the country. Our main activity is nowadays concentrated on the study of remote ecological and sanitary-hygienic consequences, on the expansion of the application of the optimum technology to other classes of physiologically active substances, on the training of cadres, on the development of specific technological regulations, and on further improvement of the aerosol technique itself.

Translated from *Uspekhi Khimii* **60** 558 (1991)

Ecological applications of the results of studies designed to assess the regulation and prediction of the stability of polymeric materials

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I should like to draw attention to a topic, not yet touched upon, which has a bearing on ecology and chemistry. The influence of chemistry on ecology should be manifested on at least three levels: the manufacture of chemicals, their exploitation, and their utilisation.

The matters discussed today in the Session concerned mainly problems of manufacture and the processes related to them. Very little has been said about the other two aspects, and yet this is a very important problem and certain approaches to its solution exist.

At the Institute of Chemical Physics, there exists a group of laboratories concerned with the problem of the regulation of the operational stability of a wide range of materials and not only polymeric materials.

The problem of prolonging the useful life of a material is in fact equivalent to increasing the scale of its manufacture and is therefore the problem of an ecologically clean method of increasing such manufacture.

However, it is not always necessary that the material should have the longest possible operational life. Very frequently a definite limited operational period is required after which the material should leave the system in an ecologically clean way. This is the second important problem on which studies are being conducted at the Institute of Chemical Physics of the USSR Academy of Sciences.

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II. INTRODUCTION OF ECOLOGICAL CONSIDERATIONS INTO CHEMICAL AND OTHER INDUSTRIES

Translated from *Uspekhi Khimii* **60** 559–564 (1991)

Certain possibilities of gas-separating membranes for the creation of ecologically clean industries

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The problems of the separation or purification of natural, technological, and exhaust gases have now become especially acute (particularly due to the imperfection of the existing technologies). Certain problems of industrial technology can be solved with the aid of the membrane separation of gases, which constitutes in essence an ecologically clean method.

The assortment of industrial gas-separating membranes, elements, and devices available throughout the world is not as yet very great but, bearing in mind certain advantages of membrane processes, many firms (chemical companies, manufacturers of membranes, suppliers of gases, and engineering firms) have expanded wide-scale research into the membrane separation of gases. According to the prediction by the Day Chemical Company, the scale of the manufacture of gas-separating modules has increased from ten million dollars in 1985 to 145 million dollars in 1990. The separation of gases with the aid of membranes is based on the different rates of transport of gaseous components through polymer membranes due to the [different?] gradients of their partial pressures (concentrations).

A characteristic feature of membrane gas separation processes is the flow regime of their operation. A readily permeable component, for example, a harmful component, can be "removed" from the stream of gaseous raw material entering the membrane module, obtaining at one outlet from the membrane module an ecologically cleaner mixture and at the other outlet (beyond the membrane) a stream enriched in the harmful component to be utilised further or used in recycling. The degrees of extraction and sampling of the components can be varied within wide limits, but, when account is taken of the driving force of the process (partial pressure), it is most convenient to use membranes for the depletion or enrichment of gaseous mixtures with a high content of the components to be separated. At the same time, thorough single-stage purification of gas mixtures by membrane methods cannot as yet compete with alternative methods, for example, the reagent procedures.

It appears that the membrane separation of gases can be used in the solution of ecological problems in the following versions: the isolation and removal of harmful components from gaseous waste; the incorporation of membrane processes in the technology for the prevention of the formation of side products; the application of autonomous membrane devices in processes for the intensification of purification stages.

Table 1. The permeability and selectivity of certain industrial gas-separating membranes.

Type of membrane	Q, litres $m^2\ h^{-1}\ atm^{-1}$					
	H_2	O_2	N_2	CH_4	CO_2	CO
Asymmetric planar polyvinyltrimethylsilane membrane (Institute of Petrochemical Synthesis of the USSR Academy of Sciences, "Plastmassy" Scientific-Industrial Association, 1975)	2500	580	160	260	2000	160
Composite polysulphone hollow fibre (Monsanto Corporation, USA, 1979)	151	22.7	3.8	6.3	104	6.6
Composite planar membrane based on a ternary copolymer comprising fluorinated polymers (Asahi Glass Company, Japan, 1982)	1900	560	140	220	2300	–
Composite planar membrane based on cross-linked polysiloxanes (Asahi Glass Company, Japan, 1980)	4100	3400	1800	5200	13000	–

In the construction of devices, these versions are achieved by inserting membrane devices (modules) in the gaseous "tails" of exhausts from technological processes, or by incorporating membrane modules in the technological scheme for the process, or by using gas mixtures prepared autonomously by membrane methods with intensification of the stages involving the purification of solid and liquid waste. The main gas separating polymer membranes used in industry are described above (Table 1).

The asymmetric planar polyvinyltrimethylsilane (PVTMS) has been developed at the Topchiev Institute of Petrochemical Synthesis (IPS) of the USSR Academy of Sciences and has been manufactured since 1975 by the "Plastmassy" (Plastics) Scientific-Industrial Association. The membrane has been used in processes designed to enrich air in oxygen, in the isolation of hydrogen from its mixtures with nitrogen, methane, and carbon monoxide, and for the separation of mixtures of carbon dioxide and methane. Certain parameters of its permeability are presented in Table 1.

The Monsanto Corporation (USA) manufactures an asymmetric composite polysulphone hollow fibre designed for the industrial separation of water-containing gas mixtures. The membrane modules of this firm are partly used also for the enrichment of oxygen in air.

The anisotropic composite planar membranes of the Asahi Glass Company (Japan) are used mainly for the enrichment of oxygen in air and in processes designed to regulate the composition of a gaseous medium.

New polymer materials for gas-separating membranes are being vigorously investigated in world laboratories. These are, for example, silane-containing block copolymers, polytrimethylsilylpropyne (it has the most effective gas-permeability parameters among the known polymers), and siloxane-containing and other polymeric materials (Table 2). It is noteworthy that the mixtures to be separated consist, with rare exceptions, of permanent gases the diffusion of which in the membrane does not entail specific interactions. On the other hand the separation of, for example, acid gases requires the creation of materials which operate stably under severe chemical conditions. This problem is at present in the development stage (see polyamidoimides in Table 2).

Table 2. Certain experimental specimens of gas-separating membranes tested in world laboratories.

Polymeric materials	Mixtures separated
Silane-containing copolymers (Institute of Petrochemical Synthesis of the USSR Academy of Sciences)	Permanent gases, hydrocarbons
Polytrimethylsilylpropyne (Sanyo Chemical Industry, Japan; Air Products, USA; Institute of Petrochemical Synthesis of the USSR Academy of Sciences)	Air, biogas
Siloxane-containing and other polymers (General Electric Corporation, USA; Polimersintez Scientific-Industrial Association, Mendeleev Moscow Institute of Chemical Engineering, USSR)	Oxygen, nitrogen, carbon dioxide
Poly-4-methylpent-1-ene (Khimvolokno Scientific-Industrial Association, USSR: Torei Company, Japan)	Oxygen, nitrogen, carbon dioxide
Poly(phenylene oxide) (General Electric Corporation, USA)	Air
Polyamidoimides (Ube Company, Japan; Institute of Macromolecular Compounds of the USSR Academy of Sciences)	Hydrogen, acid gases

One of the examples of the membrane separation of gaseous waste is the separation of biogas (Fig. 1). This problem is particularly urgent in large cities where giant plants for the processing of waste are being built. Biogas is obtained in the biodegradation processes involving the waste from animal husbandry, the manufacture of feed, and municipal waste and is formed in enormous amounts—0.5 nm^3† per kilogram of the processed raw material. Fig. 1 shows that the liquid bioprocessing products are utilised as organic fertilisers and biogas, partly used to maintain the biofermenter in the working state, is ejected as waste. Studies on the membrane separation of biogas have been initiated at the Institute of Petrochemical Synthesis of the USSR Academy of Sciences jointly with the Institute of Microbiology of the Academy of Sciences of the Latvian SSR. Preliminary estimates (Table 3) have shown that the membrane purification of biogas will make it possible to obtain a high calorie fuel, freed from hydrogen sulphide locally, for the autonomous provision of energy without any special ecological consequences. Furthermore, it is possible to obtain technical carbon dioxide.

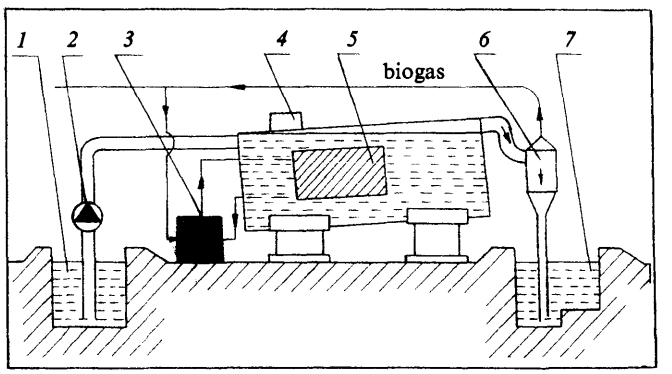


Figure 1. The biogas apparatus (Institute of Microbiology of the Academy of Sciences of the Latvian SSR): (*1*) manure storage compartment; (*2*) pump; (*3*) heat generator; (*4*) service hatch; (*5*) heat exchanger; (*6*) gas–liquid separator; (*7*) organic fertiliser storage compartment.

Table 3. Composition of biogas.

Main components	Initial biogas	After membrane purification
Methane, %	60	95
Carbon dioxide, %	40	5
Accompanying gases (H_2S, H_2, etc.), %	Up to 1	—

The heat generation by the initial biogas and the biogas after membrane purification is indicated below:

	Initial biogas	After membrane purification
Heat generation	50000 kcal nm^{-3}†	8500 kcal nm^{-3}†
	5.8 kW h nm^{-3}†	9.9 kW h nm^{-3}†

*The unit of volume is probably m^3, not nm^3 (Ed. of Translation).

One of the important ecological problems which it will be essential to solve in the next few years with the aid of membrane separation methods is that of reducing the amount of organic solvent vapours or the vapours of petroleum products ejected as waste in the form of mixtures with air. Here a typical source of pollution is not large-scale chemical plants but a multiplicity of small and medium sources—storage depots for motor fuel and filling stations, car body painting workshops in the automobile industry, furnaces for the preparation of sand moulds, etc. In the scheme applied by the Mercedes Company (Federal Republic of Germany), the organic solvent vapours are not only removed from the gaseous medium in such chambers but are also extracted for subsequent use.

Membranes based on cross-linked elastomers are usually employed for processes of this kind. For example, the separation of chloromethanes (methylene chloride, chloroform, and carbon tetrachloride) from nitrogen can be achieved with the aid of membranes based on polychloroprene rubber and its copolymers as a result of the high selectivity of the vapours in relation to nitrogen. The selectivity for gas-separating membranes usually amounts to several tens. As can be seen in Fig. 2, higher selectivities are achieved in this instance, which is extremely important since the typical concentrations of the impurities isolated from air are low.

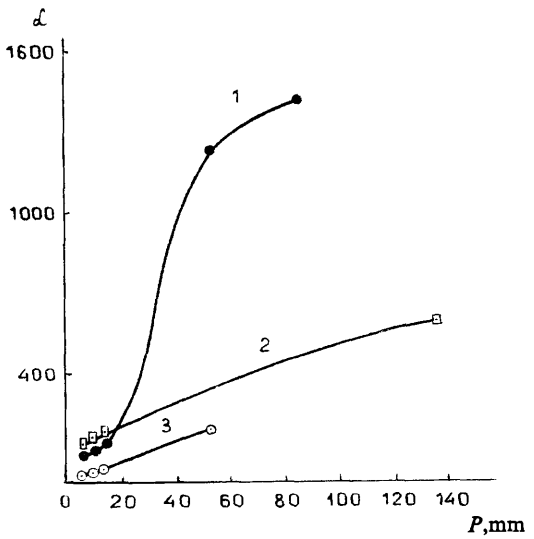


Figure 2. Dependence of the selectivity α (the ratio of the permeability of the organic solvent vapour to the permeability of nitrogen) in the separation of solvent vapours from nitrogen on the partial pressure of the vapour: (*1*) $CHCl_3$; (*2*) CH_2Cl_2; (*3*) CCl_4.

The development of membrane purification methods for gases in order to remove harmful impurities now requires the creation of highly selective and highly permeable membranes with the aid of which it would be possible to solve also the problem of the removal of acid gases from air mixtures.

As an example of the second aspect of the application of membrane processes for ecological purposes, one may consider the oxo synthesis process, i.e. the preparation of secondary alcohols and carbonyl compounds in reactions with participation of synthesis gas. In particular, in the manufacture of butyl alcohols from 2-ethylhexanol, whose output in the USSR amounts to hundreds of thousands of tonnes, the $H_2:CO = 1:1$ synthesis gas is used. On the other hand, in the steam conversion [water gas] reactions, the $H_2:CO = 3:1$ synthesis gas is obtained. Therefore, in order to obtain the synthesis gas with the required composition, one has to apply the complex technology of the copper–ammonia extraction of carbon monoxide from the stream with its subsequent injection into the initial synthesis gas in order to obtain a mixture having the required composition, for example, in the current manufacture of butyl alcohols by the "Perm'nefteorgsintez" Industrial Association.

Part of the gas resulting from the steam conversion of methane (with the composition $H_2:CO = 3:1$) is directed to the carbon monoxide isolation unit with the aid of the copper–ammonia purification. According to the specification, there should be no losses of the copper–ammonia solution, but in reality they occur and are not small. In only one industrial manufacture of the synthesis gas by the "Perm'nefteorgsintez" Industrial Association they amount to 15 tonnes annually when recalculated as metallic copper, i.e. one is dealing with waste comprising a highly toxic metal. Furthermore, ammonia compounds forming part of the composition of the copper–ammonia complex also have an ecologically harmful effect. The replacement of the absorption purification by the membrane process will not only greatly simplify the technological scheme of the process (here there is a possibility of both single- and two-stage versions with intermediate compression of the process product—hydrogen) but also fully eliminates the harmful stage involving washing with the copper–ammonia solution. Bearing in mind that similar and larger plants exist also at other sites (Angarsk, Salavat), the development of a membrane process for controlling the composition of the synthesis gas, which is now being initiated at the Topchiev Institute of Petrochemical Synthesis of the USSR Academy of Sciences in collaboration with the All-Union Institute of Petrochemical Processes, can be important both as regards the community and the protection of the environment.

As regards the third field of application of membranes, nowadays this can concern devices for the preparation of air enriched in oxygen and for the intensification of various biopurification processes. The manufacture of gas-separating devices for the enrichment of air in oxygen based on the Soviet PVTMS gas-separating membrane, the first of its kind in the world, has been initiated in the USSR (Table 4). The "Kriogenmash" Scientific-Industrial Association manufactures also MVK [MAO?—membrane air–oxygen] apparatus of this kind with a productivity of 12.5 to 300 nm^3 of air per hour, the air being enriched in oxygen up to 35%. Such autonomous sources of oxygen are designed to increase the efficiency of the aerobic biopurification of waste; they improve the parameters of other oxidation processes.

One can also imagine that membrane gas-separating devices can play a definite role in the creation of ecologically clean internal combustion engines. Estimates have shown that for this purpose it is necessary to ensure, under room conditions, streams with a flow rate amounting to tens of cubic metres per hour with an oxygen concentration up to 30%. The existing industrial membranes do not possess such capacities. Among laboratory specimens, the greatest hopes are concentrated on polytrimethylsilylpropyne which occupies an unusually high place even in the leading group of organosilicon polymeric membrane materials. Table 5 shows that its permeability is higher by an order of magnitude than the permeabilities of other

materials. If the problem of the manufacture of such a membrane can be solved, then, apart from improving the technical-economical parameters of the operation of the engine, by increasing the oxygen content and reducing the nitrogen level in the air mixture it will be possible also to reduce the ejection into the surrounding atmosphere of the combustion products in the form of hydrocarbons, nitrogen oxides, and solid carbon. The same situation arises also in fuel–energy plants.

Table 4. Membrane gas-separating devices of the MVK series designed for the preparation of air enriched in oxygen directly from the atmosphere.

Principal characteristics	MVK 0.0125	MVK 0.025	MVK 0.3
Productivity, $nm^3 h^{-1}$*	12.5	25.0	300
O_2 concentration, %, not less than	35	35	35
Specific energy consumption, kW h m^{-3}	0.35	0.25	0.14
Starting time, min	1–2	1–2	2–3

*Probably $m^3 h^{-1}$ (Ed. of Translation).

Table 5. Gas permeability coefficients (P) for organosilicon polymers.

Polymer	$10^9 P$, cm^3 cm $cm^{-2} s^{-1}$ $cmHg^{-1}$			
	hydrogen	methane	oxygen	nitrogen
Polyvinyltrimethylsilane	20	1.8	4.4	1.1
Polydimethylsiloxane	65	95	60	28
Polytrimethylsilylpropyne:				
Japan Institute of Petrochemical	690	720	400	200
Synthesis of the USSR Academy of Sciences	700	–	590	280

Thus the possibilities of ecologically clean membrane gas separation processes are associated primarily with the creation of new polymeric materials and membranes with an exceptionally high productivity and selectivity and also with the creation of membrane methods and devices in which the membrane would play not only the role of a separating element but would also be actively involved in the chemical reactions of the substances, i.e. would play the role of a membrane reactor.

Translated from *Uspekhi Khimii* **60** 565–569 (1991)

Chemical aspects of a circulating water supply

M I Kabachnik, N M Dyatlova
Nesmeyanov Institute of Organoelement Compounds,
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All-Union Institute of Chemical Reagents and Specially Pure Chemicals, Moscow

One of the most important ecological problems is that of water. Using water from various natural sources in enormous amounts, the human population partly wastes it by evaporation but most of it is returned to nature in the liquid but contaminated form. In the USSR the overall water resources amount on average to 4500 km^3 per year (4/5 corresponds to surface waters and 1/5 to subsoil waters). It is believed that a little more than 110 km^3 of water can be used annually for industrial and agricultural needs and for utilities without harming the water balance in the country. The industrial consumption of water in the USSR runs to many tens of cubic kilometres (from 40 to 60 km^3 according to different data). Approximately the same amount of water is consumed domestically by the population. The manufacture of one tonne of nickel requires on average 800–850 tonnes of water. The bleaching of 1 tonne of cotton requires 280 tonnes of water. One tonne of caustic soda requires 250–300 tonnes of water, etc. Naturally, even in related undertakings, these consumptions differ markedly. Nevertheless they are very large. A similar situation has been observed also in other industrially developed countries. For this reason, the saving of water and the fight against the exhaustion of the water resources of our planet and the contamination of water have now become one of the most important problems facing humanity.

One of the aspects of the solution of this problem involves the conversion of industrial undertakings and heating systems to a circulating water supply. Trends of this kind are characteristic of many branches of industry, but they are perhaps most characteristic of ferrous metallurgy—a large consumer of water.

The water economy in metallurgical undertakings has developed rapidly during the last decades towards the creation of a circulating water supply system.

More than one thousand circulating water supply systems have now been created in the undertakings of the Ministry of Ferrous Metallurgy of the USSR; the fraction of the circulating water supply in the overall water consumption of this branch of industry has exceeded 85%.

The conversion of the water economy of any industry to circulating schemes leads to a gradual impairment of the quality of water in the systems. As a result of the repeated employment of limited volumes of water (with a necessary external supply to make good the losses) in such systems, salts accumulate and dense salt deposits are formed on the equipment.

The formation of salt deposits in circulating water supply systems is now occurring on a wide scale. Industrial undertakings suffer annual additional costs and losses running altogether to several hundreds of millions of roubles. The removal of part of the circulating water to water reservoirs in order to reduce the content of sparingly soluble salts and thus diminish the rate of formation of deposits is used as a palliative solution. It is then necessary to

materials. If the problem of the manufacture of such a membrane can be solved, then, apart from improving the technical-economical parameters of the operation of the engine, by increasing the oxygen content and reducing the nitrogen level in the air mixture it will be possible also to reduce the ejection into the surrounding atmosphere of the combustion products in the form of hydrocarbons, nitrogen oxides, and solid carbon. The same situation arises also in fuel–energy plants.

Table 4. Membrane gas-separating devices of the MVK series designed for the preparation of air enriched in oxygen directly from the atmosphere.

Principal characteristics	MVK 0.0125	MVK 0.025	MVK 0.3
Productivity, $nm^3 h^{-1}$*	12.5	25.0	300
O_2 concentration, %, not less than	35	35	35
Specific energy consumption, kW h m^{-3}	0.35	0.25	0.14
Starting time, min	1–2	1–2	2–3

*Probably $m^3 h^{-1}$ (Ed. of Translation).

Table 5. Gas permeability coefficients (P) for organosilicon polymers.

Polymer	$10^9 P$, cm^3 cm $cm^{-2} s^{-1}$ $cmHg^{-1}$			
	hydrogen	methane	oxygen	nitrogen
Polyvinyltrimethylsilane	20	1.8	4.4	1.1
Polydimethylsiloxane	65	95	60	28
Polytrimethylsilylpropyne:				
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make good this loss by supplying fresh water to the system, which leads to partial return to open water supply systems. As industrial undertakings are converted into loss-free water utilisation schemes, it becomes urgently necessary to solve the problem of the stabilisation of the possible precipitation of deposits of salts responsible for the hardness of water, i.e. the creation of inhibitors of salt deposition and corrosion.

A similar situation has arisen in non-ferrous metallurgy, in the chemical and petroleum industry, in the systems employed in thermal electric power stations, in heat and power plants, and in other branches of industry. In all cases the organisation of an ecologically favourable circulating or closed water supply is inhibited by the abundant formation of salt deposits, whose periodic removal involves much labour and time. Hence arises the problem of preventing salt deposits, which although difficult is entirely soluble. Thus the solution of a major, one may say global, ecological problem is based on the solution of the more specific problem of inhibiting salt deposition.

The main component of salt deposits is usually carbonates (mostly calcium carbonate), formed from the hydrogen carbonates responsible for the temporary hardness of water. Procedures for the chemical prevention of salt deposition and for washing the equipment clean have been proposed at different times—for example, the acidification of water and the use of a series of polymeric inhibitors, but best results have been obtained by employing polyphosphates, which form complexes with the cations of the deposited salts. However, polyphosphates are effective only when the content of salts in water does not exceed 3 mequiv. litre^{-1} (however, many waters, especially those from artesian wells, contain a greater amount of salts). Furthermore, in all cases the effective action of polyphosphates is comparatively brief—so long as the content of salts in the circulating water does not rise to the limit indicated above (as a result of the supply of fresh water and evaporation). Finally, polyphosphates gradually hydrolyse. Thus the use of polyphosphates does not exclude measures for the removal of salt deposits. Naturally, in their presence this can be done more rarely but it is nevertheless frequent enough.

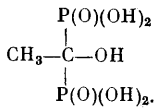
An effective procedure for combating salt deposition involves the binding of metal cations into water-soluble complexes with the aid of complexones. The disodium salt of ethylenediamine-*N,N,N'N'*-tetra-acetic acid (EDTA) (Trilon B) was used initially as a reagent of this kind. Other carboxylic acid complexones have also been proposed. However, subsequently, following the appearance of organophosphorus complexones, they were all to a large extent displaced by the latter, since these are more effective and at the present time organophosphorus complexones are in fact widely employed to inhibit salt formation in circulating and closed water supply systems.

The effectiveness of organophosphorus complexones is based not only on their ability to form stable water-soluble complexes with the majority of cations present in water, but also, and this is particularly important, on their ability to effect inhibition in substoichiometric amounts, the amount of the complexone required being significantly smaller than the amount necessary for the stoichiometric formation of stable complexes. Studies have shown that this is a consequence of the adsorption of complexones on the crystallisation nuclei of the salt, which prevents the growth of the nuclei and the formation of crystals. A supersaturated solution incapable of giving rise to a deposit is formed.

Numerous organophosphorus complexones have been tested. It was found that the most effective complexones are those whose molecules contain several (three or more) phosphonic acid groups.

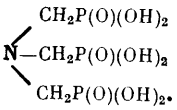
At the present time our industry produces the following organophosphorus compounds for the inhibition of salt deposition.

1. Hydroxyethylidenediphosphonic acid (HEDP):



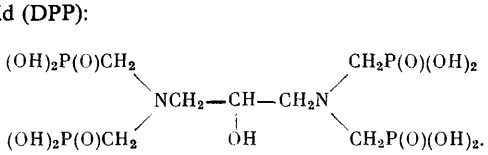
HEDP is obtained from acetic acid and phosphorus trichloride. We investigated its complex forming properties and the methods for its industrial synthesis. HEDP can be used as a salt deposition inhibitor both in a pure form and in different compositions.

2. Nitrilotrimethylphosphonic acid (NTP):



NTP is obtained from ammonium chloride, formaldehyde, and phosphorus trichloride. The extremely effective IOMS combined inhibitor of salt deposition and corrosion has been developed. This preparation contains about 80% NTP, but, since ammonium chloride (a waste product in the manufacture of polyethylenepolyamines) containing an admixture of polyethylenepolyamines is used as the nitrogen-containing starting material, the preparation contains, apart from NTP, also phosphorylated polyethylenepolyamines which have a synergistic effect on NTP. The phosphorus-containing starting material used under these conditions is phosphorous acid (a waste product in the manufacture of lauryl peroxide). This results in the preparation of an extremely cheap and extremely effective salt deposition inhibitor—IOMS.

3. 2-Hydroxypropylene-1,3-diamine-*N,N,N'N'*-tetramethylphosphonic acid (DPP):



DPP is obtained from epichlorohydrin, ammonia, formaldehyde, and phosphorus trichloride. A technical product, obtained from a crude mixture consisting of 80% of 1,3-diamino-2-propanol and 20% of polymeric products of the interaction of ammonia with epichlorohydrin, is manufactured on the basis of DPP. The phosphorylation of such a mixture yields DPP and polycomplexones. This mixture is manufactured under the name DPP-1 or FOSFANOL (a neutral form of DPP-1). The effectiveness of the technical product is higher than that of pure DPP.

Each of the proposed salt deposition inhibitors has its "speciality"—the type of salt deposits which it prevents most effectively.

The use of recipes which include, apart from organophosphorus complexones, also corrosion inhibitors, surfactants, and other ingredients has become very important.

The overall volume of manufacture of organophosphorus complexones used as salt deposition inhibitors amounts at present to several thousand tonnes annually (10 commercial brands are produced). Much experience has accumulated in industry as regards the preparation of organophosphorus complexones for the inhibition of salt deposition, in particular for the stabilisation of water by complexones in circulating gas purification cycles in blast furnaces. Complexone stabilisation of water is used nowadays in the

metallurgical plants in Chelyabinsk, Novolipetsk, Magnitogorsk, and Makeevka. Use of complexones has made the extent of the formation of carbonate deposits many times smaller.

Under the influence of complexones, the previously formed deposits, consisting mainly of calcium carbonate, undergo a change in structure, soften, and are gradually washed out of the system. It has been noted that the combination of IOMS and HEDP gives rise to a positive result even for a high carbonate hardness of the circulating water (35 mequiv. litre^{-1}).

The prevention of salt deposition permitted a reduction of the cost of maintenance by a factor of several tens. Salt deposition and corrosion inhibitors have been introduced in more than 20 metallurgical undertakings.

A second example is provided by the water supply to the gas purification equipment in ferroalloy furnaces. Provision has been made for a circulating water supply. The cooling and purification of the circulating water after gas purification are carried out in the sludge accumulator. During warm seasons, the system is operated continuously. As the temperature of ambient air is reduced during winter an intense increase in salt deposition begins on the impellers of the pumping equipment supplying water to consumers. The water pressure falls and after 5–7 days the pumps have to be switched off to clean the impellers. The cleaning is carried out mechanically by hand. The use of 1 g m^{-3} of FOSFANOL makes it possible to continue the operation without stopping for the removal of the salt deposits.

Mention should also be made of the application of HEDP in chemical factories, in heat exchange systems employing artesian water with a temporary hardness of 5–7 mequiv. litre^{-1}. The employment of polyphosphates to prevent salt deposition proved ineffective. Experience gained in the operation of the water circulation cycle with the cooling water heated to 50 °C and using HEDP demonstrated the high stabilising effect of the reagent and made it possible to abandon frequent stopping of the equipment for cleaning.

It is possible to quote many more examples. Effective results have been obtained using organophosphorus complexones in the water circulating systems of non-ferrous metallurgy, in the coal industry, in the mineral fertiliser industry, in medium- and high-pressure boiler plant, in particular, in more than 20 combined heat and power generating plants, hydroelectric power stations, and atomic power stations, in the water heating boilers of central heating systems, in cooling systems with cooling towers, in hydrotransport apparatus, etc.

The consumption of the organophosphorus complexone in circulating water supply systems is usually approximately 1–3 g m^{-3}. It is noteworthy that sometimes, together with the inhibition of the salt deposition, a diminution in the corrosion of metallic surfaces is also observed. To achieve this effect, anticorrosion additives are usually introduced into the composition.

The effect of organophosphorus complexes and salt deposition inhibitors is normally considered from the standpoint of economic results attained under these conditions: a significant diminution of the cost of prophylactic maintenance, the shortening of the periods during which the equipment remains idle, and the saving of labour, metal, water, etc. The economic effect can then run into tens and hundreds of millions of roubles. However, economy is not the only concern. The use of salt deposition inhibitors permits a very wide scale employment of circulating water supply systems and its ecological effect is hard to overestimate: the saving of water, whose resources are extremely limited, is achieved and the ejection of contaminated and mineralised waters into the environment is prevented.

Naturally, the inhibition of the formation of salts in circulating water supply systems has so far been only initiated. Although a fairly wide range of phosphorus-containing complexones have been created, on the basis of which inhibiting compositions have been developed, much work still remains to be done on the introduction into numerous water consuming industries of circulating water supply systems employing salt deposition and corrosion inhibitors, which may make a major contribution to the solution of ecological problems in our country.

Translated from *Uspekhi Khimii* **60** 570–574 (1991)

Biological purification of sewage from chemical plants

V N Koren'kov, B P Zhukov
Scientific-Industrial Combine "Soyuz", Lyubertsy

Sewage from chemical plants contains substances both in solution and in the form of suspensions including compounds which constitute explosion hazards. These substances may be present at concentrations many times higher than the maximum permissible concentration for reservoirs, and therefore it is unacceptable for sewage to be discharged without purification. The most satisfactory solution would be to utilise the substances present in the water and the purified water itself in the chemical plant thereby transforming the processes in the plants into operations generating a low level or even no effluent. In the scientific-industrial combine "Soyuz" at Lyubertsy a procedure for the treatment and purification of water and the recycling of water from industrial sewage has been developed and includes the following elements (Fig. 1):

1) Local installations for the purification and recycling of water from industrial sewage in each phase of the manufacturing process as a result of which 70% of the water and up to 90% of useful substances can be returned to the plants (such substances would otherwise have been irreversibly lost and it would have been necessary to purify 100% of the industrial waste waters containing a high concentration of toxic materials);

2) A facility for the purification of industrial sewage in plants in which suspended substances are mechanically removed leaving 30% of the effluents formed by washing of equipment, premises, and pipework, etc.;

3) Biological sewage works in which industrial and domestic waste waters are purified concomitantly so that all toxic components are rendered completely harmless;

4) Secondary purification plant and where necessary the exhaustive purification of biologically purified effluents with the return of this water to the process water of chemical and other plants.

State-of-the-art techniques and modern water purification equipment are used, for example ultra- and hyper-filtration, membrane electrolysers and electrolysers with a three-dimensional cathode, continuously operating self-washing filters, and compact sedimentation tanks.

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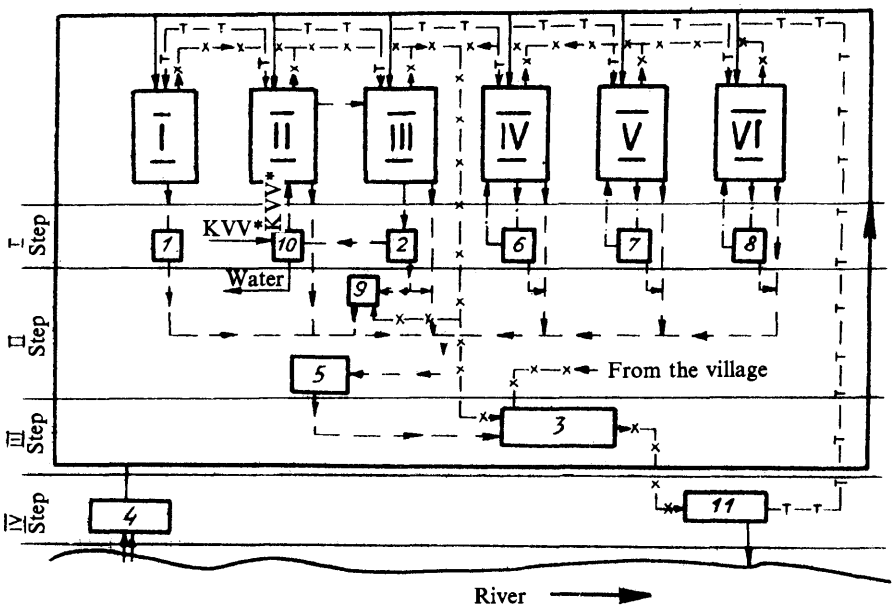


Figure 1. A four-step schematic representation of the treatment and purification of water and the recycling of water from industrial effluents: I–VI, production phases; *1, 2, 6, 7, 8, 10*, local installations for the purification and recycling of industrial wastewaters; *9*, installation for the biological purification of oxygen-containing inorganic compounds; *5*, installation for the mechnical purification of the total sewage from the plant; *3*, biological sewage works; *11*, installation for the secondary purification and exhaustive purification of sewage; *4*, water intake.

*The meaning of this abbreviation is not clear; it may refer to aluminium treatment (Ed. of Translation).

Biofilters with plastic packing, air tanks with a porous aggregate, and also a unique method involving biological reduction of oxygen-containing inorganic compounds including highly toxic hexavalent chromium and the separation of chromium as a precipitate in the form of the hydroxide, Cr(III), are used for biological purification. The latter method has been devised in collaboration with the Institute of Biology of Water Reservoirs, Academy of Sciences of the USSR. Other oxygen-containing inorganic salts of perchloric, nitric, and nitrous acids are converted into harmless chlorides and free nitrogen. This process is achieved with the aid of microorganisms isolated in the Institute of Biology of Water Reservoirs, Academy of Sciences of the USSR. This method is protected by eighteen patents published in the USA, England, France, the Federal Republic of Germany, and Italy, etc.

Heavy-duty vertical filters with a rubble packing are used for secondary purification of the biologically purified mixture of industrial and domestic effluents. Active charcoal is incorporated into the free space between the packing grains in order to achieve a high degree of purification, and the charcoal is regenerated *in situ* by a chemical treatment without the need to unload the filter. After this type of treatment the water quality meets the specifications for the water of fish-farming reservoirs (Five-day biological oxygen demand (BOD_5), 2; quantity of suspended matter, 5; nitrate nitrogen, 0.02; nitrates, 9; petroleum derivatives, 0.05 mg/litre.

The specially designed high-performance and continuously operating filters and equipment for the biological purification of water used in chemical plants have formed the basis for the creation of facilities for intensive fish farming in an enclosed recycling system. These facilities may be operated both in fish farms (for breeding young fish) and in large-scale establishmnents (for fish breeding on a commercial scale). A schematic representation of the installation is shown in Fig. 2.

The installation has a fish production capacity of 200 kg of carp per cubic metre of the reservoir per annum, whereas in fish breeding ponds the value of this parameter is no greater than 200 g/m^3 per annum, i.e. 1000-fold less productive. The installations devised are superior to the best foreign equivalents in regard to quality of recycled water, compactness, and fish production efficiency. These devices are patented in Comecon countries. More than seventeen agreements have been reached for acquiring the intensive fish farming technology designed in the scientific-industrial combine "Soyuz" in Lyubertsy. Thermal power stations have shown a particular interest in these installations.

An essentially novel and ecologically safe method for rendering waste waters harmless by the reduction of oxygen-containing inorganic compounds with open cultures of microorganisms has aroused great interest in regard to the purification of effluents from chemical plants. Waste waters from certain plants are polluted with toxic inorganic salts which are readily soluble in water and which contain bound oxygen in the molecule, for example salts of perchloric, chlorous, nitric and nitrous acids. The maximum permissible concentrations for domestic (in the numerator) and fish farming (in the denominator) reservoirs are as follows: perchlorates, 5/0.08; chlorates, 20/0.35; nitrates, 45/40; nitrites, 3.3/0.08; hexavalent chromium, 0.05/0.001.

Biochemical reduction could be the most straightforward and economical method for purification of water by removal of oxygen-containing inorganic compounds. However this type of process is

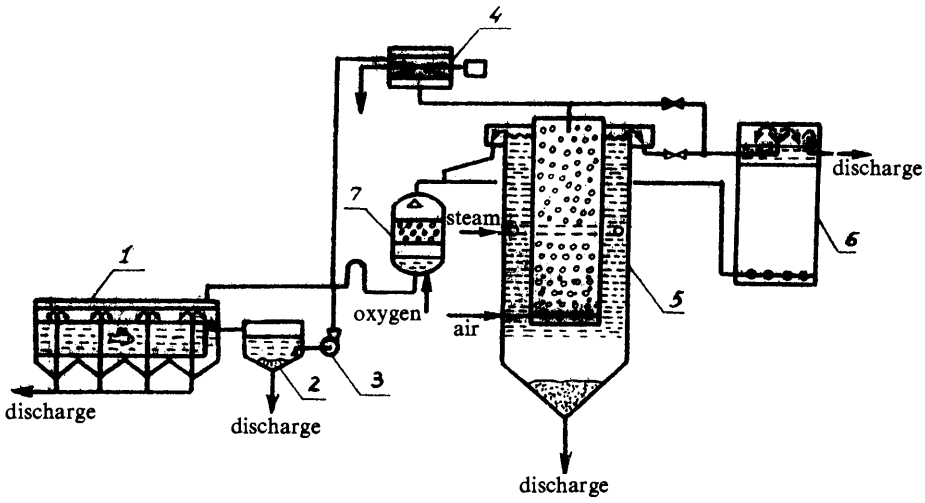


Figure 2. A schematic representation of an installation for intensive fish farming: *1*, fish tank; *2*, dirty water container; *3*, pump; *4*, continuously operating self-washing filter; *5*, aeration tank/sedimentation tank; *6*, denitrifier; *7*, oxygenator.

available for only three classes of compounds, i.e. nitrates (nitrate reduction), sulphates (sulphate reduction), and carbon dioxide (methanogenesis). Each class of compound is reduced only by a specific unique microbial culture under strictly defined conditions essential for the growth and metabolism of the microorganisms. Foreign scientists have been unable to identify microorganisms which have the ability to reduce other oxygen-containing inorganic compounds.

In order to assess the possibility of achieving the biochemical reduction of oxygen-containing anions of perchloric, chromic and other acids, the present authors have made a thermodynamic calculation of the change in the isobar-isothermal potential of the biochemical reactions occurring during the oxidation of organic substances.

It has been shown that in these reactions a whole series of oxygen-containing substances generate energy and they may be ranked in the following order of decreasing energy yield:

$$ClO_4^-,\ ClO_3^-,\ NO_3^-,\ NO_2^-,\ Cr_2O_7^{2-},\ Cr_2O_4^{2-},\ \text{and}\ SO_4^{2-}.$$

However, this does not imply that in addition to the denitrifiers and sulphate reducers there are microorganisms with the ability to reduce other anions of interest.

Nevertheless Soviet scientists in the Institute of Biology of Water Reservoirs, Academy of Sciences of the USSR, have isolated microorganisms, which have the ability to utilise the bound oxygen in salts of perchloric acid (i.e. *Vibrio dechloraticans Kusnezovi*) and also chromates and bichromates [*Bacterium dechromaticans (Rom)*][1,2].

Processes, equipment and installations for the purification of waste waters to remove these compounds with the aid of these unique strains have been developed (Fig. 3).

Optimal media have been developed for the strains discovered by V I Romanenko[3] and the morphological, cultural, and biological characteristics and sugar relationships have been studied, and the conditions required for maximum viability have been determined. The present authors have been able not only to elaborate a process but also to enhance the process in which water is rendered safe by removal of these compounds.[4]

The profile of the biochemical reduction of oxy-anions and the effect of physicochemical factors (temperature, redox potential, pH, organic substrates, etc.) on these processes have been studied in laboratory, semi-industrial and pilot-plant devices.

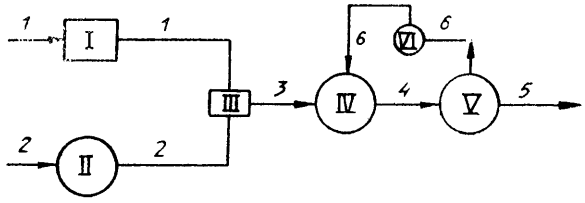


Figure 3. A schematic representation of the removal of hexavalent chromium from effluents; I, neutraliser; II, V, sedimentation tanks; III, mixer; IV, biological regenerator; VI, pump; *1*, chromium-containing waste waters; *2*, domestic waters; *3*, a mixture of chromium-containing and domestic waters; *4*, purified waters with a specific sludge and chromium hydroxide; *5*, purified effluent; *6*, specific sludge.

The process of biochemical reduction of oxy-anions can be described by a system consisting of three differential equations characterising the relationship between the rate of utilisation of the nutrient substrate, $dZ/d\tau$, the kinetics of the utilisation of chemically bound oxygen, $dE/d\tau$, and the rate of increase (or decrease) in viable specific bacteria, $dX\delta/d\tau$. By resolving this system of equations and taking into account the material balance for continuous cultivation and batch cultivation devices it was possible to obtain an equation

for the technical calculations for the installations in which salts of perchloric acid could be rendered harmless (converted to harmless chlorides) and nitrites and nitrates could be converted to free nitrogen. The nutrient substrate consisted of readily oxidisable organic substrates present in domestic effluents, surplus activated sludge, processed biofilm from normal biological sewage works, effluents from meat-packing plants, and others.

The biological method for the purification of effluents by removal of Cr(VI) devised in the scientific-industrial combine Soyuz in Lyubertsy is now being used in various branches of the national economy, since waste waters containing this harmful toxicant occur extensively not only in the chemical industry but also in a wide range of other industries (especially in the electroplating industry).

With the aid of the method recommended for the purification of chromium-containing effluents it is possible to achieve a three-five-fold reduction in expenditure on the construction of installations and engineering equipment and a five-seven-fold reduction in operating costs depends on the flow-rate of the effluents, the chromium concentration, and the required degree of purification (for each cubic metre of chromium-containing water which may be decontaminated) in comparison with the less expensive installations for the chemical removal of Cr(VI) from effluents. The cost of purifying one cubic metre of chromium-containing industrial effluent in a mixture with domestic waste water is no greater than 5–10 kopeks.

It has been confirmed by reliable medical sources that the microorganisms, which reduce Cr(VI) to Cr(III), are harmless and are not causative agents of diseases. An installation for the biological purification of water to remove Cr(VI) by a batch process has been operating trouble-free since 1974 in the scientific-industrial combine Soyuz in Lyubertsy. A facility for the continuous purification of effluents to remove Cr(VI) has been in operation for ten years in the metal-coating workshop at the "Kommunar" automobile factory in Zaporozhe providing a cost savings of 65,000 roubles. An installation for the continuous purification of ground water in order to remove Cr(VI) operating at an efficiency of 8000 cubic metres per day is now in the second year of operation in the Aktyubinsk Chromium Compound Plant (ACCP). The purified water and the chromium hydroxide obtained are used in industrial processes. A cost savings of 4.4 million roubles has been achieved. A batch process facility is being installed in the Moscow factory "Frezer". It is intended to introduce additional facilities for the removal of Cr(VI) from effluents in the automobile factory "Kommunar" and ACCP. Work will be carried out within the guide-lines of the All-Union programme "Biotekhnika" (Biotechnology) in collaboration with the Institute of Biology of Water Reservoirs, Academy of Sciences of the USSR, on the development of techniques for the removal of Cr(VI) from effluents in different branches of industry and for the reprocessing of chromium-containing dumps in ACCP which amount to five million tonnes.

An economical justification study for constructing installations in the Lyubertsy aeration station for decontaminating treated chromium-containing solutions by a biological method for 900 factories in Moscow and the Moscow district and utilising the extracted chromium is currently being carried out. The anticipated cost savings is 30 million roubles per annum. In 1988 an agreement was reached with the Italian firm Olivetti to introduce the method for biological removal of Cr(VI) in Italy. Three Italian firms are currently expressing an interest in acquiring a license.

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Translated from *Uspekhi Khimii* **60** 575–580 (1991)

The determining role of the redox process in the formation of the quality of the aqueous environment

Yu I Skurlatov
Institute of Chemical Physics, Academy of Sciences of the USSR, Moscow

One of the factors determining the adverse effect of man on the environment is the imbalance of redox processes in water reservoirs involving oxygen and hydrogen peroxide, agents which play a key role in the determination of water quality in the natural environment.

In recent years numerous articles have appeared in the literature on the determination of the content of hydrogen peroxide in different water systems, seas, and oceans[2,3] rivers and lakes,[4–7] and in rain and snow[8,9] and even in mineral ice samples in Greenland and in Antarctica.[10] All authors arrive at the same conclusion. Hydrogen peroxide is an inherent component of the natural aqueous environment. It can even be demonstrated that before the intervention of man the evolution of aerobic life on Earth occurred not only in the presence of oxygen and water but also in the presence of hydrogen peroxide.

Hydrogen peroxide in an aqueous environment may arise from four main sources: 1) entry from the atmosphere; 2) formation as a result of catalytic processes for oxidation involving oxygen; 3) formation as a result of photochemical reactions in the presence of sunlight, and 4) formation as a result of biological emission.

When the atmosphere becomes polluted there is an abrupt curtailment of the influx of hydrogen peroxide "from the sky" to the Earth's surface. In environmentally clean regions snow and rain contain $10^{-5}-10^{-4}$ M hydrogen peroxide, whereas according to the data obtained by the present author and co-workers hydrogen peroxide may be totally absent from regions subjected to atmospheric pollution. In turn this leads to a deterioration in the condition of soil ecosystems.

The present author has shown that the presence of hydrogen peroxide in moisture in the soil (in irrigation water) significantly enhances seed germination and plant growth, shortens the duration of the vegetative period, and increases the yield of agricultural crops.

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Yu I Skurlatov
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One of the factors determining the adverse effect of man on the environment is the imbalance of redox processes in water reservoirs involving oxygen and hydrogen peroxide, agents which play a key role in the determination of water quality in the natural environment.

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The present author has shown that the presence of hydrogen peroxide in moisture in the soil (in irrigation water) significantly enhances seed germination and plant growth, shortens the duration of the vegetative period, and increases the yield of agricultural crops.

An ecologically safe method for stimulating plant growth devised by the present author is being introduced in Moldova for glasshouse and field cultivation. Results obtained from trials with soya-bean and tomato plants indicate that an increase in yield equivalent to 500–700 roubles/hectare is being achieved.

Catalytic and photochemical processes involving oxygen are of great importance in the formation of hydrogen peroxide within reservoirs.

In the catalytic processes hydrogen peroxide accumulates during the oxidation of reducing substrates which are more reactive with oxygen than with hydrogen peroxide. An increase in the hydrogen peroxide content is usually found in areas in which untreated municipal sewage is discharged.

Sunlight is a determining factor in processes in which hydrogen peroxide is formed in surface waters and in summertime photochemical processes involving microscopic algae resulting in the formation of hydrogen peroxide are most important.[11] Examples in which hydrogen peroxide is formed as a secondary product of photosynthesis have been described in the literature.[12] With the aid of various microscopic algae the author has observed and characterised another effective channel through which the ultraviolet component of sunlight exerts an effect on algae.

The manner in which the hydrogen peroxide content in the natural aqueous environment changes over a 24-hour period is shown in Fig. 1. With the aid of a technique devised by the present author and co-workers[12] for the determination of hydrogen peroxide it is possible to make measurements with an accuracy of 10^{-7} M.

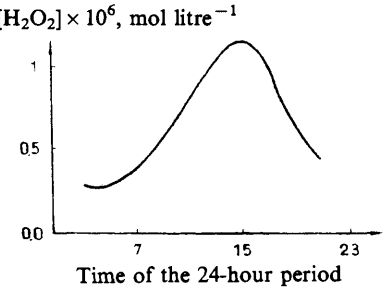


Figure 1. Diurnal course of the hydrogen peroxide content in a natural water.

The fact that the hydrogen peroxide content of natural waters is dependent on solar activity indicates that this molecule is present at a quasi-stationary level in the aqueous environment, i.e. in addition to hydrogen peroxide formation processes exist for the decomposition of hydrogen peroxide.

It has been found that both of these processes, the formation and decomposition of hydrogen peroxide, are accompanied by the efficient generation of reactive particles in the natural water and that these particles are involved in self-purification of the aqueous environment (O_2 and OH radicals and metal complexes in anomalously high oxidation states). Studies carried out by the present author and co-workers have shown that algae involved in the formation and decomposition of hydrogen peroxide promote radical and peroxidase oxidation of contaminating substances. In the summer period of the year an effective channel exists in the natural aqueous environment for the biogenic initiation of self-purification processes (Fig. 2).

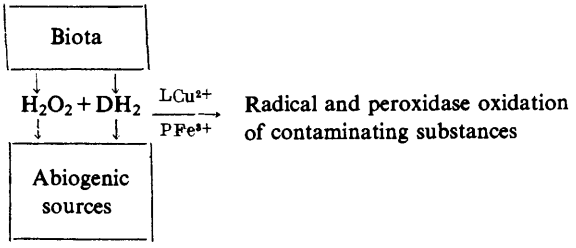


Figure 2. A chemico-biological model for the self-purification of a natural aqueous environment.

The efficiency of radical and peroxidase oxidation of contaminating substances is determined by the rate of photochemical formation of hydrogen peroxide. The present author has calculated that 10–50% of the hydrogen peroxide is decomposed in natural waters with the formation of free OH-radicals and other reactive particles.

A feature of the kinetics of hydrogen peroxide decomposition by microscopic algae is that the process is of zero or first order with respect to the hydrogen peroxide concentration, and in both cases the rate of the reaction is proportional to the algal biomass.[14]

The first-order reactions include the decomposition of hydrogen peroxide by catalase, whereas the zero-order reactions include the peroxidation of reducing substances formed in dehydrogenase reactions. The rate of the zero-order reactions is determined by the rate of formation of these substances acting as reducing agents. Under quasi-stationary conditions the rates of formation and decomposition of hydrogen peroxide are equal to:

$$W_f = k_{f,1} + k_{f,2}\,[\mathrm{B}],$$
$$W_d = (k_{d,1} + k_{d,2}\,[\mathrm{H_2O_2}])\,[\mathrm{B}],$$

so that the quasi-stationary concentration of hydrogen peroxide in the natural aqueous environment is determined by the relationship:

$$[\mathrm{H_2O_2}] = \frac{k_{f,1} + (k_{f,2} - k_{d,1})\,[\mathrm{B}]}{k_{d,2}\,[\mathrm{B}]} \approx \frac{k_{f,2} - k_{d,1}}{k_{d,2}},$$

where $k_{f,1}$ and $k_{f,2}$ are the effective rate constants for hydrogen peroxide formation, and $k_{d,1}$ and $k_{d,2}$ are the rate constants for hydrogen peroxide decomposition.

The main conclusion from this simplified picture is that two situations may arise in the aqueous environment depending on whether the flow of hydrogen peroxide or reducing substances is predominant.

The redox state exhibits a diurnal or seasonal course in accordance with the change in solar activity and water temperature. It has been found that the transition of the environment from a state in which hydrogen peroxide is present in the water to a state in which reducing substances (which readily interact with hydrogen peroxide) are present is of great significance for aqueous ecosystems. When quasi-reducing conditions are formed in the water, the water

becomes toxic for organisms which undergo intensive water exchange with the environment.

Fish larvae in the early stages of development obtained from artificially breeding sturgeons (Chondrostei) and phytophagous fish serve as a bio-assay of the change in redox state of the aqueous environment (Fig. 3).

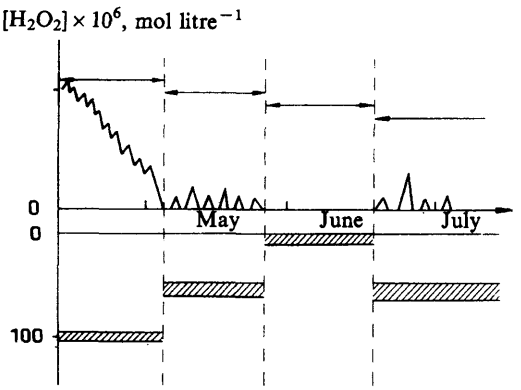


Figure 3. Seasonal time-course of the redox-state and toxicity of the aqueous environment in reservoirs in which blooms of blue-green algae have developed.

Under conditions in which toxic reducing conditions have been formed in the water, addition of hydrogen peroxide to the water leads to the normalisation of larval development. The present author and co-workers have developed and introduced into VORZe Fish Breeding Stations a method for breeding larvae of sturgeons which is based on the addition of further quantities of hydrogen peroxide to the water in which toxic reducing conditions have arisen.

By comparing the results obtained from the determination of the content of hydrogen peroxide in the Volga water with data on the death rate of larvae in Fish Breeding Stations it was possible to conclude that the seasonal changes in the redox state in the Volga began in 1976. Prior to this data the factory produced more than twelve million sturgeon fry per annum, whereas after this data this figure was less than eight million. By addition of hydrogen peroxide to the water it has been possible to breed more than five million additional physiologically sound Caspian sturgeon fry (an increase of more than one million fish above the previous maximum value).

Evidently a change in the redox state of the aqueous environment is a decisive factor in the reduction of the breeding potential for fish which spawn in the summer period of the year.

Two years ago a new problem arose with sturgeons. Stratification of muscle tissue in sexually mature fish and egg resorption was observed. Apparently this phenomenon was also associated with the disruption of the redox state in the Volga which occurred in 1976, since the commercial returns on the fish (catches) begin precisely within 10–12 years. In fact now the results of those impairments in the physiological development of the fish larvae which occurred in the larval stage can be seen.

The blue-green algae act as generators of reducing substances which leads to a change in the redox state of the natural environment.[15] Under conditions of interspecies competition they release into the environment certain substances which readily interact with hydrogen peroxide (Fig. 4).

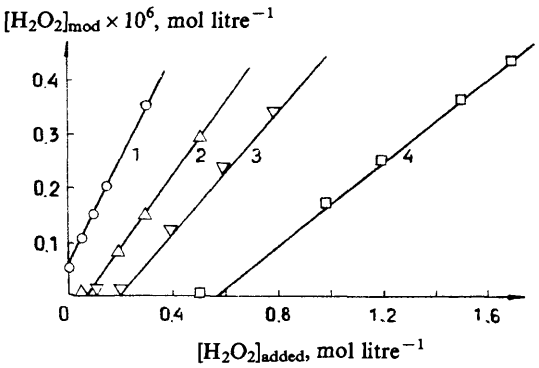


Figure 4. Interaction between hydrogen peroxide and substances acting as reducing agents which were released by blue-green algae (dark conditions).

Note. The key to the numbered plots are not given in the original manuscript (Ed of Translation).

The rate of generation of the reducing substances is determined by the ecological factors, temperature and illumination.

Although the formation of reducing conditions in the water is not accompanied by any significant changes in hydrochemical parameters, several adverse consequences immediately arise.

1. The hydrogen peroxide disappears, the hydrogen peroxide which is essential for the normal operation of physiological processes in organisms with an intensive water-exchange mechanism (the same fish larvae in the early stages of development).

2. There is a transition of copper into the biologically unavailable non-reactive reduced form, apparently in the form of a complex with sulphydryl compounds. Consequently respiratory apoenzymes may be synthesised and these apoenzymes contain no copper in the active centre in the early stages of development of the aquatic organisms. Such cases have been described in the literature in regard to plant cells.[16] It is of great interest that when the biosynthesis is terminated the appearance of copper in the medium does not lead to the activation of the apo-enzyme.

3. It is possible that the reducing agents themselves, which are involved in the formation of the reducing state of the aqueous environment, have a toxic action. One cannot rule out the possibility that substances released by blue-green algae into the environment constitute one variety of the so-called algotoxins.[17] Research workers in many countries throughout the world have studied the algal toxins, which appear in reservoirs in which blooms of blue-green algae have arisen. Cases in which large numbers of birds and animals have perished are known and there have been instances of human food poisoning when water from "blooming" reservoirs has been consumed.

4. There is a sharp decline in the self-purifying capacity of the aqueous environment. Under these conditions toxic compounds of natural or anthropogenic origin may accumulate in the water.

5. The development of a pathogenic microflora is found, and the reducing environment favours the development of these organisms. Cases of large-scale outbreaks of human diseases such as heptatitis, cholera, amoeboid meningitis, etc. have been reported. It has been suggested that the death of large numbers of Baltic seals from distemper was associated with the blue-green algal blooms in the Baltic Sea. One should note that even in small quantities hydrogen peroxide inhibits photosynthesis in blue-green algae and suppresses the mass development of the algae. Thus the control of processes which determine the content of hydrogen peroxide in the natural environment is an urgent problem.

The present author considers that one of the factors which promote an imbalance of reservoir redox processes, in addition to the regulation of river discharge and contamination of waters with nitrogen- and phosphorus-containing mineral compounds, is the fact that the possible effect of the redox state of the municipal effluents purified by biological methods has not been taken into account.

The studies carried out by the present author on the municipal sewage works in Belgorod showed that under oxygen deficient conditions before transfer to the aeration taken reducing substances appear in the effluents which are toxic to aerobic organisms and which can be titrated with hydrogen peroxide. Furthermore these toxic substances partially pass through the biochemical sewage purification plant. At the same time the readily oxidisable compounds are retained in the aeration tank and on entry into a reservoir these compounds would promote the formation of hydrogen peroxide and detoxify the reducing toxins. This implies that the sewage plant for the biological purification of municipal effluents may act as a kind of filter which inhibits the entry of hydrogen peroxide into the water thereby exerting a pronounced effect on the redox processes within the reservoir.

This suggestion is not without foundation. One may recall that sturgeons began to perish in the Volga in 1976. In the same year sewage plants for the biochemical purification of effluents of large cities in the Volga basin came into operation.

A new consequence of the imbalance of redox processes within the reservoirs and the associated radical-mediated processes in natural waters was the appearance of the super-oxidising state of the aqueous environment in a number of reservoirs. This was most pronounced in the Pripyat and Dnepr rivers after the Chernobyl disaster. The super-oxidising state apparently arises during extreme intensification of radical-associated oxidation processes. The carriers of superoxidised equivalents are sorbed on to suspended particles. The nature of these components has not been precisely determined but EPR data indicate that they could be microcolloidal particles of manganese in mixed oxidation states (+3, +4).

During the formation of the superoxidised state of the environment in the water adult breeding fish {phytophagous and fish caught in a fine-mesh [sic. A type of fish? (Ed. of Translation)] net} begin to perish in fish farms and in natural reservoirs. The addition of reducing agents, for example ascorbic acid, to fish farming ponds in which the superoxidised state has been formed, leads to the normalisation of the situation.

Thus redox processes and the associated radical processes play an exceptionally important role in the formation of the quality of the natural aqueous environment and in the resolution of problems of nature conservancy. The latter is associated with the intensification of purification of effluents, the regulation of water quality in fish farms, the improvement of water quality in irrigation farming, the development of water-monitoring systems, and prevention of blooming in reservoirs used as sources of drinking water, etc. The increasing ecological pressures in many regions of the USSR dictates the need for a further extension of studies in the field of hydrochemical processes. Hopefully a real key for the control of the quality of natural waters will be found.

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Translated from *Uspekhi Khimii* 60 581–585 (1991)

Problems of risk and safety in the chemical-forestry complex†

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Undertakings of the chemical-forestry complex in our country constitute a serious potential threat to the lives of the service personnel and the population in the adjoining regions. The principal trend in the development of such undertakings involves an increase in output from different plants, an improvement in technological parameters (temperature, pressure, and concentration), the processing of a large amount of materials, and the accumulation in technological areas of an appreciable amount of inflammable, explosive, and toxic chemicals.

This fact requires a serious analytical approach to the development of technological processes and of equipment used in the latter and also to the planning of industrial developments taking into account the consequences which may arise in incidents of various degrees of seriousness, starting from slight leakages, failure of hermetic seals in the reaction equipment, and going as far as large scale explosions and fires.

It is noteworthy that, unfortunately, in the Soviet Union there have been in this respect virtually no systematic studies based on unique scientifically well-founded principles and the results of incidents occurring in different undertakings are not considered as a whole. At best they are retained in the subdivisions of various ministries and are inaccessible. On the other hand, one cannot fail to note that in the industrially developed countries very much attention has been devoted to the problem of risk and safety, including the ecological safety of chemical undertakings— programmes are being developed at the governmental level, being financed both by the government and individual firms. For example, in the EEC countries alone three programmes have been realised recently and the fourth, concerned with problems of the safety of chemical industries and the prevention of accidents, is being carried out. A series of centres for the study and prediction of catastrophes have been created in the USA at well known universities and in major companies. Specialist journals are being published and specialists are being trained. The importance and urgency of this problem were emphasised at a conference held in 1987 in Rome, where more than 140 reports representing virtually all the industrially developed countries were delivered.

It is important to emphasise that the relevant research is based on a systematic approach to ensuring safety at all stages of planning and exploitation: in the normal, pre-accident, and accident regimes with localisation of the consequences of the accident including its organisational aspects.

The estimation of risk and the adoption of appropriate measures designed to diminish it constitute one of the main aspects of the procedures for ensuring the safety of the control of processes in devising plans for coping with accidents and in planning new industries. The stages in the assessment of risk are as follows:

1. Identification of the danger in which one usually employs "denial tree" and "events tree" methods or denials type analysis. The necessity to examine the entire spectrum of the possible types of danger (from minor frequently occurring breakdowns to major and rare accidents).

2. Analysis of the consequences of accident situations based on the mathematical models devised taking into account the severity, danger, and type of incident.

3. Analysis of the frequency of incidents in which "denials or events trees" are also used.

4. Estimation of the degree of risk as a combination of the frequency of the event and the severity of its consequences. Naturally, all the studies are being prosecuted with a wide-scale employment of computer systems.

More than 60 data banks concerning incidents in chemical undertakings as well as 120 data banks concerning dangerous chemicals are known to exist abroad at the present time. Programs for the abolition of major incidents in chemical plants for the manufacture of herbicides, in petrochemical complexes, etc. have been developed in detail. In individual instances the expenditure on the application of methods for the analysis of the risk in technological processes and industries reaches 20–25% of the total cost and yet it pays for itself in the course of a short period (5–6 years) of operation.

Unfortunately, the trends which can be clearly traced in the activities of the research organisations in the world are much less pronounced in the activities of the corresponding organisations of the Soviet Union, although the general trends in the development of the technosphere in chemical industries are approximately the same in our country. As an example, one can show that the proportion of factories and their output have been increasing in the petrochemical complexes of developed countries: in the USA, Canada, and the Soviet Union (Fig. 1).

It has to be said that petrochemical complexes constitute a very serious risk. For example, the petrochemical complex located close to Leningrad in the town of Kirishi contains approximately 500 000 tonnes of combustible petroleum products in an area of approximately 1.5 km^2. If one admits the theoretical possibility that these petroleum products can form a gas–air mixture, then the power of its overall explosion will be approximately equivalent to the explosion of a 3–5 megatonne nuclear device. Naturally, the consequences of such an accident would be felt over distances running into many tens of kilometres.

At the same time one cannot fail to note that experience gained in the work of organisations associated with the creation of specialist engineering techniques in our country and in the first place in space rocket engineering (much experience has been accumulated in a series of organisations associated with the creation of the space rocket technology in our country including the safe exploitation of both the rocket themselves and of the launching equipment) merits continuous attention specially under the conditions of the developing changes. It is now appropriate and necessary to pose the question concerning the use of this experience for reducing the degree of risk and increasing the safety of chemical industries. For example, at the State Institute of Applied Chemistry Scientific-Industrial Association (SIAC SIA‡) and also in the organisations working in cooperation with the latter, extensive researches have been conducted and are

†This seems to be a euphemism for the rocket fuel industry (Ed. of Translation).

‡Russian abbreviation NPO GIPKh (Ed. of Translation).

being conducted, including large-scale experiments, into the potential danger of chemical compounds used in specialist technology (rocket fuel, etc.). A broad spectrum of inflammable and explosive properties of various metallic and non-metallic materials is being investigated; systems have been created whereby one can analyse the possibility of the development of a thermal explosion as the most typical cause of many accidents; programs have been developed whereby it is possible to create mathematical models which effectively reproduce the real situations frequently observed in reality. Thus, detailed fundamental studies on the interaction of self-inflammable components with nitrate oxidants made it possible to demonstrate clearly the impossibility of the detonation of this system even when the components are mixed rapidly. This in turn led to a multibillion economic gain in the creation of a whole series of launching systems.

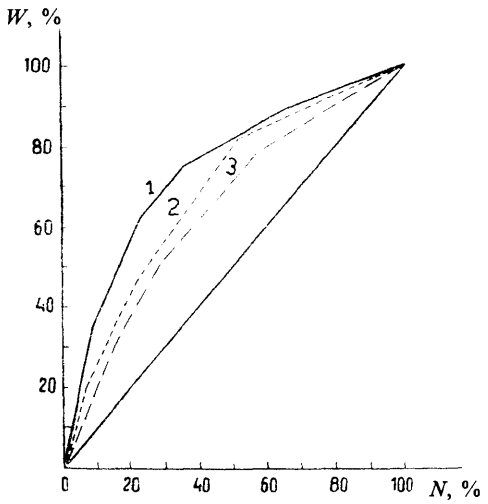


Figure 1. The increase in the power (W) and the fraction of factories (N) in petrochemical industries throughout the world: (*1*) USA, 1985; (*2*) Canada, 1984; (*3*) USSR, 1985.

In many accidents which have occurred in our country on military firing ranges and in the course of special large-scale experiments (for example, in the simulation of the break up of a rocket in the tube of a submarine) a virtually complete agreement between prediction and the real consequences of accidents of this kind was demonstrated. Detailed investigation of the transient processes in the combustion and detonation of liquid and gaseous oxygen and hydrogen led to the creation of reliable fire and explosion warning systems in the "Energy"–"Storm" complex known throughout the world.

As regards considerations with a direct bearing on chemical industries, one should note that the most typical cause of accidents is inadequate knowledge of the relevant chemistry and also of the physical processes in various stages of potentially dangerous industries. For example, in the manufacture of hydrogen peroxide by the isopropyl method (Kuibyshev) there have been several accidents of various degrees of severity associated with the fact that in the various stages of the study of this process the side products arising from the oxidation of isopropyl alcohol by hydrogen peroxide were undetected. These peroxide compounds are typical initiating explosives as regards their characteristics and their accumulation in the stagnant zones of any kind of apparatus, starting with columns and extending to pumps, inevitably leads to an accident. The understanding of the mechanism of this phenomenon made it possible to take necessary technical measures which reduced the risk and danger in this industry and in recent years we have fortunately not had any such incidents.

A similar typical error, made in the research stage, consists in the fact that sometimes no account is taken of the possibility of the formation of explosives in other systems. For example, in 1988 an explosion occurred at the Kropotkin chemical factory. Studies conducted at the SIAC SIA showed that, apart from the target reaction designed to produce polyfurite, a polyfurite–sodium perchlorate explosive mixture is also formed. Perchlorates accumulated and, in combination with the combustible substances, generated an explosive substance which was the cause of the explosion. The use of perchloric acid in this industry is the main source of risk.

The second cause of accidents is that the probability of the occurrence and thermodynamics of reactions leading to side products, whose heats are sometimes greater than that of the main reaction, are not always accurately calculated. We again refer to the experience gained at the SIAC SIA: a serious explosion with the breakup of the apparatus and of the building in the manufacture of perfluoro-oenanthic acid occurred in October, 1986 at the experimental factory in Dzerzhinsk. The heat of the main reaction, for which the apparatus was designed and in relation to which the entire technological process had been tested, did not exceed 6 kcal mol^{-1}:

$$2CF_3(CF_2)_5COOCH_3 + KBH_4 + 2CH_3OH \rightarrow$$
$$2CF_3(CF_2)_5CH_2OH + KBO_2 + 2C_2H_5OH + 6 \text{ kcal mol}^{-1}.$$

It has now been established that, together with the main reaction, there is a possibility of a side reaction between methyl perfluoro-oenanthate and potassium perborate in the presence of methanol, whose heat is 50 kcal mol^{-1}:

$$2CF_3(CF_2)_5COOCH_3 + KBH_4 + 3CH_3OH \rightarrow KF + BF_3 +$$
$$+ C_6F_{14} + C_3F_8 + H_2O + 6CO + 4CH_4 + 2H_2 + 50 \text{ kcal mol}^{-1}.$$

The reaction takes place when the synthetic process is carried out in a reactor whose size differs significantly from that of the analogous reactor used in the laboratory method and leads to a thermal explosion in air of the products of the synthesis.

In research and particularly in planning studies, very little account is taken of secondary factors in accidents. In particular, the failure of the hermetic seal in a 50 m^3 vessel (and this is still a very small volume) filled with a combustible gas, for example, natural gas or any other hydrocarbon, leads to burns and damage felt over a distance of approximately 3 km.

Fig. 2 presents curves for the variation of pressure in the shock wave front on detonation and the explosive pulse in this case. Here no account was taken of the fact that many factors — temperature inversion, wind, accidental ground features, secondary fragments, etc. — make an additional "contribution" and intensify the effect of the explosion and hence must be taken into account in assessing the risk of a real accident of this kind.

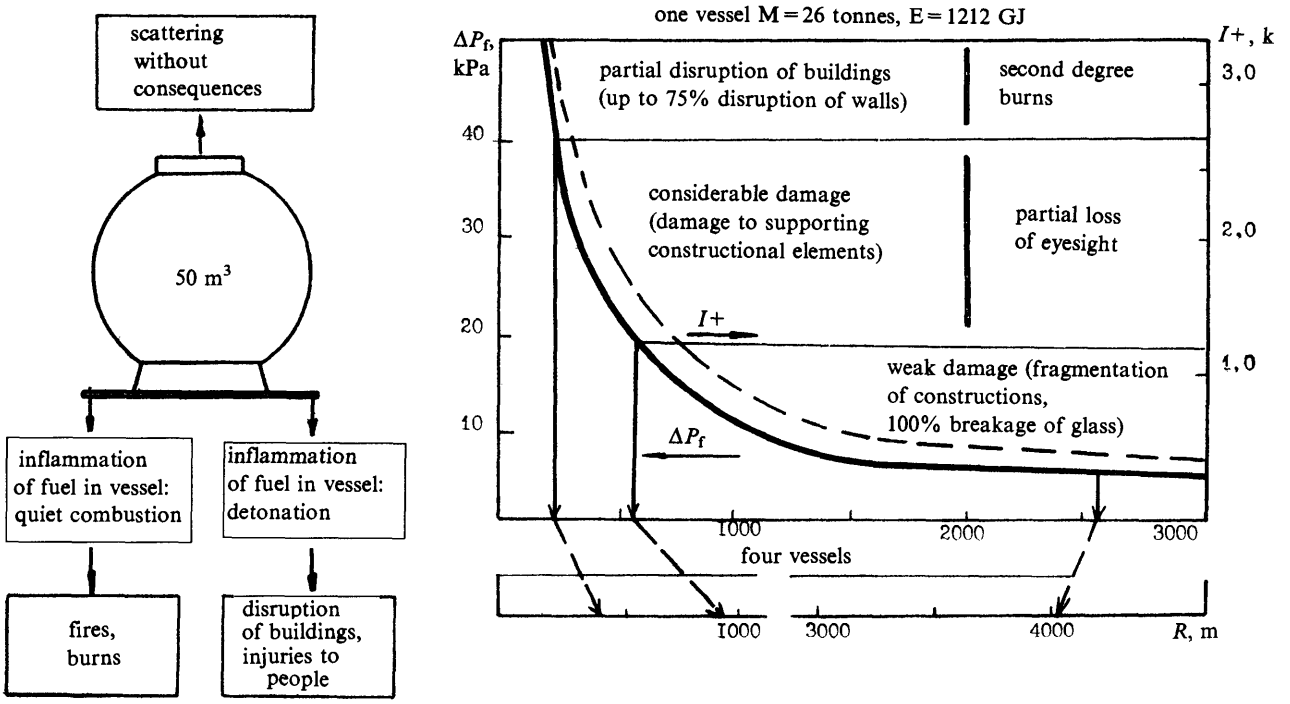


Figure 2. Danger of failure of the hermetic seal and explosion of a container (V = 50 m^3); Δ_{p_f}, change in pressure in shock wave front; I, explosion pulse; R, radius of action.

The pollution of the environment by chemical products during various accidents is also a serious risk factor and requires continuous study.

The most important field of research, which in our country also lags in its development, involves the creation of systems for the automated control of processes which would make it possible to assess not only the occurrence of a process "post factum" but also the onset of a pre-accident situation and on a time scale such that it would be possible to localise these accident situations by altering the technical parameters.

Thus one is dealing with the creation of not simply automated control systems but systems for the early identification of processes, especially in those stages where they are potentially dangerous. It is noteworthy that, for the solution of the set of problems listed above, concerning the questions of safety of industry, including chemical industries, it will be desirable to make use of the existing experience in the organisation of similar studies already gained abroad.

Such experience also exists in the Soviet Union. In particular, methods for dealing with leakages of rocket fuels have been developed in the course of many years at the SIAC SIA. These methods included both technical aspects for the abolition of the consequences of such leakages and provided for all the organisational measures. It has to be said that the many breakdowns which have occurred, for example, as a result of railway accidents, were made good fairly rapidly and without human casualties. Such experience should be transferred also to chemical undertakings.

Here it is useful to point to the relationship between the conditions governing the occurence of modern accidents and the structure and expenditure on their prevention. We may note that the present expenditure does not yield the required effect because it is concentrated on technical systems and there has been virtually no expenditure on the training of directing personnel to take control of safety measures. The tragic events in Chernobyl and the earthquake in Armenia showed how important it is, in the initial stages of the development of catastrophes, to establish control by means of a set of measures and to control large masses of people in a state of psychological stress in order to diminish the consequences of the catastrophe.

Thus it is evident that we are faced by the necessity to develop significantly the studies in the field of risk and safety in the industries of the chemical-forestry complex. Such studies should be given priority by the government. One may propose the following subdivisions of research of this kind:

1. The construction of computational-theoretical models and the determination of risk factors in accident situations in chemical industries.

2. The creation of a data bank of starting materials, intermediates, and final products designed to ensure the construction of a safety system.

3. The improvement of existing methods and means and creation of new ones for the determination of the characteristics of the danger associated with chemicals.

4. The creation of a single methodology for the localisation and abolition of the consequences of explosions and emissions of toxic substances.

5. Estimation of the economic effectiveness of the measures designed to ensure the safety of chemical industries.

6. Analysis and expert assessment of measures designed to improve the ecological aspects and safety of the existing chemical undertakings. Events of recent years — numerous accidents and even catastrophes — which we have witnessed and in which we have participated, demonstrate that the development of this priority field of research can not be put off.

Translated from *Uspekhi Khimii* **60** 586–594 (1991)

Solid phase chemical reactions and new technologies

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Principles for carrying out chemical reactions in solid bodies are considered in this paper as is the design of new technologies and materials based on the previously unknown phenomena which we discovered when studying reactions in the solid phase.

Modern chemical science has developed in the last 200–300 years on the basis of experiments performed while observing natural phenomena and appropriate special experiments. This knowledge became the basis of modern chemistry. However all the reactions which were observed in nature and studied under laboratory conditions proceeded mainly either in the gas or liquid phases or in solution, in melts or on the surface of a solid body. As a rule chemical reactions do not proceed or proceed extremely slowly in the bulk of a solid body because of the absence of diffusion of reactants to one another and diffusion of the reaction products. Alchemists even said that a solid body was death for chemistry since it had no motion. Several years ago we showed successfully that if a shear deformation was brought about in a solid body then at the point of shear deformation chemical reactions took place in it at extremely high rates. As is shown in Fig. 1, together with the shear stress τ there is also a certain pressure p applied to the substance being investigated in order that the system is not destroyed at the time of shear deformation. Before passing to a systematic presentation of the results of these experiments it is necessary to check that a shear deformation can be brought about in solid bodies in industry as under laboratory conditions.

Bridgman's anvil is shown in Fig. 2. The test sample (1), a substance or mixture of substances in which a chemical reaction is to be effected, is clamped between two anvils (2) of tempered steel. One of them (in the given case the lower) is rotated about its axis generating a shear deformation. This laboratory machine permits work with gram quantities. A similar shear deformation may be effected by pressing the solid test substance through a cone under high pressure (Fig. 3). Depending on the relationship $\lambda = S_1/S_2$ it is possible to vary the size of the shear deformation but the applied pressure p determines the rate of deformation. In this case it is possible to work with tens of grams of substance. There is also a series of other devices enabling experiments to be carried out under laboratory conditions. Industrial machines have been developed capable of processing tons of substance per hour. Extruders are such machines (Fig. 4). The rotating screw generates the required pressure and passes the substance into the gap formed between the stationary body of the extruder and the rotating bit of the screw. Two- and multiscrew extruders also exist where special 'cogs' effect shear deformation. At present tens of machines have been constructed in which solid phase chemical reactions can be effected under laboratory and industrial conditions.

The basic rules for carrying out solid phase chemical reactions are now considered. It has been shown that almost all reactions known in inorganic and organic chemistry will proceed under conditions of shear deformation in solid bodies. We have successfully studied hundreds of reactions such as polymerisation processes, addition, substitution and decomposition reactions, etc.

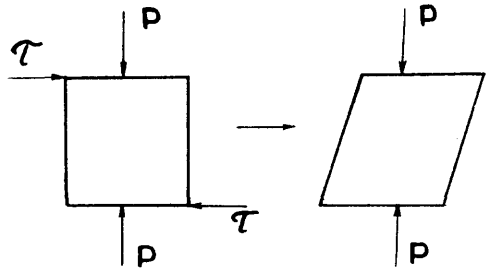


Figure 1. Schematic representation of the combined influence of pressure and shear deformation.

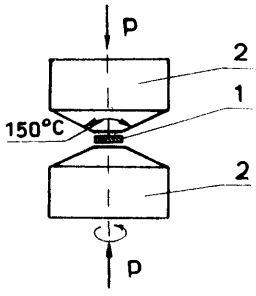


Figure 2. Bridgman's anvils.

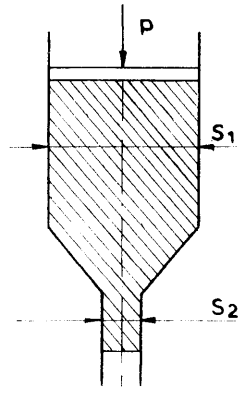


Figure 3. Outline of cone extruder.

A typical 'kinetic' curve of a solid phase reaction occurring under the action of shear deformation is shown in Fig. 5. In contrast to classical chemical kinetics the angle of rotation of the anvil and not

time is disposed on the abscissa, i.e. a value proportional to the shear deformation. The yield of product is on the ordinate as usual. All the chemical reactions studied by us proceed in accordance with the typical 'kinetic' curve.

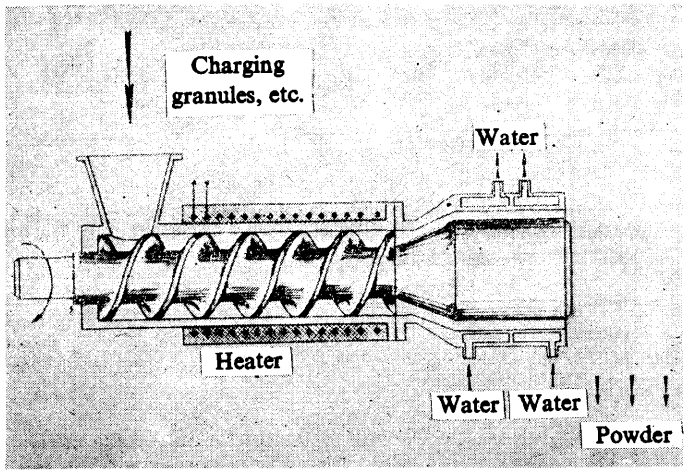


Figure 4. Extruder.

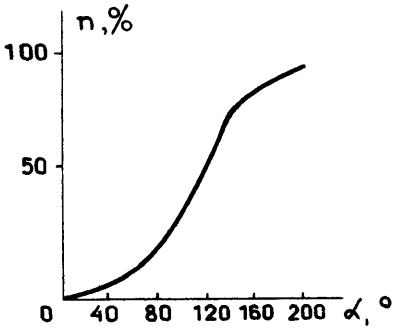


Figure 5. Dependence of polymer yield on the angle of rotation of the anvil (t = 20 °C, P = 10 kBar).

The most characteristic features of solid phase chemical reactions are as follows.

1. Simple compression of the sample by extremely high pressure does not induce a chemical reaction. After removing the shear deformation a long stay under high pressure also does not lead to an increase in product yield, i.e. there is no poste-effect. The direction of the deformation also does not influence the size of the yield. At a given value of deformation the yield will be the same independent of the rotation of the anvil to left or right or after many changes in the direction of rotation.

2. The rate of chemical conversion in solid bodies on shear deformation is extremely high in comparsion with the reaction rate in liquid and even more so than in the gas phase. Under isothermal conditions the reaction rate in a solid body is 3–8 orders of magnitude greater than in the liquid phase.

3. Under the conditions indicated the usual concept of 'catalysis' and 'catalyst' lose their classical sense. Reactions proceed without a catalyst although some special additives may influence the course of the process but this is an action on the mechanism.

4. The extent of chemical reaction is proportional only to the size of the shear deformation.

$$W = \frac{c_0 - c}{c_0} \sim \alpha,$$

where W is the extent of the reaction, α is the shear deformation, c_0 and c are the initial and running concentrations respectively.

The chemical reaction rate is proportional to the deformation rate.

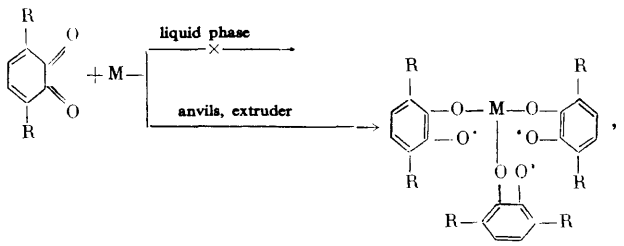
$$V \sim \frac{d\alpha}{dt}.$$

5. Mass transfer processes under the conditions indicated also have special features which are impossible to explain within the framework of the usual diffusion of molecules and atoms in solid bodies. Consequently it is impossible to use the generally accepted concept of a diffusion coefficient for the quantitative characterisation of the rate of mass transfer. Nonetheless using the concept of 'reduced diffusion coefficient' it is possible to compare the rate of mass transfer in a solid body at the point of shear deformation with the usual diffusion coefficient. It turned out that the value of the reduced diffusion 'coefficient' was 8–10 orders of magnitude greater than the diffusion coefficient in the same solid body without shear deformation and 3–5 orders of magnitude greater than the diffusion coefficient of the same molecules at the same temperature in the liquid phase.

The values given for the relative reaction rates and diffusion 'coefficients' were determined qualitatively and consequently are characterised by lower values. They may in fact be much greater. The reaction rate is determined as the total quantity of substance resulting from unit volume in unit time. However as was shown above the reaction rate is determined by the deformation rate and in the sample (tablet) being investigated the deformation rate varies from the centre to the periphery when rotating one of the anvils from zero to a maximum at the edge of the sample. Furthermore a large gradient in deformation rate is displayed across the thickness of the sample. Consequently the values given for the chemical reaction rate and the mass transfer rate represent only the lower limit of these values.

6. One of the main problems of chemical science is the determination of the course of a chemical reaction. Consequently it comprises many strictly established chemical rules specified thermodynamically or kinetically by the features of the chemical process. Numerous experiments by us have shown that these laws and empirical rules of conducting chemical reactions, which have been discovered when investigating processes in liquid and gaseous phases, are very frequently also displayed in the solid phase. There are several cases when a reaction does not proceed in a solid body as predicted by classical chemistry. For example quinone reacts with

powdered metals (aluminium, chromium, iron, etc.) and forms a free radical with three unpaired electrons:



where R = $C(CH_3)_3$; M = Al, Cr, V, Mo, etc. Evidently the analogous reaction does not proceed in the liquid phase by virtue of the fact that an aluminium atom is not able to lose 3 electrons sequentially and quadrimolecular reactions are never observed in chemical kinetics.

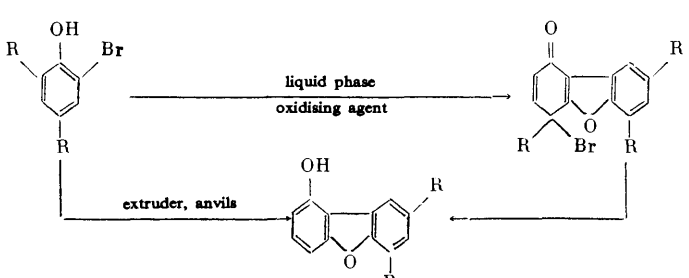
7. In solid phase chemical reactions, as a rule, there are few intermediate reaction products (the final product is generally formed straight away). In the liquid phase

$$A \xrightarrow{K_1} B \xrightarrow{K_2} C \ldots \xrightarrow{K_n} X,$$

and in the solid phase A → X where K_i is the rate constant.

This is linked with the fact that the time for carrying out a chemical experiment is comparable with the time characteristics of the sequential intermediate reactions ($\tau = 1/K_i$). It is evident that in the liquid phase all the intermediate products (B, C, etc.) disappear after a long time and only the final product remains in the system.

8. In the solid phase the reaction rate constant is several orders of magnitude greater than in the liquid phase. Consequently in the latter case the characteristic reaction time becomes much less than the time of the experiment and the formation of only the final reaction product is observed. One of such cases is shown below when the formation of an intermediate was not observed on carrying out the reaction in the solid phase.



where R = t-Bu.

9. The rates of chemical, metallurgical, biological, enzymic and other processes depend on temperature and as a rule the reaction rate grows as the temperature is increased (Arrhenius rule):

$$V \sim e^{-E/kT},$$

where E is the energy of activation.

The size of the energy of activation (it may have a value of a few to tens of kilojoules per mole) characterises the rate of increase of reaction rate with rise in temperature. That is why some processes accelerate rapidly and others less so with increase in temperature. As a rule however all accelerate.

It turns out that in solid phase chemical reactions occurring under the action of shear deformation the activation energy is zero. Reaction rates do not depend on temperature in the temperature range from −196 to +200 °C. This is a characteristic of numerous reactions, such as addition, dissociation, substitution, polymerisation, etc. It is necessary to record specially that in solid phase chemical reactions the energies of activation are zero not only in exothermic but also in endothermic processes. The absence of activation energy in exothermic reactions is explained by the reacting molecules being deformed in the pliable deformation of a solid body. These deformed molecules or combinations of deformed molecules already have sufficient energy to surmount the kinetic barrier (ε) (Fig. 6). But in the case of endothermic processes, in addition to the kinetic barrier, a barrier exists linked with the size of the dissociation energy (Q). The overall energy equation is

$$E = \varepsilon + Q.$$

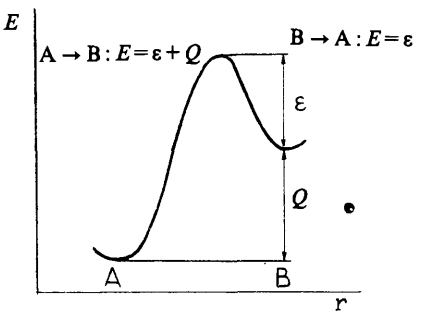


Figure 6. Dependence of the potential energy of the system along the reaction coordinate.

In solid phase endothermic reactions the energy of activation is also zero. This indicates unequivocally that among the deformed molecules (excited as a result of elastic deformation) or combination of molecules there are some in which the accumulation of total energy is greater than ε + Q. It is evident that the number of these molecules is not great since it is difficult to accumulate a large quantity of energy in the system because of the incompressibility of solid bodies at moderate pressures (tens of kilobars). That is why the extent of reaction in endothermic processes is insignificant.

It is therefore seen that the absence of an energy of activation in solid phase chemical reactions is a very important feature. It was shown by special experiment that this phenomenon is not linked with local heating in a friable solid body at the time of deformation. The portion of the volume being heated is too small to explain the absence of an energy of activation within the framework of these concepts.

As has been shown the rate of a solid phase chemical reaction is proportional to the deformation rate. Industrial machinery and laboratory equipment have upper limits for rates of deformation consequently they also have an upper limit for reaction rate. As indicated these rates are 5−8 orders of magnitude greater than the rates of these reactions in the liquid phase. It is evident that if the deformation rate can be successfully increased it should be possible to bring about solid phase chemical reactions at even greater rates than those indicated above.

About 50 years ago Bridgman showed that if a solid body or powder is pressed between two anvils then the system loses mechanical stability above a certain critical pressure and is destroyed with scattering of the solid particles. Our investigation showed that the critical pressure for bursting depends on many factors particularly on the thickness of the tablet being tested (h) (Fig. 7). It turned out that a minimum value of h_{cr} exists below which the system does not burst even at very high pressures (maximum pressure was 30 GPa in the case in question). However h_{cr} is not a strictly limiting value. If there is shear deformation as well as pressure then the system loses mechanical stability at a thickness lower than h_{cr}. In this case a thickness (h_{cr}^{o}) exists at which even a shear deformation does not lead to bursting. It turns out that the critical bursting pressure also depends on the diameter and mass of a tablet, the rate of loading the system, the nature of the substance, small additions and many other factors apart from the tablet thickness. Thus above the continuous curve (Fig. 7) the system is mechanically extremely unstable and leads to bursting, but below the curve it is stable.

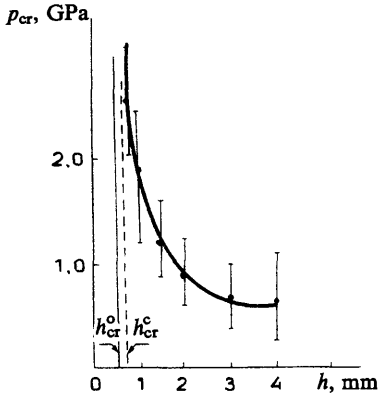


Figure 7. Dependence of critical explosion pressure p_{cr} on tablet thickness.

Our qualitative investigations showed that the duration of these bursts was much less than 10^{-5} to 10^{-6} sec (it is possible that the real time was less than 10^{-8} and 10^{-9} sec).

The investigations showed that under the indicated conditions the same reactions take place as under the action of shear deformation but their time course was not seconds or tens of seconds but less than 10^{-6} sec. This is like the so-called detonation reactions when the rate of propagation of the chemical reaction is greater than or equal to the rate of propagation of sound in the same solid body. Evidently simple long term compression without mechanical bursting (below the lower continuous curve in Fig. 7) does not lead to chemical reaction.

Endothermic reactions occur on mechanical bursting because mechanical energy accumulates in a solid body on compression (possibly in the experimental equipment generally) and this mechanical energy is transformed directly into chemical energy. As is seen from Table 1 the limit (critical bursting pressure p_{cr}) does not depend on temperature in the range −78 to +80 °C.

The reaction yield also does not vary. As was shown above the yield in endothermic reactions is naturally so low because the energy stored in the system is also little. So long as a reaction is weakly exothermic, such as hydrolysis and neutralisation reactions (see below), then after the same time of bursting (10^{-6} sec) the yield is almost 100%. This is linked with the fact that there is no need to put additional energy into the system while carrying out the reaction, on the other hand energy, although little, is evolved. It is only necessary to overcome the kinetic barrier which, as has been shown, does not exist in solid phase reactions.

Table 1. Bursting reactions.

Substance	Bursting pressure, 10^2 MPa		
	−78° C	room temperature	80° C
$CuSO_4 \cdot 5H_2O$	7.5	7.5	7.0
$CuCl_2 \cdot 2H_2O$	15	8	7.5
$Na_2SO_4 \cdot 10H_2O$	3	3	− *
$Na_2CO_3 \cdot 10H_2O$	4	4	− *
$MnSO_4 \cdot 5H_2O$	7	7	7
$ZnSO_4 \cdot 7H_2O$	11	9	6
$NiSO_4 \cdot 7H_2O$	9	10	5.5
$CoSO_4 \cdot 7H_2O$	7	6	4.5
$FeSO_4 \cdot 7H_2O$	11	13	15
$MgSO_4 \cdot 7H_2O$	7.5	9.5	− **
$Al(NO_3)_3 \cdot 9H_2O$	8.5	3.5	− *
$KAl(SO_4)_2 \cdot 12H_2O$	7	6.5	5
$Cr_2(SO_4)_3 \cdot 6H_2O$	17	17	−***
$KCr(SO_4)_2 \cdot 12H_2O$	13	17	8
$(NH_3)_2Fe(SO_4)_2 \cdot 6H_2O$	8	5	5

* No burst, sample was irrigated.
** Two sequential bursts at pressures of 3 and $15 \cdot 10^2$ MPa.
*** Burst occurs only on dropping pressure.

In the case of strongly exothermic reactions (a heat effect for the reaction amounting to hundreds or thousands of kilojoules) in addition to a detonation rate for the course of the reaction the formation is observed of a shock wave leading to destruction of the anvils and most of the experimental equipment. Metallothermic reactions are such reactions when one metal by virtue of its own high reactivity reacts with oxides, sulphides or sulphates of another metal and replaces it.

$$M^1 + M^2(X) - M^1(X) + M^2,$$

where X is $(O)_n$, $(S)_m$ or $(SO_4^{2-})_u$, etc. (n, m, u are integers).

An enormous quantity of non-ferrous and rare elements are produced by means of metallothermy at the present time. This industry has developed successfully at home and abroad for more than ten years. The mechanism and kinetics of these reactions are consequently well known.

The characteristic feature of metallothermic reactions is that they are, as a rule, strongly exothermic. The reactions shown below are also extremely exothermic.

$$CuSO_4 + Al \rightarrow ?$$
$$CuSO_4 + Mg \rightarrow ?$$
$$Fe_2O_3 + Al \rightarrow ?$$
$$Fe_2O_3 + Mg \rightarrow ?$$

The composition and quantities of the reaction products are still not strictly established.

Under uniaxial compression of mixtures of these powders (particle size from 0.1 to 1 mm) at room temperature the system loses mechanical stability (explosion) at the point of reaching a pressure equal to p_{cr} and as a result of the vigorous reaction a detonation occurs with destruction not only of the anvils but also of most of the equipment. It must be noted that each detonation leads to the destruction and scattering of reaction products which markedly hinders investigation of them.

Metallothermic reactions have been studied in a detailed manner by scientists all over the world for over a hundred years. It has been established that under the usual conditions the reaction is initiated at 1100–1200 °C and spreads at a rate of millimetres per second. The temperature at the spreading front of an exothermic reaction is 2000–2500 °C.

In the present case reaction is initiated at room temperature and is complete after less than 10^{-6} sec, consequently the propagation rate is kilometres per second. It must be noted particularly that although the dimensions of the reacting solid particles are comparatively large (diameter ~1 mm) the reaction successfully reaches an advanced stage of completion after so short a time.

Combination of the results obtained indicates that in the given case the detonation course of the chemical reactions occurs not as a result of high temperatures with subsequent heating of the unreacted layer as happens on thermal spreading but isothermally at low temperature like the usual solid phase chemical reaction, a significant portion of the thermal energy is evolved after completion of the reaction.

In the case of strongly exothermic reactions (metallothermic for example) the time for completion of the process is less than 10^{-5} to 10^{-6} sec. The propagation rate will be of the order of kilometres per second (anvil diameter 1 cm) and not millimetres per second as in thermal propagation. On the other hand the proceeding of a solid phase chemical reaction at detonation rate, isothermally, at low temperatures shows unequivocally that in solid phase reactions a mechanism exists for an ultra high speed process without initial heating up of the system, i.e. not linked with the Arrhenius rule. This is also indicated by the fact that in the reactions investigated the sizes of the reacting particles were of the order of 1 mm but the reaction went to completion. Complete conversion of the system at the molecular level had occurred after a time of less than 10^{-5} to 10^{-6} sec.

The detonation course of metallothermic reactions in solid bodies is accompanied by destruction of the anvils and of the equipment generally. This indicates that under the given conditions a mechanism exists for the transformation of chemical energy (reaction thermal effect) directly into mechanical energy without high temperatures and without the formation of a gaseous phase.

The conversion of the chemical energy of a reaction into mechanical is usually effected in the following manner. In a closed volume in the gas phase or under conditions when a gas phase is formed, the thermal energy evolved as a result of a chemical reaction heats the system, the pressure in the system rises enabling mechanical work to be carried out. In the case of solid phase chemical reactions it is seemingly necessary to assume formation of a shock wave directly at the time of the process. As was shown above in the case of decomposition (endothermic process) the reverse process occurs, mechanical energy is converted directly into chemical energy without initial heating of the system.

Let us consider the possibility of using the results obtained from investigating solid phase chemical reactions such as the higher mixing rate (diffusion 'coefficient') in comparison with liquid phase reactions, the independence of the rate of chemical conversion on temperature, the absence of catalysts, etc., in the technology of manufacture of useful substances and materials.

In modern industry (chemical, metallurgical, building materials, cellulose–paper, etc.) enormous quantities of solvent and catalyst are used for the optimum conduct of a process in the liquid phase and processes are carried out at extremely high temperatures. The need to use solvents, catalysts and high temperatures becomes superfluous for a solid phase process.

Investigations have shown that the known industrial processes may be carried out at room temperature without using solvents. The manufacture of soap has been known to man from ancient times. The process reduces to the addition of water to solid fat and solid ash and the mixture is boiled to form soap. Soap is manufactured by this technology up to the present the only difference being that solid alkali is used in place of ash. We have developed an industrial method of soap manufacture in a solid phase without solvent. At the present time a dry method of making paper from wood pulp has been developed similarly.

On the basis of the ideas described above a new physical elastic deformation method of crushing has been developed. It must be noted that contemporary crushing machines (ball mills, vibration mills, disintegrators, etc.) have an extremely low performance. When crushing synthetic and natural polymers (resins, wood, polymers, cellulose, etc.) by the elastic deformation method performance is increased by more than an order of magnitude.

Mixtures rather than individual polymers are widely used in industry at the present time to obtain new materials and articles made of them. Usually two basic methods are used. These are fusing and mixing or precipitation from a common solvent. Both methods have several technical, economic and qualitative drawbacks.

As has been shown the rate of mixing is sharply increased in the solid state on shear deformation. The very same occurs with macromolecules. Consequently a new technology for obtaining polymeric mixtures has been successfully created.

The use of solid phase chemical processes in industry may therefore lead to the creation of new, ecologically clean and energetically advantageous processes.

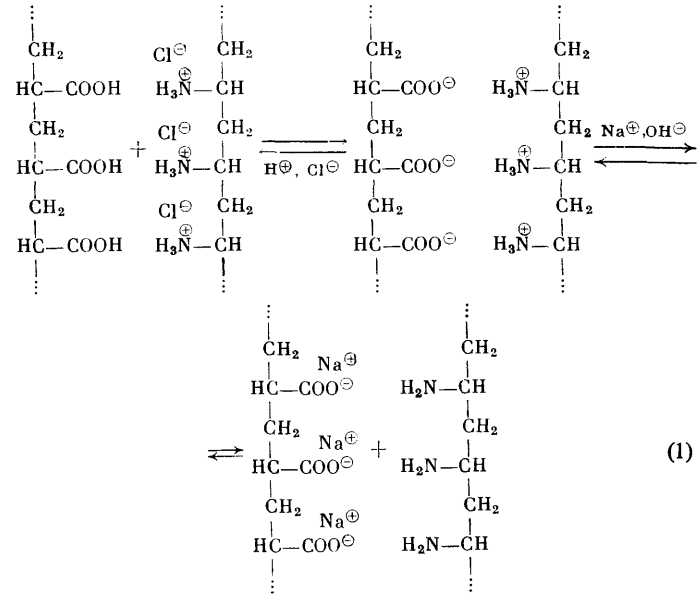
Translated from *Uspekhi Khimii* 60 595–601 (1991)

Polyelectrolytes in the solution of ecological problems

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Polyelectrolytes have been used traditionally for the decomposition of colloidally disperse systems and for structure formation in the latter. We have shown in recent years that the use for such purposes of polymeric complexes formed by the interaction of two oppositely charged elecrolytes—polyelectrolyte complexes (PEC)—leads to qualitatively new possibilities in this field.

The interaction of linear polyelectrolytes bearing unlike charges is due to the occurrence of reversible reactions involving the formation of new bonds between chemically complementary units of the reacting molecules. The reaction between polyacrylic acid (PAA) and polyvinylamine (PVA) is illustrated schematically below:



(1)

Fig. 1 (curves *1* and *2*) illustrates the dependence of the degree θ of the interpolyelectrolyte reaction (1) on the pH of the reaction medium. The degree of reaction (1) is understood as the fraction of the units of the polymeric acid or base which have formed salt linkages with the units of the oppositely charged macromolecule, i. e.

$$\theta = c_k c_0,$$

where c_k = [$-COO^-H_3N^+-$] is the concentration of the interpolyelectrolyte salt bonds and c_0 the concentration of the units of the polymeric acid or base in the reaction system. Evidently the degree of reaction (1) increases and reaches the high value θ = 0.8 within a narrow pH range (1–2) (curves *1* and *2*), while the degree of ionisation α of the corresponding weak polyelectrolytes (curves *3* and *4*) increases monotonically over a wide range of the pH of the reaction medium. This demonstrates the cooperative character of the interpolyelectrolyte reaction and the anticooperative character of the charging process involving free polymeric acids and bases. The cooperative nature of the interpolyelectrolyte reaction is responsible for the exceptionally high stability of the polyelectrolyte complexes within certain pH and ionic strength ranges. In such media, polyelectrolyte complexes are capable of swelling to only a limited extent and give rise to a kind of plastic hydrogel. At the same time, at salt, acid, or alkali concentrations exceeding critical values, the equilibrium in reaction (1) shifts to the left, the interpolyelectrolyte salt linkages holding together the polyions break, and the polyelectrolyte complexes are converted into a soluble state.

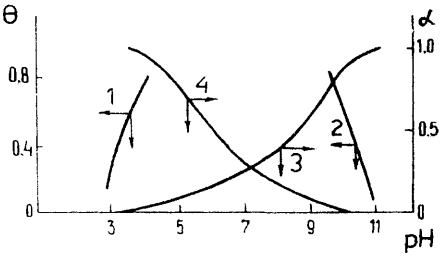
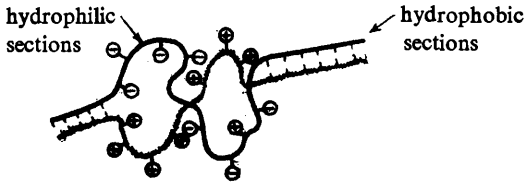
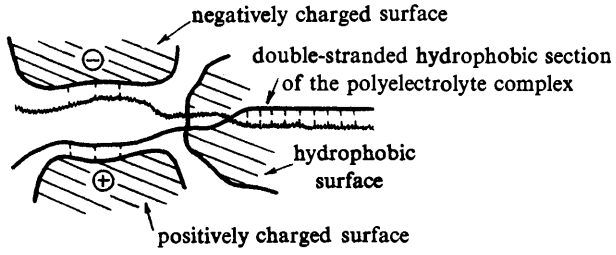


Figure 1. Dependence of the degree of the interpolyelectrolyte reaction θ between equimolar amounts of high-molecular-weight polyacrylic acid and polyvinylamine hydrochloride (curve *1*) and between sodium polyacrylate and polyvinylamine (curve *2*) on the pH. Dependence of the degree of dissociation α of polyacrylic acid (curve *3*) and polyvinylamine (curve *4*) on the pH. Concentration of polyelectrolytes 0.02 M; c_{NaOH} = 0.2 M; c = 0.1 M; t = 20 °C.

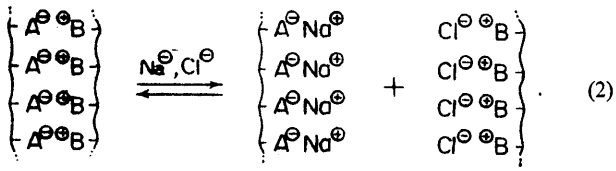
The polyelectrolyte complexes contain hydrophobic regions made up of paired sections of the complementary chains and hydrophilic sequences of ionogenic groups formed by disconnected sections of oppositely charged polyions. A fragment of a polyelectrolyte complex molecule is illustrated schematically below:



Sections of different nature in the swollen polyelectrolyte complex are capable of changing places with one another at a high rate. These structural features of polymeric complexes impart to the latter the unique capacity to be adsorbed on surfaces of different nature and to become adapted to varying external conditions in the contact zone. A fragment of a polyelectrolyte complex in contact with different particles of the disperse phase may be represented as follows:



The technology of the preparation and application of polymeric complex binders is extremely simple. It can be reduced to the preparation of dilute aqueous solutions of a mixture of polyelectrolytes in which the electrostatic interaction between oppositely charged polyions is prevented by shielding due to low-molecular-weight salts, for example, mineral fertilisers. The binder is then introduced into the disperse system, the solution being sprayed onto the surface of the soil or ground by means of any spraying technique. On subsequent washing of the treated layer with water, for example, by spraying or by rainfall, the shielding electrolyte is diluted and removed from the sphere of reaction (2):



(2)

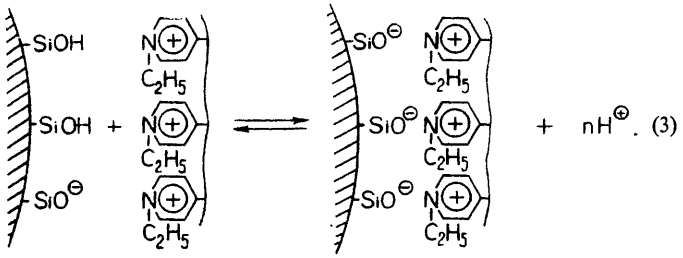
The equilibrium in reaction (2) is then displaced to the left, i.e. towards the formation of the polyelectrolyte complex. The resulting polyelectrolyte complex gel is capable of repeatedly drying out and becoming moist without impairment of adhesion properties, i.e. of the quality of the reinforced layer. Various low-molecular-weight organic and inorganic substances, for example, fertilisers, plant growth stimulators, herbicides, and other physiologically active compounds, can also be incorporated in the polyelectrolyte complex gels. For this purpose, it is sufficient to simply add them to the initial solution. The substances immobilised in the polyelectrolyte complex are then capable of being transferred from the polyelectrolyte complexes to the surrounding medium at a controlled rate.

By virtue of these properties, the polyelectrolyte complexes have been used successfully as structure-forming agents for soils to prevent their erosion by water and wind and to achieve a simultaneous increase in fertility. In the soil-polymer crust, the particles of the disperse phase are linked to one another by thin layers of the polyelectrolyte complex. Such crusts are not broken up by strong winds and rain. The procedures described have been applied successfully, for example, to grass over the sloping sides of earth channels. Polymeric complexes introduced onto the surface of the ground prevent its wind and water erosion during the period necessary for the growth and development of the grass cover. This makes it possible to tidy up reclamation systems incomparably more economically and effectively than can be done by traditional procedures. Polymeric complexes have also been widely tested as agents for the prevention of the washing away of soils and the subsequent crust formation on cotton seedlings and also as agents preventing the blowing away of the protecting banks in vineyards by hurricane force winds (up to 30–40 m s^{-1}).

It is significant that all these antierosion measures can be applied with a very low consumption of polymers (from 20 to 100 kg ha^{-1}). Simultaneously with the main effect, a marked stimulation of planned growth and development is observed. Treatment of cotton fields with polymeric complexes after sowing enhances the development of the root system and improves the capacity of the cotton plant for germination. This favourable effect of the polyelectrolyte complexes on germination can be to a large extent explained by the greenhouse effect of the soil-polymer crust, which retards the evaporation of moisture from the surface of the soil.

In the solution of ecological problems, one can use as polyelectrolytes both synthetic industrial polymers, for example poly(diallyldimethylammonium chloride) (commercial name—VPK-402), poly(dimethylaminoethyl methacrylate), hydrolysed polyacrylonitrile (HYPAN), as well as the products of the modification of natural polymers, for example, cellulose. The use of the waste from major industries for such purposes is especially attractive. For example, oxidised ligands, which are the products of the treatment of wood, can be used as polyanions. These water-soluble polymers, which pollute the environment, can be extracted quantitatively from the waste of the cellulose-paper plants in the form of an insoluble complex which can be used, in its turn, as a structure-forming agent.

Linear polyelectrolytes are capable of reacting effectively with oppositely charged colloid particles. We established that this interaction is described satisfactorily within the framework of the idea that there is cooperative electrostatic attraction between the units of the linear polyelectrolyte and the oppositely charged ionogenic groups distributed on the surface of the colloid particles. A reaction of this type between polysilicic acid (PSA) and the linear poly(*N*-ethyl-4-vinylpyridinium bromide) (QPVB) polycation is illustrated in Scheme 3. Reaction (3) results in the formation of polymer-colloidal polyelectrolyte complexes, whose composition is determined by the state of ionisation of the units of the linear polyelectrolytes and of the ionogenic groups distributed on the surface of the colloid particle:



(3)

Fig. 2 illustrates the dependence of the degree of the polymer-colloid reaction between the polyelectrolyte complex and QVPB on the pH (curve *1*). Evidently, as in the case of interpolyelectrolyte reactions, the formation of the polymer-colloid polyelectrolyte complex is accompanied by an appreciable increase in the degree of ionisation of the surface silanol groups of polysilicic acid (cf. curves *2* and *3*). It is seen from the above figure that the degree of reaction (3) in terms of the linear polymer (curve *1*) increases with increase in pH to the higher value (QPVB) = 0.7 at pH 9. This means that in alkaline media most of the units of the linear polycation are linked by salt bonds with the surface of the colloid particles. The relatively small steepness of the θ–pH curves, i.e. the low cooperativity of the polymer-colloid reactions is a consequence of the conformational non-complementarity of the interacting components—linear macromolecules and compact colloid particles. The conformation of the linear macromolecule, incorporated in the particles of the polymer-colloid polyelectrolyte complex, is characterised by the presence of a large number of loops. In other words, the set of its conformations is appreciably depleted compared with the set of conformations of a similar macromolecule in a dilute solution. A natural consequence of this is the tendency of the particles of the polymer-colloid polyelectrolyte complex to aggregate and form larger particles—floccules. Thus the flocculation of the colloid systems when the latter interacts with linear polyelectrolytes is in fact caused by the impairment of the thermodynamic quality of the solvent in relation to the chains linked to the surfaces of the colloid particles and hence by the spontaneous segregation of the adsorbed macromolecules as a concentrated phase. In the large

associated species (floccules) formed under these conditions, the colloid particles are separated from one another by polymer layers swollen to the maximum extent and formed by sections of the adsorbed polymer chains which on adsorption failed to come into contact with the surfaces of the colloid particles.

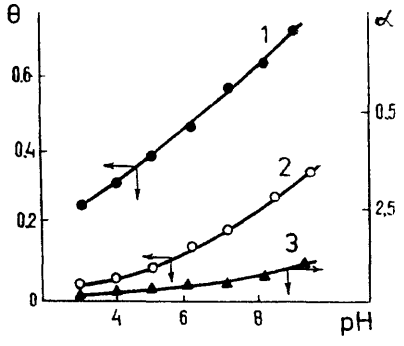


Figure 2. Dependence of the degree of the polymer-colloid reaction between QPVP and the polysilicic acid sol [*1*, θ(QPVP); *2*, θ(PSA)] and of the degree of dissociation of the surface silanol groups of the polysilicic acid sol (curve *3*) on the pH; c(QPVP) = 0.0025 M; degree of polymerisation of QPVP = 2500; sol particle radius = 56 Å; t = 20 °C.

note that the high rate of deposition of the disperse particles and the quality of the clarification of the colloid systems persist over a wide range of variation of the concentrations of a polycomplex flocculant of this kind. In addition, this makes it possible to avoid the undesirable effects due to the partial stabilisation of dispersions on exceeding the dose of the flocculant.

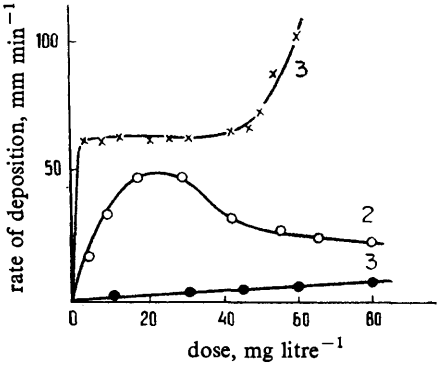
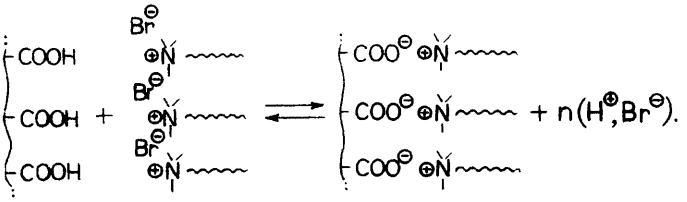


Figure 3. Flocculation of the sludge from the elutriation crust of the lanthanide ores from the Belozimsk deposit; sludge concentration 10 wt.%; particle size 70 μm: *1*, HYPAN; *2*, VPK-402; *3*, HYPAN; VPK-402 = 1:1.

By virtue of the ability of linear electrolytes to react with colloid particles, they are used as flocculants for the intensification of the processes involving the separation of highly disperse suspensions and emulsions. This is required, in the first place, for the creation of closed water circulation systems in undertakings of the mining industry. As an example, one may quote the successful use of the Soviet-produced industrial polycation VPK-402 in the Lovozersk mining-enrichment plant as a flocculant in connection with the establishment of a closed water circulation. The joint use of oppositely charged polyelectrolytes proved to be particularly effective. This makes it possible to reduce by an order of magnitude the consumption of polymer-flocculants with the simultaneous appreciable increase in the rate and quality of the clarification of dispersions. This was demonstrated in relation to the thickening of the highly disperse fraction of the ore from the Beloziminsk deposit (Fig. 3). Fig. 3 shows that the introduction of polymeric anions, for example HYPAN, hardly alters the rate of deposition of colloid particles (curve *1*). On the other hand, linear polycations play the role of flocculants (curve *2*). However, an increase in the content of VPK-402 above a certain optimum amount is again accompanied by a decrease in the rate of deposition and also in the quality of the clarification of the colloid system, i.e. under these conditions the polycation functions as a stabiliser of the disperse system. A qualitatively different flocculation picture is observed when linear polyelectrolytes bearing unlike charges are introduced jointly (curve *3*). In this case the rate of separation of the disperse phase is much higher than in the case where only the polycation is used and the effect indicated is attained with appreciably lower consumptions of the jointly applied oppositely charged polyelectrolytes compared with the cationic flocculant (cf. curves *2* and *3*). It is important to

Linear polyelectrolytes are able to interact cooperatively with oppositely charged micelle-forming surfactants. Such a reaction between polyacrylic acid and dodecyltrimethylammonium bromide (DDTMAB) is presented below:



(4)

As in the case of reactions between chemically complementary linear macromolecules, the polyelectrolyte—surfactant reaction is characterised by a high cooperativity (Fig. 4). The degree of such reaction increases sharply within a narrow range of the pH of the reaction mixture. The degree of dissociation of the polymeric acid incorporated in the polyelectrolyte complex particle then exceeds the degree of dissociation of the free polymeric acid at the same pH (cf. curves *1* and *2*). This results in the formation of stable polymeric polyelectrolyte—surfactant complexes stabilised by the hydrophobic interactions of the alkyl substituents in the surfactant with one another and with the hydrophobic sections of the chain in addition to the salt bonds formed between the ionogenic groups of the linear macromolecule and the diphilic surfactant ions. Such polymeric complexes are formed at a surfactant concentration in the solution lower by two and more orders of magnitude than the critical concentration for a micelle formation (CCM) for the same surfactant. This makes it possible to employ polyelectrolytes for the

effective extraction of surfactants from spent waters. The polymeric complexes isolated under these conditions are in their turn highly effective flocculants capable of decomposing simultaneously mineral dispersions and emulsions of organic substances. This has been demonstrated in experiments on the purification of spent waters in the rolling mills of the Moscow "Serp i molot" (Hammer and sickle) factory.

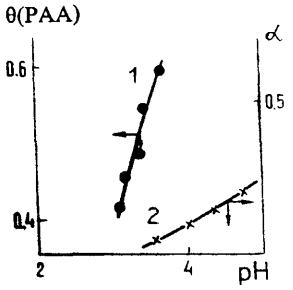


Figure 4. Dependence of the degree of reaction θ between equimolar amounts of polyacrylic acid and dodecyltrimethylammonium bromide (DDTMAB) (curve *1*) (polyacrylic acid and DDTMAB concentrations 0.03 M) on the pH; dependence of the degree of dissociation α of polyacrylic acid (curve *2*) on the pH; c_{NaOH} = 0.1 M; *1*, 20 °C.

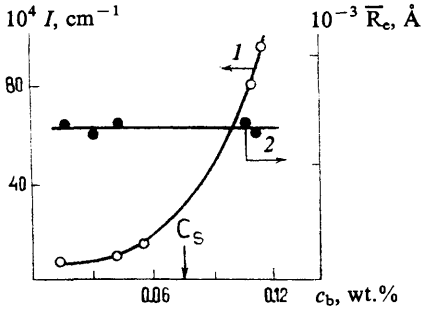


Figure 5. Dependence of the integral intensity of the scattered light *I* (curve *1*) and of the microemulsion drop size ($\bar{R}_e$) (curve *2*) on the amount of emulsified benzene (c_b); composition of the polyelectrolyte complex [PMANa]/[DDTMAB] = 0.2; [PMANa] = 0.03 M; [DDTMAB] = 0.03 M; pH 5.7; t = 20 °C.

The diphilic surfactant ions in the particles of such polymeric complexes are segregated into intramolecular micelles whose size and morphology are determined by the composition of the polymeric complex and the degree of polymerisation of the linear polyelectrolyte. By virtue of the presence of the intramolecular micellar phase, the polyelectrolyte–surfactant polymeric complexes effectively solubilise organic substances which are sparingly soluble in aqueous media, with formation of thermodynamically stable microemulsions of the "oil–water" type. Fig. 5 presents the dependence of the integral intensity of scattered light (curve *1*) and the drop size of microemulsions (curve *2*) on the amount of emulsified benzene. Eviently the size of the drops of the benzene microemulsion in water, stabilised by the complex of sodium polymethacrylate (PMANa) and the surfactant, is independent of the amount of emulsified benzene, while the integral light scattering intensity increases with increase in the amount of emulsified hydrocarbon. It is noteworthy that microemulsions are formed at a hydrocarbon concentration appreciably lower than that of the saturated solution of the hydrocarbon in water (c_s). This means that the drops of the microemulsion consist of a solution in the hydrocarbon of fragments of the polymeric acid bound to the aliphatic groups of the surfactant. The microemulsion particles can be readily separated from the aqueous medium, for example, by adding small amounts of polycations to the system. Thus the polymeric complexes of linear polyelectrolytes with micelle forming surfactants can be used to extract sparingly soluble organic compounds from aqueous media.

Polyelectrolytes have been used successfully also for the extraction of metal ions from aqueous media. Cross-linked polymers, capable of forming complexes with transition metal ions, including heavy metals, are widely used for this purpose. It has been found that the degree and rate of extraction of the metal can be increased by an order of magnitude by using a simple but effective method of "adjusting" the polymeric sorbent to a particular ion. This procedure consists in the fixation of the optimum conformations of the sections of the chains which arise in the polymer-metal complex formed by the linear polyelectrolyte. The complex is then cross-linked. The resulting complex-forming cross-linked polymer "remembers" the optimum structure and in subsequent cycles behave as an "adjusted" highly effective polymeric sorbent.

Translated from *Uspekhi Khimii* **60** 602–609 (1991)

New metal- and carbon-containing catalysts for the catalytic removal of harmful impurities from industrial gaseous waste

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Topchiev Institute of Petrochemical Synthesis, USSR Academy of Sciences, Moscow

The intensification of economic activity has led in recent years to dangerous ecological complications in many regions of our country. Emission into the atmosphere of gaseous waste comprising nitrogen and carbon oxides, carbon disulphide, organic sulphides, hydrogen cyanide, ammonia, and acetylene, which are present in the industrial waste from chemical, petrochemical, gas, and metallurgical industries, in automobile exhausts, in the exhausts from thermal power stations, etc., has given rise to especially great fears.

The incorporation in the processing treatment and the increase in the degree of utilisation of new types of petroleum, gas condensites, and accompanying gases with a high content of hydrogen sulphide and mercaptants are characteristic of the petroleum processing and gas industries in the USSR. For example,

effective extraction of surfactants from spent waters. The polymeric complexes isolated under these conditions are in their turn highly effective flocculants capable of decomposing simultaneously mineral dispersions and emulsions of organic substances. This has been demonstrated in experiments on the purification of spent waters in the rolling mills of the Moscow "Serp i molot" (Hammer and sickle) factory.

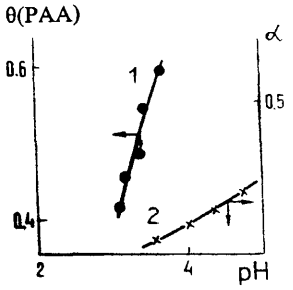


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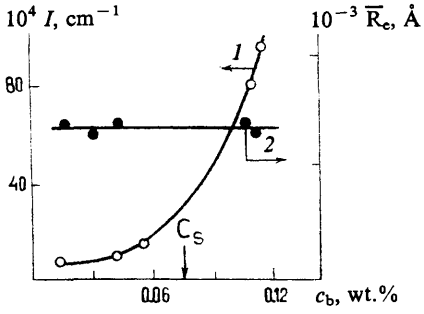


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New metal- and carbon-containing catalysts for the catalytic removal of harmful impurities from industrial gaseous waste

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The intensification of economic activity has led in recent years to dangerous ecological complications in many regions of our country. Emission into the atmosphere of gaseous waste comprising nitrogen and carbon oxides, carbon disulphide, organic sulphides, hydrogen cyanide, ammonia, and acetylene, which are present in the industrial waste from chemical, petrochemical, gas, and metallurgical industries, in automobile exhausts, in the exhausts from thermal power stations, etc., has given rise to especially great fears.

The incorporation in the processing treatment and the increase in the degree of utilisation of new types of petroleum, gas condensites, and accompanying gases with a high content of hydrogen sulphide and mercaptants are characteristic of the petroleum processing and gas industries in the USSR. For example,

promising petroleum deposits (Tengiz, Zhanazholsk) and gas condensate deposits (Karachanak, Astrakhan, and Orenburg deposits and the adjoining petroleum deposits), characterised by great depths of deposition (3500–5500 m), high pressure at the outlet from the well (50–90 MPa) and an elevated temperature (80–125 °C) as well as a high gas factor (600–900 m^3 $tonne^{-1}$), contain between 5 and 30 wt.% of hydrogen sulphide and 2–15 wt.% of carbon dioxide together with methanethiol, carbon disulphide, and other harmful substances.

The effluent and blast gases in the majority of chemical industries, coke-chemical factories, and other industrial objects also contain considerable concentrations of impurities comprising carbon disulphide, mercaptans, nitrogen oxides, etc. The existing methods of extraction, storage, transport, and processing do not ensure the maintenance of an ecologically safe situation in regions where these products are extracted and processed.

The exhaust gases from internal combustion engines and thermoelectric power stations also make a considerable contribution to the contamination of large cities, especially Moscow, by gases. Nitrogen oxides, formed on combustion of diesel fuel, masoute, and especially natural gas constitute a specially great risk to the health of the population. Thus the change in the fuel used by thermoelectric power stations to natural gas increased almost by an order of magnitude the concentration of nitrogen oxides; their concentration in the centre of Moscow exceeds severalfold the limiting permissible concentration (LPC). It is sufficient to say that one thermal power station with a power output of 300 MW releases annually 194 tonnes of nitrogen oxides, 497 tonnes of sulphur dioxide, and 630 tonnes of carbon monoxide. Polycyclic aromatic hydrocarbons, also formed on incomplete combustion of diesel fuel, are no less dangerous. The limiting permissible concentrations of these compounds are 10^{-6} mg m^{-3}, which is smaller by six orders of magnitude than the concentration of, for example, carbon monoxide and nitrogen oxides.

Several versions of catalytic systems based on precious metals have now been developed abroad; all the automobiles produced must be fitted with them. Unfortunately our country lags appreciably in this respect.

A characteristic feature of the majority of industrial gaseous waste in modern industries is their multicomponent nature, which complicates the solution of the problem of their chemical deactivation by means of a series of different chemical reactions leading to the formation of both harmless and new dangerous substances. For example, when the gas contains components such as sulphur dioxide, hydrogen sulphide, carbon dust (C), and carbon monoxide at the usual process temperatures (200–500 °C), there is a possibility of the occurrence of tens of reactions of this type. Some of them are presented in Table 1.

The picture becomes even more complicated if nitrogen oxides or ammonia are present. In the general case, the situation reduces to the occurrence of a whole sequence of oxidation-reduction reactions, where the compositions of the intermediate and final products are fairly complex or cannot be predicted beforehand. In order to determine the final mixture composition, it is insufficient to know only the initial concentration; the concentrations of the substances are a function of time, local temperature gradients, and the specific features of the action of the catalysts. And yet ecological problems require the virtually complete neutralisation of harmful components; the concentrations of most of them should not exceed tenths or even hundredths of a milligram per cubic metre. A certain polyfunctionality is therefore required from the catalysts employed, including a combination of catalytic and adsorption activities.

Such properties are possessed, in particular, by activated charcoals, but their availability and cost preclude their wide scale employment for the purification of large volumes of industrial gaseous waste.

Table 1. Certain possible reactions of the components of ecologically harmful gas mixtures.

Reaction	Heat change, kcal	Free energy change ΔF^0, kcal mol^{-1}
$2H_2S+SO_2 \rightarrow 2H_2+^3/_8S_8$	–	−16.5
$H_2S+^1/_2O_2 \rightarrow S+H_2O$	+53	–
$H_2S+^3/_2O_2 \rightarrow H_2O+SO_2$	+124	–
$2H_2S+O_2 \rightarrow 2H_2O+S_2$	+106	–
$2H_2S+SO_2 \rightarrow 2H_2O+^3/_2S_2$	−11.45	−3.52
$SO_2+2CO \rightarrow 2CO_2+^1/_2S_2$	–	−41.09
$CO+^1/_2S_2 \rightarrow COS$	–	−17.25
$C+S_2 \rightarrow CS_2$	–	−3.75
$CO_2+C \rightarrow 2CO$	–	ΔH^0=40.79
$2SO_2+2C \rightarrow 2CO_2+S_2$	–	–

We suggested that synthetic metals and carbon-containing catalysts with adsorption and polyfunctional catalytic activities be used for these purposes. They are formed in the catalytic decomposition of hydrocarbons on *d* metals within a certain temperature range. In essence, this phenomenon takes place in virtually each industrial process involving the catalytic processing of a hydrocarbon-containing raw material (catalytic cracking processes, dehydrogenation, reforming, etc.) and is well known as an extremely undesirable process leading to the saturation of catalysts by coke; it entails the loss of their activity and necessitates the regeneration of the catalysts. Systematic studies on this process, carried out by numerous investigators,[1–4] showed that the formation of carbon is a process which takes place in accordance with definite rules and can be fully controlled. The structure of the carbon formed then depends both on the nature of the metal and on the carbon deposition conditions.

A typical dependence of the degree of conversion of hydrocarbons into activated charcoal on temperature passes through an extremum (Fig. 1). The optimum temperatures for a number of oxides (Fig. 1*a*) and hydrocarbons (Fig. 1*b*) are described by general relations in terms of the variables optimum temperature–logarithm of the heat of formation of acetylene from the given raw material (Fig. 2). The optimum temperatures also differ for the same raw material and different metals. We obtained general criterial relations for a multiparameter system of this kind, from which it is possible to find the conditions governing the preparation of the activated charcoal. This makes it possible to predict the process and to control it. It was shown that, for example, in the case of C_8H_{10} the optimum calculated temperature is 757 K, while the experimental temperature is 768 K.

The activated charcoal obtained was studied by various physicochemical methods. The elemental composition, the specific surface, the valence state of the metal, and the X-ray diffraction characteristics of the carbon were investigated.

It was established that metals are present as a rule in the finished catalyst in the zerovalent (reduced) state but have a distorted crystal lattice (Table 2). In the case of iron and cobalt, the formation of carbides and cementides was observed, which does not happen in the case of nickel. The metal particles are distributed throughout the catalyst bed with formation of 100–250 Å clusters. The following structural characteristics were determined from the X-ray diffraction patterns for catalytic carbon: the interplanar spacings d_{002}, the size of the coherent scattering regions (CSR), the size of the pseudocrystallites L_c and L_a, and the diffraction coefficient M characterising the degree of organisation of the carbon atoms to form a graphite-like structure. Table 2 shows that no appreciable correlation is observed between these characteristics and the nickel content in the catalytic carbon.

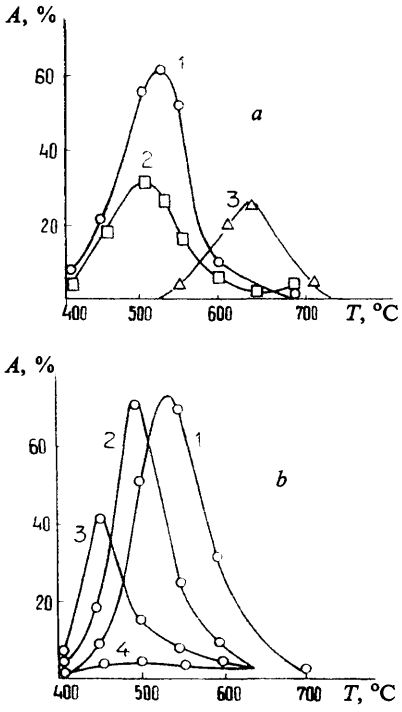


Figure 1. Temperature dependence of the yield of the activated carbon: *a*, for metal oxides (*1*, NiO; *2*, Co_2O_3; *3*, Fe_2O_3); *b*, for hydrocarbons (*1*, C_6H_6; *2*, cyclo-C_6H_{12}; *3*, C_7H_{16}; *4*, $C_3H_5CH_3$).

We shall now consider the principal results obtained in the study of the activities of catalysts both in model mixtures under laboratory conditions using a pulse method and in industrial gaseous waste (Table 3).

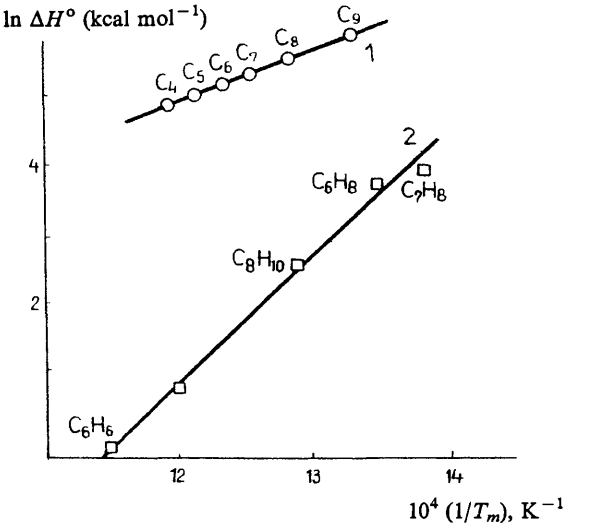


Figure 2. Dependence of the heat of formation of the carbon material ($\Delta H°$) on the optimum process temperature (T_m) for various hydrocarbons: *1*, paraffin; *2*, cyclic (aromatic and unsaturated) hydrocarbons.

Table 2. X-Ray phase analysis of catalytic carbon (DRON-2, Cu K_α line).

c_{Ni}, wt.%	S_{sp}, $m^2 g^{-1}$	d_{002}, Å	L_c, Å	L_a, Å	M, %	Ni	
						CSR, Å	d, Å
0.9	166	3.45	88	94	92.5	–	2.037
2	161	3.46	87	100	91.0	360	2.041
2.8	156	3.41	103	95	92.0	210	2.034
4.5	146	3.41	116	95	87.0	275	2.033
6.0	135	3.42	100	100	91.7	290	2.035
10.0	74	3.40	110	90	82.5	200	2.032
100	–	–	–	–	–	–	2.03

It is also seen from the data presented that, as the hydrocarbon accumulates, the specific adsorption surface increases and the concentration of the metal diminishes, the metal being highly dispersed by the growing carbon.

The specific surface of the catalyst depends on the matrix employed, but it does not as a rule exceed 240–260 $m^2 g^{-1}$ (according to low-temperature nitrogen adsorption data), i.e. is significantly lower than the specific surface of activated charcoal (600–800 $m^2 g^{-1}$). The electron photomicrograph in Fig. 3 shows metal-containing carbon fibres.

Oxygen is absorbed at temperatures in the range 300–350 °C. When the catalyst specimen is treated with oxygen at 300 °C, the evolution of carbon dioxide is not, however, observed. Oxygen is consumed in the oxidation of the nickel reduction centres. At higher temperatures, oxygen is also consumed in the oxidation of the carbon of the catalyst, which results in the evolution of carbon dioxide.

Carbon monoxide is absorbed at temperatures in the range 200–550 °C. Under these conditions, the main reaction product (carbon dioxide) begins to evolve from 300 °C upwards.

Carbon dioxide is absorbed by the catalyst in the temperature range from 20° to 250 °C, the maximum corresponding to 50 °C (1.22 $cm^3\ g^{-1}$). At a temperature above 200 °C, carbon dioxide may be removed by thermal desorption.

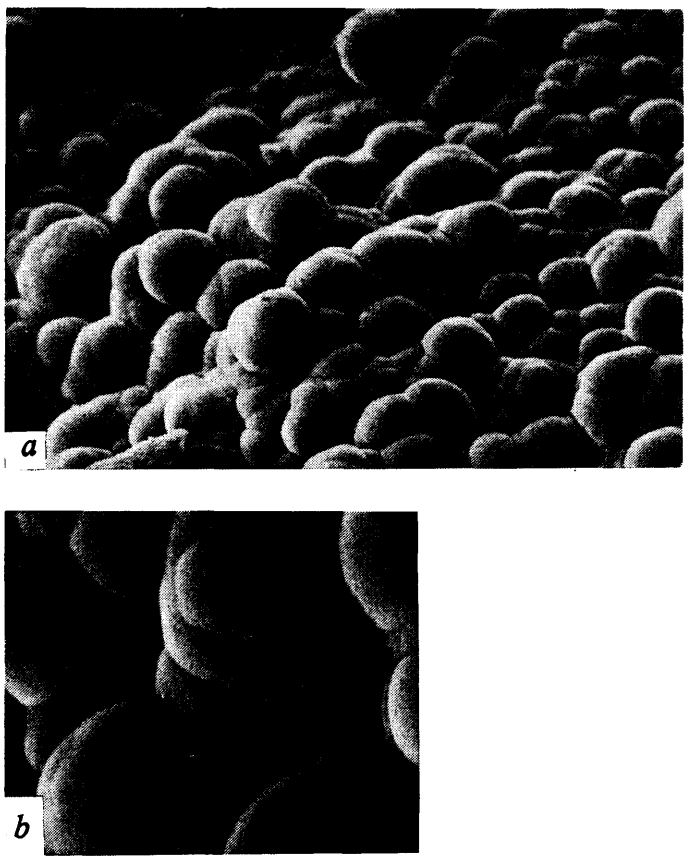


Figure 3. Photomicrographs of the catalyst (on a γ-Al_2O_3 carrier); magnification $\times 350$ (*a*) and 1400 (*b*).

Nitric oxide is absorbed in the temperature range 50–250 °C, the maximum degree of absorption being observed at 150 °C (1.54 $cm^3\ g^{-1}$). Molecular nitrogen is evolved in the same temperature, its amount diminishing with increase in temperature (from 5.0×10^{-2} cm^3 at 50 °C to 0.6×10^{-2} cm^3 at 250 °C). Nitrogen and carbon monoxide and dioxide are evolved on thermal desorption (in the temperature range from 150 °C to 500 °C).

It is of interest to note that the absorption of nitric oxide on activated charcoal does not begin until 200 °C (also with evolution of nitrogen).

In the absence of an oxidant, hydrogen sulphide is poorly adsorbed on the various catalysts tested and does not decompose. In the presence of various oxidants (air, sulphur dioxide), the decomposition of hydrogen sulphide is observed even at room temperature with formation of elemental sulphur (mainly S_8). The amount of adsorbed hydrogen sulphide on the treated catalyst does not exceed 6%. The most active of the catalysts investigated (carbon-saturated γ-Al_2O_3 containing 4.5% of nickel) converted (before breakthrough) 3000 volumes of gas.

Table 3. The activities of catalysts in relation to certain gases.

Gas	Absorption temperature, °C	Chemical reaction temperature, °C	Main product
Oxygen	300–350	>300	Carbon dioxide
Carbon monoxide	200–250	>300	Carbon dioxide
Carbon dioxide	20–250	—	—
Nitric oxide	50–250	>50	Nitrogen
Hydrogen sulphide	20 (pore)	>20*	Sulphur (S_8)
Ammonia	20–450	>20*	Nitrogen
Methane	450–600	>450	Carbon monoxide, carbon dioxide, water
Carbon disulphide, hydrogen cyanide	20	—	Carbon disulphide, hydrogen cyanide

*In the presence of oxidants.

Table 4. Composition of gaseous waste (temperature 350–1100 °C).

Substance	Content, mg m^{-3}
Hydrogen sulphide	360
Sulphur dioxide	60
Carbon monoxide	7.3
Nitrogen oxides	306
Ammonia	197
Benzene	474
Hydrogen cyanide	4
Benzopyrene	0.21
Oxygen and nitrogen	residue

Ammonia is absorbed over the entire experimental temperature range (the maximum is at about 100 °C). Ammonia is an effective reducing agent, which reduces the metal, carbon oxides, and nitrogen oxides. Thermal desorption begins at 450 °C with evolution of nitrogen into the gas phase.

Methane is absorbed at fairly high temperatures (450–600 °C), carbon monoxide and dioxide being evolved into the gas phase. The same products are also formed on thermal desorption. The same temperature range is characteristic of the activity in relation to the methane–nitric oxide mixture.

A catalytic effect was not observed in relation to mercaptans, carbon disulphide, and hydrogen cyanide. Mercaptans, using butanethiol as an example, are not absorbed, while carbon disulphide and hydrogen cyanide remain on the catalyst in the adsorbed form. Aliphatic and aromatic alkyl-substituted hydrocarbons are also effectively adsorbed. The strength of adsorption of hydrogen cyanide is confirmed by the fact that it is desorbed at a temperature above 200 °C. However, these compounds can interact on contact with oxidising gases.

The results obtained in preliminary tests on catalysts in industrial gaseous waste from the Moscow Coke–Gas Factory (MCGF), the Kashirsk Thermoelectric Power Station, and the Cellulose Industry in Krasnoyarsk are presented below. Table 4 gives the composition of the effluent gases from the MCGF.

As a result of the application of the catalyst, hydrogen sulphide, hydrogen cyanide, and nitric oxide are eliminated from the gases (Table 5).

Table 5. Results of tests on new catalytic systems (MCGF).

Source of waste	Ecologically harmful impurity	Catalyst operating conditions		Impurity concentration, mg m^{-1}		Duration of operation before breakthrough	Efficiency of purification, %
		space velocity, h^{-1}	temperature, °C	before purifcation	after purification		
Straight run coke gas	Hydrogen sulphide	300	20	3000	0	312	100.0
Reverse run coke gas	"	470	20	30	0	816	100.0
Straight run coke gas	Hydrogen cyanide, hydrogen	300	20	1000	2.8	1440	99.7
Reverse run coke gas	"	100	20	171	6.0	1440	99.8
	Acetylene	300	200	800	82.7	1440	89.7
	Nitrogen oxides	2000	300	0.21	0.065	1440	69.0
Industrial waste at the MCGF	Ammonia	300	500	1500–78 500	64–28 500	1440	84.0–99.9
Removal of ammonia from aqueous solution by bubbling	"	300	500	134 000	600	1440	96.4
Petrol engine	Nitrogen oxides	12 000	180	1600 ppm	140 ppm	1440	91.0
Stand with UMZ-416 engine	Carbon monoxide	12 000	270	3500 ppm	170 ppm	1440	95.0
Manufacture of viscose	Carbon disulphide	1000	20	1300	50	1	96.1
	"	1000	20	500	9	1	98.2

The advantages of the catalysts described above are as follows:

availability and the possibility of obtaining them directly in the factory, since this requires only a carrier, a hydrocarbon gas, a metal salt, and plant of suitable size and of a relatively simple design;

a lower cost than that of activated charcoal, which makes it possible to organise a large scale industrial production without a large capital expenditure;

the possibility of using spent catalysts, already containing metals, as carriers;

the use of catalysts makes it possible to combine adsorption and catalytic purification processes;

The solution of the problem of the elimination of ecologically harmful impurities from gaseous waste can be reduced (in view of the multifunctional nature of the catalyst) to setting up a balance between oxidative and reductive components. This provides a simple and effective lever for controlling the process, can guarantee the reliability and quality of the purification, and creates conditions for automating the purification processes and the monitoring of the chemical composition of the waste.

The large scale employment of the systems developed requires the creation and organisation of the production of standard apparatus for coating inorganic materials with carbon. At the present time, there exists only laboratory apparatus as well as the plant at the MCGF, which has made it possible to produce one tonne of the catalyst. It is necessary to solve a series of technological problems (in particular, the problem of the additional aerodynamic resistance to the effluent gases) and to develop methods for the regeneration of the catalysts. Furthermore, it is essential to develop apparatus for the rapid analysis of the effluent gases before and after purification, a computer technique, and a module for the automatic control of the purification processes.

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Translated from *Uspekhi Khimii* **60** 610–619 (1991)

Membrane technology in the resolution of nature conservancy problems

S F Timashev
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1. The potential of membrane technology and certain examples

In future membrane technology could provide the basis for resolving a number of ecological problems in many branches of industry and agriculture. Practical experience throughout the world has highlighted examples of how membrane technology may be used on the industrial scale in order to resolve ecological problems.

First of all there is the project in the USA now in its final stages in which the salinity of the Colorado river has been reduced from 1.5 g^{-1} to approximately 0.7 g^{-1} (i.e. in regard to salt content the water has been converted to drinking water). A similar water processing facility is now under construction in the town of Hume (Arizona state) close to the border with Mexico. In this case part of the river discharge will be channelled through the desalination plant where blocks of membrane assemblies for reverse osmosis are located and have an operating efficiency of 400 thousand cubic metres per day. Under these conditions the solvent (water) is forced through the membranes in the presence of a high osmotic pressure (the operating pressure is usually approximately 3–5 MPa) while salts

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The solution of the problem of the elimination of ecologically harmful impurities from gaseous waste can be reduced (in view of the multifunctional nature of the catalyst) to setting up a balance between oxidative and reductive components. This provides a simple and effective lever for controlling the process, can guarantee the reliability and quality of the purification, and creates conditions for automating the purification processes and the monitoring of the chemical composition of the waste.

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are retained. The flow of desalinated water will be mixed with the untreated portion of the Colorado river discharge so that the river water in Mexico has an acceptable salt content.

The future possibility of combining complexone (based on organophosphorus compounds) stabilisation (prevention of salt deposition) of water† with membrane treatment of water in circulating water supply systems by means of ultrafiltration, electrodialysis, and reverse osmosis should be considered. This approach would be even more attractive, since in the case of water stabilisation by complexones part of the circulating discharge would inevitably have to be replenished and the organophosphorus compounds would remain outside the water circulating system.

Reverse osmosis installations are also used for generating large volumes of drinking water, and this process is carried out in Saudi Arabia in plants for the distillation of briny waters in which approximately 10^4 m^3 of water are produced each day. There is a clear awareness of the severity of problems associated with water supplies in the USSR especially in Southern regions. Adequately large reserves of brackish water (approximately 3–6 g l^{-1}) have been located, so that attention may be focused on the supply of water to rural areas which would be ecologically safe as a result of the use of membrane techniques. The success of the respective developments will apparently be determined not only by the availability of high performance membranes (with respect to operating efficiency, selectivity, chemical and thermal output, stability, mechanical properties) but also by the creation of high-capacity membrane devices and by the supply of essential equipment including heavy duty pumps.

It is noteworthy that progress has already been made in the USSR in resolving water supply problems. In Tambov the Rodnik type of electrodialysers fitted with ion-exchange membranes MK-40 and MA-40 and with an operating efficiency of 1–4 m^3 h^{-1} (a product of the scientific-industrial complex Plastmassy, Scientific Research Institute of Plastics) have been in full-scale production since 1974. These facilities provide a reliable supply of drinking and household water produced from brackish waters of artesian boreholes for more than one million inhabitants of rural localities in Kazakhstan, the land along the Volga, the Ukraine, Kalmykin, and Central Asia.

The main electrodialysis installations for demineralisation of water for the requirements of the Prikumskii plastic factory are currently operating. These facilities (operating efficiency is approximately 50 m^3 h^{-1}) reduce the salt content from 0.75–0.8 g l^{-1} to 0.1 g l^{-1}. In this case a certain portion of the demineralised water is used in low pressure steam boilers, while the remaining portion of the water after secondary purification by ion-exchange is utilised for the industrial manufacture of ethylene oxide. The significant reduction in the amount of waste waters attained with the aid of this type of water treatment technology has a favourable ecological effect.

Academician A V Fokin‡ has already indicated in an earlier report that losses of mercury in Soviet plants during the production of one tonne of caustic soda (a total quantity of more than 0.5 million tonnes per annum) reaches 600 g, whereas in foreign countries the loss of mercury during the production of caustic soda is more than an order of magnitude lower. Apparently the only answer to this problem would be to convert to the production of caustic soda under clean conditions with the aid of membrane techniques. By adopting such a strategy there would still be many problems to surmount, despite the purchase of perforated carboxyl-containing membranes and electrolysers from the Japanese firm, Asaki Glass. It is noteworthy that the world-wide production of "membrane" caustic reached approximately 4.5 million tonnes per annum in 1988. [1]

In a number of major chemical and petrochemical plants membrane techniques are now being introduced for the extraction of exploitable components from process gas mixtures which, in addition to saving resources, enables harmful gaseous discharges to the atmosphere to be reduced or eliminated. The American firm Monsanto uses membrane assemblies with an operating efficiency of up to 2.8 × 10^4 m^3 h^{-1} as a result of which up to 9% of the hydrogen not utilised in the chemical transformations can be returned to the manufacturing process and up to 99% of the hydrogen may be concentrated and subsequently utilised for the synthesis of ammonia and methanol and for hydrorefining and hydrogenolysis. A high order of cost savings is being attained in Saudi Arabia where the firm "Chieda" has built an air separation plant for generating high purity oxygen (1200 tonnes per day) and nitrogen (10^4 m^3 h^{-1}) in a petroleum chemistry complex (plants for the production of ethylene, ethylene glycol, and low density polyethylene). In this regard certain achievements in the Soviet Union are noteworthy. Gas separation membranes made of polyvinyltrimethylsilane and gas-separating membrane devices have been developed§. Assemblies, which are commercially available from the scientific-industrial complex "Kriogenmash", are used for the biological purification of waste waters, oxygenation of water for the artificial breeding of fish and other living organisms, for medicinal purposes, and for the generation of a controlled gas phase during the storage of different kinds of agricultural produce and for other purposes. Other examples in which membrane technology may be effectively employed could be given.

2. Resolution of fundamental problems in membrane separation. The basis of the development and extensive exploitation of membrane technology for a wide range of practical purposes

Advances in membrane technology will only be possible as a result of a comprehensive study of a broad range of scientific problems, and the wide experience of many foreign firms supports this view. The main problems will be briefly listed.

1. Problems associated with the production of materials (organic polymers, inorganic material particularly ceramics) for membranes. In this case one has in mind a broad range of problems concerning membrane material science which relate to the selection of conditions for the synthesis and treatment of materials and to the formation of membranes and their modification (volume, surface).[2,3].

† See the paper by M I Kabachnik and N M Dyatlova "Chemical Aspects of a Circulating Water Supply" in the present issue.

‡ See the article by A V Fokin "Protection of the Environment and Chemical Ecology" in the present issue.

§ See the article by N A Plate, V V Teplyakov, V S Khotimskii, and Yu P Yampol'skii "Certain Possibilities with Gas-separating Membranes for the Creation of Ecologically Friendly Plants" in the present issue.

2. Problems associated with the physical chemistry of membrane separation. This group of questions includes attempts to determine the nature of the selectivity of the transport of a given component through the membrane and the determination of the structure of membranes in various three-dimensional scales (beginning with nanometres) and relationships between the structure and functional characteristics of the membranes.[4,5] The mechanisms of transport of ions and molecules within different types of synthetic membranes vary. "Particle size" effects play a major role in microfiltration (particles in the 0.02 μm – 10 μm range are retained) and ultrafiltration (particles typically with a mass of 500 daltons to 0.1 μm in size[5]) processes. However even in the case of ultrafiltration surface force fields, the interaction (Coulomb, dispersion, and "structural"[6]) between particles passing through the membrane pores and the surface of the pore have a significant effect on the efficiency of the separation process. Therefore modification of the surface of the pores (for example by grafting of charged and polar functional groups) may significantly alter the retention effect.

Fields of surface forces are exerted in a particular way in reverse osmosis processes, when under the influence of high osmotic pressures the solvent or individual components of a complex solvent are pressed through the submicropore or subchannel system. In this case the efficiency of the separation (when specifications are met in regard to chemical and mechanical stability of the selective layer in the membranes) is dependent on the topology of paths along which the solvent flows and on the fields of surface forces created by the functional groups within the material used.

In a large proportion of currently available processes for electrodialysis, electrolysis, gas separation, and pervaporation (evaporation through non-porous "diffusion" layers) drift diffusion transport through membranes occurs, so that the effect of membrane separation is determined for various components in the mixtures by the differences in the permeability constants (P) of the material from which the membrane is made. These values are obtained as the product of two factors, a thermodynamic factor (the solubility constant of a component in the given material, the Henry constant) and a kinetic factor (diffusion coefficient, electrical mobility, etc.). In a number of cases the mutual action of the penetrating components have a significant effect, for example on account of the plasticisation of the polymeric matrix, when one of the components dissolves in the latter.

Even at this level of factual description of cross-membrane transport many problems arise which are associated with the need to have an adequate understanding of the technological parameters of the membranes and with the determination of routes for increasing the efficiency of membrane separation, mainly on account of the selection of materials for membranes. The problems increase immeasurably on transition to regimes of intensive mass-transfer through the membrane (high current densities flowing through the membrane, high operating pressures), when the above-mentioned quasi-equilibrium representations are found to be inadequate. Under these conditions the selectivity of the separation may be determined entirely by kinetic factors and may be dependent to a greater extent on the membrane structure in different spatial scales, and on the condition of the membrane surface and the interphase boundaries in the body of the membranes.[4] By gaining an understanding of the nature of the above-mentioned features of the transport process the membrane material and the surface of the membranes can be realistically modified with the objective of obtaining membranes with specified characteristics.

New qualitative relationships and hence new advances in research in the development of new-generation membranes may be elaborated, when barrier membrane structures are used for the separation of mixtures, i.e. ultrathin layers of submicroscopical thickness (10 – 100 nm) made from organic or inorganic materials formed on ultrafiltration and microfiltration supports. In this case the permeability of the membrane layer to a particular type of particle is dependent on the ratio of two spatial scales: the minimal length of a_0, the average distance between centres of localisation of the particle moving in the membrane and also the correlation length, ξ, the characteristic degree of the structural heterogeneity of the barrier layer within the limits of which "coherence" is realised. On scales greater than ξ the system is homogeneous, and therefore the permeability constant P of membranes with a thickness $d \gg \xi$ has the normal meaning. However, when $d < \xi$, the parameter P is not a constant value, since the flow of particles through the membrane under stationary conditions is dependent on the value d according to the non-traditional method (the fractal mode of transport). On account of the difference in the values of the probabilities of the elementary jumps for the various particles, the local heterogeneity of the layer structure is "felt" in different ways by the different types of particles passing through the membrane. Thus the barrier layer may for example consist of a homogeneous system for certain particles, $i (d \gg \xi_i)$, but may constitute a fractal system for other particles, $j (d < \xi_j)$. Thus one might conclude that there is possibly a relationship between the selective permeability of the different types of particles and the thickness of the barrier layers. This may serve as a basis for the targetted search for barrier structures, which are highly permeable and highly selective with respect to specific components and which have different chemical properties and a different three-dimensional structure.

3. Questions concerning the optimisation of separation processes. The advantages of membrane techniques for resolving specific problems concerning the isolation or concentration of the required components from a gas or liquid mixture may be totally realised only when the process as a whole is optimised. In this case combined (integrated) process diagrams may be obtained specifying the use of other process units (distillation, rectification, etc.) in addition to membrane blocks (in general with membrane cascades including recycling[7]).

These complex strategies may be fulfilled by means of mathematical modelling of the processes and the creation of a bank of models for membrane-sorption processes and cross-membrane transport of components in the mixtures. All of the advantages of membrane technology can be exploited only when the process flows, equipment construction, types of membranes, and process arrangements are optimised with the aid of the mathematical models derived.

3. Prospects for the use of membrane technology to resolve ecological problems

Academician I V Petryanov-Sokolov commented on the essential strategic direction for scientific studies against a background of imminent ecological calamities. "There is no process which does not require continual monitoring..." One might anticipate that through the extensive use of membrane separation techniques it should be possible to come close to confirming this principle in real-life situations. Several Soviet developments, which could form the basis of ecologically acceptable processes, are indicated below.

A) The elaboration of basic membrane technology processes for the extraction of utilisation of ammonia from gasous and liquid discharges from chemical and metallurgical plants

In present-day manufacture of ammonia (plants for the synthesis at an output of approximately 450 tonnes of ammonia per annum are used) there are no closed-up material cycles in relation to ammonia. A certain proportion of the circulating gas mixture, the so-called blow-off gases (approximately 7–8 thousand $nm^3\ h^{-1}$) are led out of the synthetic cycle in order to prevent the accumulation of secondary gases above a particular level (approximately 10%) and tank gases are released from the storage tank (approximately 2.5 thousand $nm^3\ h^{-1}$). After the ammonia has been condensed (by cooling to 243–248 K), the ammonia content in the blow-off and storage tank gases is 1.4 and 10.7 vol.%, respectively. The ammonia is either burned in the jets of tube furnaces for natural gas conversion, which leads to further losses of the original raw material and to marked contamination of the environment with oxides of nitrogen¶, or is washed with water with the formation of ammonia water (approximately 3–6 vol.% ammonia) which in many cases is regarded as liquid sewage.

In this regard the close-up of material cycles with respect to ammonia is a key priority from the ecological standpoint (with an unquestionable saving of resources) and could be achieved if highly selective membranes were used for the extraction of ammonia from tank and blow-off gases and also from the ammonia, liquid sewage of the plant.

Ecologically important problems are associated with the operation of gaseous nitration processes which are still used, i.e. the chemico-thermal treatment of steel items, in order to increase their strength, corrosion resistance, and durability by saturation of the surface layer with the nitrogen formed during the thermal dissociation of ammonia, which is present among the operating gases used. An important defect of nitration technology is the partial (approximately 50%) thermal dissociation of ammonia, as a result of which the remaining portion of ammonia is burned with the formation of oxides of nitrogen. There is obviously a need for close-up of the ammonia cycle in this case also, since the annual demand for ammonia is $3-4 \times 10^6\ m^3$ on the premises of the Ministry of Automobile and Agricultural Engineering alone. The need to isolate ammonia from gas mixtures also arises in a number of biotechnology processes.

Membrane technology may be used for the separation of mixtures containing ammonia, in order to surmount this complex of problems. The membrane used for this purpose could be formed from hollow fibre, which has anomalously high permeability and selectivity parameters with respect to ammonia ($P_{NH_3} \approx 5\ m^3/(m^2\ h\ atm.)$, $\alpha = P_{NH_3}/P_{H_2} \approx 10^3$). This type of membrane is under development at present in the Karpov Scientific-Research Institute of Physical Chemistry in collaboration with a number of other organisations, i.e. the Kiev Branch of the All-Union Scientific-Research and Design Institute of Synthetic Fibre, the "Khimvolokno" scientific-industrial complex, the Okhtinsk scientific-industrial complex "Plastopolimer", the State Scientific-Research and Design Institute of the Nitrogen Industry and Products of Organic Synthesis, the Moscow Engineering and Physics Institute, and the Institute of Chemical Physics, Academy of Sciences of the USSR. [8,9] The membranes are based on a perfluorinated sulpho-containing copolymer with a high thermal and chemical stability. Effective methods for modifying the copolymer have been found, adhesive fillers have been developed for gas separation membrane elements, and processes have been designed in which gases are separated in hollow fibre membrane modules using different flow diagram arrangements for organisation of the process. In contrast to known membranes based on polyfluoroethylene resin[10] this membrane is not susceptible to the marked effects of plasticisation and its properties are not altered, when the composition of the ammonia-containing mixture is changed. Trials performed on membranes and gas-separating elements based on these materials have shown that in principle it is possible to surmount the above-mentioned problems on the industrial scale in regard to resource saving and the prevention of harmful wastes from entering the environment.

B) Elaboration of membrane technologies for the extraction and concentration of "acid" components from gas mixtures

In recent years serious ecological problems have arisen in regard to the processing of certain gas-bearing formations mainly in the Orenberg and Astrakhan regions. The main cause of the ecological hazard is the low standard of technology employed for recovery of the gas and also the equipment used which results in the discharge of hydrogen sulphide, sulphur dioxide and carbon dioxide into the atmosphere. Sulphur dioxide is also released into the atmosphere from many industrial plants. Discharge of this gas by thermoelectrical power stations amounts to more than eight million tonnes in the USSR [11] and integrated mining and metallurgical works (Norilsk and others)† discharge several million tonnes. The problems of extraction and concentration of acid gas are especially acute in ferrous metallurgy sites, for example sulphur dioxide in coke chemical plants and carbon dioxide in blast furnaces. Gaseous discharges from motor transport are also known to present a serious hazard to the natural environment.

The release of ecologically harmful components, including acid gases, into the atmosphere has serious consequences. The hazards are mainly acid rain, which is a threat to soil bacteria and causes degradation of the topsoil, and also the greenhouse effect as a result of the release of carbon dioxide.

Apparently it will be possible to eliminate some of these problems in future[12–14] with the aid of membrane technology (it is hoped that in this regard the major successes will be associated with the use of catalytic methods for the recovery of acid gases). Although at present there are essentially no large-scale industrial installations in operation for the entrapment and concentration of the components in aggressive acid gases (sulphur dioxide, hydrogen sulphide, oxides of nitrogen), intensive research in underway in many parts of the world in the search for high-efficiency membranes for acid gases, and line diagrams are in preparation for membrane processes and membrane-sorption and other combined installations.

Of the membranes developed in the USSR for extraction of aggressive acid gases and gas mixtures generated by the various plants, and "Seragel" type membranes are noteworthy.[15] These membranes are highly selective for sulphur dioxide and hydrogen sulphide. In addition membranes for hydrogen sulphide and carbon

¶ Apparently discharges of oxides of nitrogen together with emergency discharges of ammonia in the Shchekin industrial complex "Azot" caused irreparable damage to Tolstoy's farm in Yasnaya Polyana.

† See the article by K I Zamaraev, "Development and Introduction of Catalytic Methods for the Detoxification of Discharges from Industry and Motor Transport" in the present issue.

dioxide which are based on aromatic polyamidoimides obtained from solutions of polymers in N-methylpyrrolidone are of interest.[16]

The American firm Bend Research has designed a membrane, which is highly selective for hydrogen sulphide ($P_{H_2S}/P_{CO_2} \approx 30$) [17] and which consists of a gelatinoid layer containing an alkylpyrrolidone or an alkyl phosphate carried on an asymmetrical cellulose support. In earlier reports[18,19] it has been shown that membranes based on heat-resistant and chemically stable perfluorinated copolymers ("Nafion") are highly efficient in regard to the extraction of acid gases. These copolymers contain sulphonic acid groups with carriers containing amino groups and anion-exchange groups with quaternary ammonium bases. In these cases[18] difficulties are encountered in the determination of specific pathways for the modification of these types of materials and the elaboration of thin-layer (< 50 μm) membrane technology. Thus there would appear to be great potential in the use of hollow fibre modules with membranes based on perfluorinated ionomers for the extraction of acid gas and also for the extraction of ammonia. In these types of materials the gas molecules are transported through a system of submicroscopic canals[4] and the diffusing molecules undergo reversible binding with functional groups or the carriers. In this case certain components may be selectively controlled by altering the moisture content of the membranes.[20] One might suggest that, in addition to the above-mentioned aggressive components (hydrogen sulphide, sulphur dioxide, and ammonia) and carbon dioxide, membranes based on perfluorinated ionomers, which constitute a class of relatively heat resistant and chemically stable polymeric membranes, may (with certain modifications) also be used for the extraction of oxides of nitrogen and carbon monoxide (in the presence of nitrogen) from gas mixtures, for the separation and concentration of certain hydrocarbons, and for drying gases. The above-mentioned studies emphasise the interest in perfluorinated materials containing functional groups as membranes which may be used for the separation of the most aggressive and ecologically harmful components from gaseous media. Apparently in future in addition to hollow fibre membranes flat composite membranes with a selective layer formed from solutions of perfluorinated ionomers will be manufactured (for roll modules).

C) Design of a process of membrane electrolysis in alumina production

A membrane electrolysis process in which the recuperation of alkali is a major component of the technology for the recovery of industrial products in alumina production is being developed by the State Scientific-Research and Design Institute of the Rare Metals Industry, the Institute of Metallurgy and Enrichment, Academy of Sciences of the Kazakh SSR, and alumina plants within the Ministry of Metallurgy of the USSR.

In addition to the question of resource savings the treatment of soda-sulphate mixtures, which are formed during the recovery of sulphide-containing bauxites in a number of aluminium plants in which alkali is completely regenerated (ten–twelve thousand tonnes in terms of 100% caustic on average in each factory), has a very marked ecological impact. Trials with electrolysis using perfluorinated ion-exchange membranes in an installation at an alumina works in the Urals aluminium factory have shown that in principle it is possible to attain almost total regeneration of alkali with the concomitant production of gypsum. Broader objectives have been set for the use of membrane electrolysis for reprocessing carbonate-sulphate, chloride-carbonate, and chloride-sulphate mixtures and also alkaline aluminate solutions.

D) Replacement of ion-exchange cycles by continuous membrane processes in the production of riboxine

A preliminary analysis of the existing technologies for the production of riboxine in plants in which medicinal preparations are manufactured has shown that the use of electrodialysis may significantly reduce losses (reaching almost 50%) of the main product and significantly reduce the ecological hazard presented by the plant on account of the elimination of discharges of water used for the regeneration of ion-exchange columns. The technology of demineralisation by electrodialysis may provide the basis for this and a number of other biotechnological processes.

E) Processes for the treatment of industrial waste waters involving the extraction of valuable components

It is noteworthy that among many plants of this type in existence throughout the world including those in which electrodialysis is employed (see for example Ref. 21) processes are being designed involving the use of impregnated liquid membranes, which contain a solution of a complex-forming agent and an ionophore in an organic solvent, which is injected into the pores of the membrane support. By creating in these systems a counter (antiport) flow of ions of like sign (for example M^{n+} and nH^+) or a unidirectional flow (symport) of ions of opposite sign (M^{n+} and nOH^-) it is possible to achieve a high degree of extraction of the required component (Cu^{2+}, Cr^{3+}, VO_2^{2+}, etc.) from the original solution. In this way copper has been extracted from wash waters in electroplating shops.[22] Porous hollow fibres made from polypropylene have been used as a hydrophobic matrix, the impregnated phase being a solution of di(2-ethylhexyl)-phosphoric acid in n-dodecane. A pH value of 3–5 was maintained in the feeder solution. When sulphuric acid is used in the recipient solution, up to 99% extraction of copper, a toxic component of waste waters, was attained, which corresponded to a residual copper concentration at the normal BOD level. In this case a saturated solution of copper sulphate was obtained in the recipient solution. The demineralised water from which the copper had been removed was returned for use as the wash water and the saturated solution of copper sulphate was used for the periodic adjustment of the composition of the electroplating baths. There is an obvious need to employ this type of technology in industry in the USSR from the standpoint of resource saving and ecology.

One should note two additional general factors.

1. Attainment of ecological objectives is impossible in the absence of any novel techniques and equipment for the continuous monitoring (analytical chemical) of the composition of the environment (atmosphere, reservoirs, land) which permit rapid determinations, and which are reliable and simple to operate. One is essentially concerned with the design and production of a new generation of analytical facilities, i.e. chemical membrane sensors, miniature, highly sensitive devices for the direct, selective, and fully automated determination of chemical compounds in industrial systems and natural specimens. In these devices film (membrane) coatings made from organic and inorganic materials with increased permeability constants with respect to particular environmental components (molecules, ions) are used as barriers separating the environment under analysis from the recording system (semiconducting oxide films, field-effect transistors, etc.). With the aid of these systems it will be possible to monitor rapidly and continuously the chemical composition of liquid and gaseous natural media and industrial discharges down to trace concentrations. Unfortunately studies and developments of this nature are not in

progress in the institutes of the Section of General and Industrial Chemistry, Academy of Sciences of the USSR.

2. As regards solving ecological problems we have no right to procrastinate. It is our duty to our fellow-countrymen and to the world community to exploit to the maximum all available means for construction plants which discharge little or no wastes, in order to reduce the concentration of harmful and toxic components in the environment. This is a very complex problem, which is compounded by the fact that the Soviet authorities at present have no effective mechanisms which help industrial enterprises and factories to become interested in exploiting the achievements of science which are targetted towards the resolution of acute ecological problems. It would seems that, if there are no such mechanisms available, they must be created or at least their creation must be encouraged.

In a present-day assessment of the economic efficiency of technological processes the actual damage which they inflict upon the natural environment (in the mining of exploitable minerals, during the disposal of industrial wastes, at water intakes, etc.) and the expenses which the complete restoration of the environment would demand are not taken into consideration. If in future the objective (by introduction of appropriate laws by the Supreme Soviet of the USSR) will be to take into account this hazard in an adequate manner‡ during the planning of the various technological projects and to weigh the economic advantages against the effects of such projects, the economic advantages of fulfilling many technological plans will be viewed in a completely different light. The need to uphold a way of life with resource-, material- and energy-saving and environmentally acceptable technologies (in particular membrane technology) is undoubtedly becoming a vitally important issue for factories and industrial enterprises. It is precisely this type of revaluation of the technical level of a diverse range of manufacturing processes under Soviet conditions which may open up a route to new technologies.

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‡ In accordance with the currently operating procedures for assessing economical damage inflicted upon the environment, a fine of approximately one rouble must be payed by an industrial plant or establishment for one tonne of salts discharged into an open reservoir.

Translated from *Uspekhi Khimii* **60** 620–626 (1991)

Development of ecologically balanced industrial technology for obtaining chlorine-containing monomers

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Plans for the development of the national economy foresee the promise of a radical upheaval of technological processes based on the more progressive achievements of the work of fundamental and applied scientific investigators. Chemical technologies occupy an important place when putting this programme into effect, and safeguard practically all regions of society. Halogen-containing compounds play an important role in industrial manufacture. This is particularly so for organochlorine compounds which are involved in a number of the largest multitonnage products. It is also known that their manufacture yields many ecological problems which are difficult to resolve. Thus the manufacture of polyvinyl chloride, which reaches a world volume of more than 20 million tons per year, yields up to 9% practically unusuable waste products. It is possible to regard as ecologically unbalanced the current manufacture of several other organochlorine substances, particularly chloroprene, the monomer for obtaining rubbers possessing several desirable properties (oil stability, ozone-stability, incombustibility, elasticity).

A set of studies has been carried out in the Institute of Chemistry of the Bashkir Scientific Centre, Urals Division of the Academy of Sciences of the USSR which were directed towards the creation of technological processes for obtaining chlorine-containing products allowing for modern ecological requirements.

As the basis of our concept we rejected gas phase or other high temperature reactions which are not as a rule capable of high selectivity. It is clear that under conditions of effecting multitonnage technology each percentage point of selectivity causes either the appearance of an enormous quantity of waste products or their abrupt curtailment. We included within our interests the technology of making unsaturated chlorohydrocarbons of composition C_2-C_4 which have high practical value.

Since the selectivity of these chemical processes is determined by the elimination of hydrogen halide from compounds obtained by the previous chlorination of the corresponding organic compounds, attention was paid mainly to the development of catalysts guaranteeing high yields of the desired products. At the same time serious attention was paid to the technological aspects having no less important value in the creation of ecologically safe manufacture. We therefore started from the premise assumed by us of the priority of liquid phase methods effected under mild conditions. The use of the closed cycle principle was an important concept. Thus sodium chloride was formed on alkaline dehydrochlorination and does not usually find regular use. In our scheme high purity sodium chloride is obtained, it may be used for electrolysis, for making sodium carbonate by the Solvay process and even in the food industry.

High efficiency catalysts guaranteeing practically complete selectivity for the alkaline dehydrohalogenation reaction have been developed by us based on new concepts in interphase catalysis. This unique phenomenon of organic synthesis discovered in the seventies immediately attracted the attention of numerous investigators who directed their work both to its use in the synthesis of various organic compounds and to establishing the mechanism for carrying out the catalytic process.[1–3] It is known that various quaternary compounds such as crown ethers, polyethyleneglycol, etc. display catalytic activity in interphase reactions and are widely used. Analysis of the known work on the theoretical aspects of catalysis of interphase reactions shows that there is no unequivocal understanding of the role of catalysts at present.

In our view the generally accepted concept, according to which anion exchange is the initial catalytic act in interphase processes catalysed by quaternary compounds, particularly quaternary ammonium salts, has not been argued sufficiently. Confirmation of the formation of the corresponding ion pairs in the organic phase by deprotonation of the substrate has not been confirmed by reliable proof. On the contrary there are ideas on the formation of alkoxides from the corresponding quaternary ammonium salts and alcohols in the presence of concentrated aqueous solutions of alkali metal hydroxides. All this indicates the absence up to the present of a theory explaining reliably the rules of interphase catalysis.

Since quaternary ammonium salts are widely used in practice as catalysts because of their availability and fairly high catalytic activity, our attention was concentrated on these compounds during the investigation.

The known high catalytic effect of tetraalkyl(trialkylbenzyl)-ammonium alkoxides in the dehydrohalogenation reaction of polyhaloalkanes under the action of concentrated aqueous solutions of NaOH served for a while as the reason for the direction of our investigations.[4]

Some data obtained on dehydrochlorinating 1,2-dichloroethane are shown for illustration (Table 1).

Table 1. The effect of anion structure on the rate (W) of formation of vinyl chloride (temperature 50–55 °C, molar ratio C_2H_4 : NaOH = 1 : 2, NaOH — 50%, reaction time 30 min, quantity of catalyst 0.3 mol%).

Catalyst	10^4 W, mol litre^{-1} sec^{-1}	Dichloroethane conversion, %
$(C_2H_5)_3NCH_2C_6H_5{+}Cl^-$	8.6	28.5
$(C_2H_5)_3NCH_2C_6H_5{+}CH_3O^-$	13.9	45.7
$(C_2H_5)_3NCH_2C_6H_5{+}C_2H_5O^-$	16.8	56.3
$(C_2H_5)_3NCH_2C_6H_5{+}C_4H_9O^-$	20.7	68.1
$(C_2H_5)_3NCH_2C_6H_5{+}C_7H_{15}O^-$	21.7	71.6
$(C_2H_5)_3NCH_2C_6H_5{+}C_6H_5CH_2O^-$	31.6	99.5
$(C_2H_5)_3NCH_2C_6H_5{+}ClC_6H_4CH_2O^-$	37.9	99.7 *
$(C_4H_9)_4N^+OH^-$	9.3	30.8
$(C_4H_9)_4N^+Cl^-$	9.2	30.6
$(C_4H_9)_4N^+Br^-$	9.6	31.8

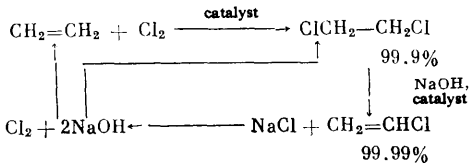
* Reaction time 24 min.

As is seen from the data of Table 1 tetraalkyl(trialkylbenzyl)-ammonium alkoxides display significantly higher catalytic activity compared with other quaternary ammonium salts. It was natural to study this phenomenon deeply in competing β-elimination and

nucleophilic substitution reactions having in mind the constantly increasing ecological requirements for the manufacture of unsaturated C_2-C_4 chlorohydrocarbons. Absolute priority was given to a fundamental investigation of the mechanism of the catalysts found since according to our concept it must have a general character independent of the type of interphase reaction. In addition a true understanding of the catalytic process creates a basis for its control. The conclusion drawn from our investigations was that the catalysis of β-elimination is effected not by the individual quaternary ammonium salts but by the formation of complexes by them.[5-8]

The reaction occurs synchronously in the organic phase and on the surface separating the phases. The principal complex is an associate of the quaternary ammonium salt and proton-donating compounds. Associates are solvated in the organic phase with the organohalogen substrate and interact with organic base on the phase separation surface. The mechanism proposed excludes anion exchange of the catalyst as the initial catalytic act. It is also important that the catalytic activity of the complex is determined both by the basicity of the proton-donating component and by the charge on the nitrogen atom in the tetraalkyl(trialkylbenzyl)-ammonium cation. The presence of an allyl substituent increases catalytic activity appreciably (allyl effect). On this basis a series of highly effective and readily available catalysts for β-elimination in polyhaloalkanes has been developed. The application of these catalysts to the process of obtaining vinyl chloride by the alkaline liquid phase dehydrochlorination of 1,2-dichloroethane affords virtually the first ecologically clean technology.

We are proposing a new strategy for industrial establishments making polyvinyl chloride based on closed cycles with complete chlorine consumption at the place of manufacture. One such cycle comprises the preparation of chlorine and sodium hydroxide by electrolysis, the selective chlorination of ethylene and the dehydrochlorination of 1,2-dichloroethane, and preparation of polymer by ecologically pure technology and, finally, the return of sodium chloride to electrolysis. The efficiency of the process may be judged from the stage of synthesising vinyl chloride. A reactor with a working volume of 1 m^3 has a throughput of 20 000 to 40 000 tons per year. Since the monomer is obtained with a purity never previously achieved in industry the waste products are reduced to a fraction of a percent. The manufacture of polyvinyl chloride resin suitable for making articles of the highest quality and a long use period may be developed from the high purity monomer. The preparation of articles for medicinal techniques, including single-use syringes, is a particularly important use for high purity polyvinyl chloride. The ecologically balance cycle developed for obtaining vinyl chloride may be depicted schematically in the following manner.



Two equivalents of sodium hydroxide are formed at the electrolysis stage for each equivalent of vinyl chloride. This is one of the positive factors in the organisation of the manufacture of unsaturated organochlorine monomers with complete consumption of chlorine. In this case half of the quantity of sodium hydroxide obtained becomes a commercial product. Comparative data are given in Table 2 which characterise the features of vinyl chloride manufacture by the gas method and by the liquid dehydrochlorination of dichloroethane.

$$CH_2Cl—CH_2Cl \begin{cases} \longrightarrow CH_2=CHCl + HCl, \\ \longrightarrow CH_2=CHCl + NaCl. \end{cases}$$

Table 2. Technological process for obtaining vinyl chloride.

Main features of manufacture	Gas phase method	Liquid phase dehydrochlorination of dichloroethane
Reaction selectivity, %	95–98	99.99
Dichloroethane conversion, %	50–60	99.5–99.6
Conditions:		
Temperature, °C	500–550	55–60
Pressure, atm	20–30	without pressure
Unutilisable waste products, thousands of tons per 10 million tons	500–110	1–2

Such features of existing processes as the incomplete conversion of the initial dichloroethane and the high temperature and pressure, are some of the factors raising the price of the final product and complicating the overall maintenance of the technological process. The large quantity of waste products also compels critical treatment of this technology. The structure and composition of the waste products are such that the problem of their utilisation has not been solved and it is doubtful whether it may be solved in a forseeable time. There are harmful organochlorine products, spent sulphuric acid and 'sooty-resinous pulp' (according to the terminology of the production workers) among the waste products. Special areas are separated off for the burial of similar 'gifts'. Consequently the start-up of pilot-plant equipment to operate at the Kaustik Sterlitamaksk Industrial Company is an urgent requirement. The putting into operation of new technology is impossible without its careful analysis under factory conditions. Here it is necessary to add that the unit cost of vinyl chloride obtained by the technology proposed allowing for capital outlay and profit rate will be several percent lower than by the gas phase method. From the ecological point of view the technology proposed by us is preferable.

The closed cycle concept proposed by us has also been suggested for the manufacture of chloroprene rubber. We are convinced that the adoption of our proposal will loosen the stiff ecological knots tying the technology used at present.

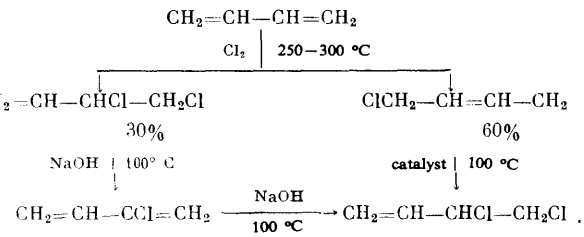
Data from operating a pilot-plant indicate that technology giving almost 10 times less chlorine-containing waste products and leading to practically zero quantities of waste water may be possible. It is extremely important to simplify the technological process, to miniaturise the devices and to replace alloy by more available materials. In addition provision is made in the proposed process for the preparation of dichlorobutane, which is not manufactured in the USSR.

Our principle of operation has replaced the high temperature vapour phase by liquid phase processes taking place under mild conditions which we have applied to the chlorination of butadiene. This step in the existing industrial synthesis of chloroprene, which yields an extremely large quantity of waste products and direct losses (the recurrent result of being out of order due to corrosion of expensive imported compressors and other equipment), is converted

by our proposed catalytic liquid phase method into a step clearly moving the ecological characteristics of the whole technology in a better direction. It therefore turned out to be important that the products of more extended chlorination resulting without fail in the gas phase chlorination of butadiene, were completely absent. As a result of this the need to create special places for burial was reduced.

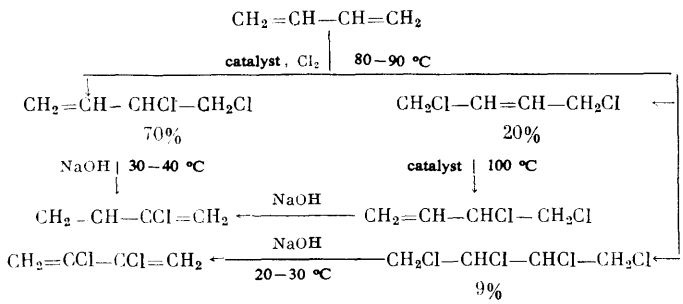
The features of the process for obtaining chlorine-containing monomers by the existing manufacture and by the method developed by us are shown below.

Existing technology



Unutilisable waste products are 7–9% on chlorination, the total quantity of waste products is 250 kg per ton of chloroprene.

Method developed by us



Unutilisable waste products are 0.5–1% on chlorination. Total quantity of waste products are 20–30 kg per ton of chloroprene.

New catalysts have enabled the development of ecologically clean technology for the synthesis of Triallate, an effective herbicide against wild oats. The process is characterised by little waste and a high quality product. The key problem in this technological process is the synthesis of 1,1,2,3-tetrachloropropene from 1,2,3-trichloropropane. This is a four-step process [reactions (1)–(4)], the step selectivity is low, which gives a large quantity of unutilisable chlorine-containing waste products. To this it is necessary to add a large volume of waste water containing harmful and as yet unidentified contaminants.

$$CH_2Cl-CHCl-CH_2Cl \xrightarrow[90\ ^\circ C]{NaOH} \underset{70\%}{CH_2=CCl-CH_2Cl}, \quad (1)$$

$$CH_2=CCl-CH_2Cl \xrightarrow{Cl_2} \underset{25\%}{CH_2Cl-CCl_2-CH_2Cl}, \quad (2)$$

$$CH_2Cl-CCl_2-CH_2Cl \xrightarrow{Cl_2} \underset{35\%}{CH_2Cl-CCl_2-CHCl_2} + HCl(?), \quad (3)$$

$$CH_2Cl-CCl_2-CHCl_2 \xrightarrow[90\ ^\circ C]{NaOH} \underset{71\%}{CH_2Cl-CCl=CCl_2}, \quad (4)$$

$$(iso\text{-}C_3H_7)_2NH + COS + NaOH \rightarrow (iso\text{-}C_3H_7)_2N-\overset{\overset{O}{\|}}{C}-SNa \xrightarrow{CH_2Cl-CCl=CCl_2} \rightarrow \underset{85\%}{(iso\text{-}C_3H_7)_2N-\overset{\overset{O}{\|}}{C}-S-CH_2-CCl=CCl_2}. \quad (5)$$

In addition the final step is characterised as unstable due to the lability of the intermediate product, which also reduces the manufacturing efficiency.

The new technology developed by us and tested in laboratory and pilot-plant equipment possesses high selectivity at all steps and is illustrated in the scheme shown below. It must be stressed that the catalysts found proved to be extremely effective particularly at the step of obtaining Triallate.

$$CH_2Cl-CHCl-CH_2Cl \xrightarrow[catalyst]{NaOH} \underset{98-99\%}{CH_2=CCl-CH_2Cl}, \quad (6)$$

$$CH_2=CCl-CH_2Cl \xrightarrow{Cl_2} \underset{92\%}{CH_2Cl-CCl_2-CH_2Cl}, \quad (7)$$

$$CH_2Cl-CCl_2-CH_2Cl \xrightarrow[catalyst]{NaOH} \underset{96\%}{CH_2Cl-CCl=CHCl},$$

$$CH_2Cl-CCl=CHCl \xrightarrow{Cl_2} \underset{98-99\%}{CH_2Cl-CCl_2-CHCl_2}, \quad (9)$$

$$CH_2Cl-CCl_2-CHCl_2 \xrightarrow[catalyst]{NaOH} \underset{100\%}{CH_2Cl-CCl=CCl_2}, \quad (10)$$

$$(iso\text{-}C_3H_7)_2NH + COS + CH_2Cl-CCl=CCl_2 \xrightarrow[0-10\ ^\circ C]{catalyst} \rightarrow \underset{98-99\%}{(iso\text{-}C_3H_7)_2N-\overset{\overset{O}{\|}}{C}-S-CH_2-CCl=CCl_2}. \quad (11)$$

The advantage of the developed technology is a sharp drop in waste products and also an appreciable reduction (6–7 times) in the quantity of waste water. The process achieves an ecological balance previously inaccessable.

The examples given graphically demonstrate the unlimited possibilities for chemistry to solve ecological problems in practice. It is necessary to carry out an analysis of the existing technology, to develop processes absolutely acceptable from the point of view of preserving the environment and to develop, together with ministries, a long-term plan of fundamental and applied investigations directed towards the creation of chemical processes new in principle. A fairly radical reconstruction of the chemical industry must be expected in line with trends in the development of modern science and chemical technology and the urgently dictated requirements of ecology.

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Brief communications

Translated from *Uspekhi Khimii* **60** 627–628 (1991)

Catalytic systems for the purification of industrial effluent gases

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The elimination of toxic impurities from industrial effluent gases constitutes an important ecological problem which has hitherto been solved to only a slight extent in our country. Such purification is desirable when the concentration of impurities in air exceeds the limiting permissible concentration (LPC) but is not sufficiently high to make their trapping economically viable. One of the most rational ways of removing such impurities involves, in the given instance, extensive catalytic oxidation.

The specific features of the catalytic purification under industrial conditions consists in the fact that the composition of the impurities removed is in general extremely complex and varied. The extensive oxidation of the effluent gases of different composition can be most effectively achieved with the aid of platinum and palladium catalysts containing the active metal, at a concentration amounting to a fraction percent, on porous and metallic carriers. These catalysts are capable of effecting a stable acceleration of the reaction at low temperatures with conversion of the impurities to give concentrations of the latter corresponding to the LPC and with conversion of functional compounds into non-toxic substances. Some of the effective catalysts are reforming catalysts (AP-56 and its later analogues) extracted from industrial apparatus after deactivation. They retain a high stable activity in extensive oxidation processes. The use of catalysts on a metallic support instead of porous carriers is more useful, since it rules out the blocking of the pores by industrial dust and increases the period of the operation of the catalyst.

Systematic studies on the separate and joint oxidation of toxic impurities under stationary and non-stationary conditions on industrial catalysts have been carried out in recent years at the Zelinskii Institute of Organic Chemistry of the USSR Academy of Sciences jointly with the Dzerzhinsk branch of the NIIOGAZ. These investigations made it possible to establish kinetic models of the extensive oxidation of various classes of compounds (paraffins, aromatic hydrocarbons, aldehydes, alcohols, acids, esters, and organic nitrogen compounds), to discover their common features and significant differences, and to develop a theory of the kinetics of catalytic reactions of mixtures of organic compounds. The latter permits the prediction, on the basis of experimental data for the reactions of individual compounds, of kinetic models for the reactions of mixtures of these substances with the aid of the idea that there is a simple mutual influence in the surface layer of the catalyst.

On the basis of the kinetic models obtained, the Dzerzhinsk branch of the NIIOGAZ together with the Institute of Organic Chemistry of the USSR Academy of Sciences achieved the catalytic purification of the effluent streams of air in the manufacture of synthetic aliphatic acids at the Novokuibyshevsk petroleum processing factory (with a turnover of 240 000 roubles annually) and also additional purification on horizontal and vertical machines for the enamelling of cable at the Moldavkabel' and Moskabel' factories with a turnover of 30 000 – 50 000 roubles annually).

Translated from *Uspekhi Khimii* **60** 629–630 (1991)

Water-soluble polymers for the purification of waste water

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The high anthropogenic stress arising from large cities, industrial undertakings, and large animal husbandry complexes has led to an unsatisfactory state of the water system in many regions of the USSR. An unsatisfactory ecological situation has arisen in the Lake Ladoga – the Neva – Bay of Finland system. The natural capacity of the water system for adaptation has reached its limit.

The question of the purification of large volumes of waste water has arisen. The situation is aggravated by the necessity to disinfect these waters to remove the pathogenic microflora and to achieve its detoxification by removing heavy metal salts which enter the water mainly from industrial undertakings.

The most acute problem is that of the processing and utilisation of deposits from urban purification plant, hundreds of tons of which are carried away to waste dumps because they cannot be converted into fertilisers owing to their high content of heavy metals and pathogenic microorganisms.

One of the most important stages in the processing of deposits from purification plant is their conditioning and dehydration, which is achieved with the aid of high-molecular-weight water-soluble polymers — flocculants, ensuring the rapid coagulation and precipitation of suspended particles and promoting thereby the dehydration of the deposits. The efficiency of the flocculant is determined by its molecular weight and also by its charge. The higher the molecular weight of the flocculant, the lower its amount required for the conditioning of the deposit and for the shortening of the duration of the process. Cationic polyelectrolytes with a molecular weight of at least $10^6 \times (6-10)$ proved to be the most effective.

Bearing in mind the marked variations in the composition of the contaminants and in the properties of the deposits as a function of the waste ejected into water, flocculants of different types are widely used abroad. Despite the fact that the requirement for them runs to tens of thousands of tonnes, high-molecular-weight flocculants are

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not manufactured in the USSR. In the purification of drinking and waste water, imported flocculants are mainly employed, a large amount of foreign currency being expended annually for their purchase.

Ultra-high-molecular-weight neutral, cationic, and anionic polymers, which proved to be effective flocculants for the conditioning of waste water deposits in Leningrad, the waste waters from animal husbandry complexes, and also from a number of paper and aluminium-magnesium industries, have been synthesised by novel methods at the Institute of Macromolecular Compounds of the USSR Academy of Sciences. The foundation for the development of a broad assortment of flocculants for different purposes was thereby laid at the Institute.

The "Akromidan-LK" flocculant, which is not inferior to foreign products in its efficiency and in a number of characteristics is superior to them, was most widely tested under different conditions. At the present time a technology for the manufacture of this flocculant is being developed and an experimental plant is being designed in which it is proposed to develop an industrial technology and to produce experimental batches of flocculants for wide scale testing.

In order to organise a wide scale industrial manufacture of new highly effective flocculants, it is essential in the first place to initiate the commercial manufacture of the starting material—amino-acrylates, the plants for the manufacture of which are at present moth-balled. This will make it possible to achieve the industrial production of Soviet highly effective flocculants and to solve the problem of providing flocculants for the existing technology for the dehydration of deposits both on urban purification plants and on purification plants of animal husbandry complexes and paper industrial undertakings.

Translated from *Uspekhi Khimii* **60** 631–632 (1991)

A new chemical technology—the basis of technological processes for the protection of nature

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The dramatic situation as regards the pollution of soil, water containing areas, and air caused by the industrial and agricultural activities and the ejection into the domestic environment of an enormous amount of organic and inorganic substances, various types of dust and gaseous, liquid, and solid products have made it urgently necessary to create fundamentally new technologies designed to protect nature and in many cases to save it.

Such a new technology, which may serve as a foundation for nature-protecting technological processes, is the controlled release technology (CRT). The physicochemical basis of the TRC is spontaneous processes—diffusion, osmosis, and dissolution, described by thermodynamic, Fick, and van't Hoff laws.

The control of the above processes using for this purpose the specific properties of high-molecular-weight compounds (matrix, transport, and constructional) will make it possible to construct entropic macromolecular chemical engines for the long-term and controlled metered injection of chemically and biologically active substances into any medium involving activity (the organism, soil, water-containing area, reactor, etc.). Macromolecular chemical engines (MCE) function without external energy sources as a result of the difference between the chemical potentials in the medium and in the MCE and by virtue of the increase in entropy in the "MCE—disposal medium" macrosystem.

The controlled release technology and macromolecular chemical engines can find and are finding applications in various branches of engineering and the national economy: plant cultivation, animal husbandry, the fishing industry, veterinary science, the health service, the food industry, in chemical engineering processes, in long term food storage, in protection against corrosion, and in autonomous systems, i.e. systems where prolonged controlled injection of various preparations is required: medicinal drugs, fertilizers, pesticides, biostimulators, inhibitors, catalysts, insecticides, herbicides, etc.

The use of the CRT in any of the fields listed above leads to the creation of new technological processes with the following features: ecological cleanliness—by virtue of the possibility of injecting the useful substance at a specified point in a strictly defined amount in the course of a specified period; the saving of resources—as a consequence of the elimination of the non-productive consumption of useful substances involving a balance between the rate of consumption and injection of the required components (for example, fertilizers); energy saving—as a consequence of the absence of the need for external energy sources to permit the functioning of controlled release polymer systems.

In support of the above postulates, three developments concerning the protection of soil, animals, and water containing area may be briefly described: the study and the cultivation of vegetables (cucumbers, tomatoes) by a non-traditional procedure, prophylaxis of strongyloidosis in cattle, and the development of polymeric devices for the measured microinjection of biologically and chemically active substances into water-containing areas.

It was shown in relation to the examples quoted that, in the growing of tomatoes and cucumbers on APION devices (devices for the metering of fertilisers), the consumption of fertilisers is reduced to the biologically necessary level (by a factor of 5–15), the crop is increased, the quality of the produce is improved, and the ecological cleanliness of the technological process is radically improved.

In the therapeutic and prophylactic treatment of cattle with the aid of LAUS devices (devices for the metered release of an antihelminthic preparation in the animal's stomach), the weight increment in the animals fed on pastures increases, and the quality of the pastures is improved by the faeces containing the antiparasitic preparation.

By ensuring prolonged metered injections at a specified rate of molluscocidal preparations into water-containing areas or flowing water systems with the aid of supercharged polymer pumps, one prevents the spreading of severe infective diseases of animals and humans without damaging the aquatic and terrestrial inhabitants of the ecosystem.

Overall, on the basis of the controlled release technology, it is possible to develop radically new technological processes, generating significant ecological, social, technical and economic effects and being directly designed to perform nature protecting functions, the husbanding of resources, and the maximum improvement of the human environment.

Translated from *Uspekhi Khimii* **60** 633 (1991)

Development of new ecologically clean technologies in the manufacture of nitric and sulphuric acids

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Studies on ecologically clean manufacturing processes are being developed in several directions in the Laboratory of Macrokinetics of the Division of the Institute of Chemical Physics of the USSR Academy of Sciences. The first concerns the creation of new technologies in the manufacture of sulphuric acid. Using a special reactor and a stoichiometric mixture of sulphur dioxide, oxygen, and water vapour as the reaction mixture, it has been possible to organise the process in such a way that the sulphur dioxide [trioxide?] formed in the reaction combines with water and condenses on the cold walls of the reactor. As a result, it is removed from the reaction, leads to no aftereffect, and does not inhibit the reaction. The advantages of this method are evident. Firstly, it has been possible to raise the concentration of sulphur trioxide from 10 to 66% and to reduce significantly the dimensions of all the gas connecting tubes. Furthermore, such a technology makes it possible to organise a closed cycle and hence to go over a completely waste-free manufacturing process.

Yet another way of obtaining sulphuric acid is undergoing laboratory tests at the present time and consists of the following steps: if a stoichiometric SO_2+O_2 mixture is frozen until solid, is irradiated with a light flux, and is then rapidly warmed, a reaction takes place at a high rate and with a high yield as a result. This procedure for the synthesis of H_2SO_4 has been tried in several laboratories.

Finally, yet another aspect of such investigations is associated with the safety of the operation of chemical reactors and of power engineering.

During the last decade, we have been actively concerned with the study of ebullition, which is a field seemingly very remote from chemistry. However, it was found that ebullition crises are surprisingly analogous to processes such as combustion and detonation, i.e. the traditional objects of study at the Institute of Chemical Physics.

The latest results achieved in this field suggest that in the immediate future we shall apparently be able to describe and understand the physics of the dangerous phenomenon of the vapour-phase explosion.

III. INTRODUCTION OF ECOLOGICAL CONSIDERATIONS INTO POWER ENGINEERING AND TRANSPORT

Translated from *Uspekhi Khimii* **60** 634–648 (1991)

Problems of the development of catalytic after-burners for the exhaust gases from automobiles and of alternative ecologically clean fuels

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The exhaust gases from internal combustion engines are the principal source of harmful pollutants in the atmosphere. Unfortunately, our Press has devoted little attention to this factor. The main bulk of publications objecting to the pollution of the atmosphere refer to the chemical industry and electric power stations. However, in reality the pollution of the atmosphere by automobiles is incomparable in terms of scale to the harmful effects of the chemical industry. In the chemical industry, pollution is more local and can be more readily detected by smell and colour than the automobile exhausts and for this reason is more likely to attract the attention of journalists.

The approximate composition of the spent gases from petrol engines is presented in Table 1. The composition of the gases naturally varies as a function of the type of engine and, in particular, the nature of the fuel. After catalytic cracking, petrol contains more paraffins and, after reforming it contains more aromatic compounds, etc. Most of the gases listed in Table 1 have no colour or smell.

According to an estimate,[1] in the USA there are 5.5 times more motor cars (110 million) than in the USSR (20 million). However, as a result of measures taken for the strict control of exhaust gases each automobile in the USA emits at least four times less harmful substances than in the USSR. The damage to human health in the USSR due to the pollution of the atmosphere caused by the exhaust gases from engines is estimated to cost 60 million roubles annually. It has been suggested that the overall scale of pollution of the atmosphere in 1990 will amount to 242 million tonnes, including 172 million tonnes due to motor cars. The exhaust gases from internal combustion engines are responsible for more than 70% of diseases among children. The incident of lung cancer and also the number of spontaneous miscarriages have increased. It is believed[1] that 68% of all the human diseases are induced by breathing poisoned air.

The interaction of nitrogen oxides NO_x with hydrocarbons under the influence of solar radiation induces the appearance of the so-called photochemical smog. Thus the exhaust gases from automobiles are particularly harmful in poorly ventiliated cities with a large amount of solar radiation such as Log Angeles, Alma-Ata, and Tbilisi. We emphasise yet again that smog is caused not so much by chemical or power industry as by motor cars.

I. Norms for the emission of toxic products

The principal methods for reducing the toxicity of autombile exhaust gases involve the improvement of engine design, the introduction of electronic devices for regulating the composition of gases, the improvement of the composition of fuel, and catalytic purification. The first studies on catalytic purification date back to the 1920s and systematic studies in this field were initiated in 1949 by E Houdry (USA).[2] However, the widescale incorporation of the results of these studies did not begin until the end of the 1970s after the U.S. government introduced controls for the emission of toxic substances and reduced the permitted norm (limit) for the latter.[2] Since then the norms for the emission of toxic substances have been continuously made more strict (Table 2).

The reason for this process has been the sharp impairment of the state of the atmosphere in cities with heavy motor traffic. The adoption of clean air laws and the stage by stage increase in the rigour of standards have led to serious steps being taken in the USA as regards the problem of the purification of motor car exhaust gases. In the course of an approximately 20 year period of observations, the level of emitted incomplete combustion products from newly produced motor cars has been reduced by a factor of ~ 10 and the level of nitrogen oxides has been reduced by a factor of 3–4.

Even more strict standards as regards nitrogen oxides have been adopted in Japan (Table 2). In Western Europe the 1988 norm is less rigorous but since that year newly produced automobiles in Europe began to be fitted with catalytic after-burners. There has been a corresponding diminution in the use of ethylated petrol and in 1990–1991 it should cease altogether. The norms for emitted gases in Western Europe gradually approach the American and Japanese ones. Application of norms to emissions has also been introduced in the USSR (Table 3).

It is essential to note that, owing to the complexity of the procedure for the determination of the exhaust gases (special equipment, driving cycles, etc.), the certification of a given model as regards toxicity and the issue of a special certificate guaranteeing that the automobile meets the specified ecological parameters at least

in the course of a guaranteed distance (80–160 km) have come to be generally adopted. Since the renewal of car fleets and models in Western markets takes on average 3–5 years, this specifiction of norms ensures the maintenance and in many cases the improvement of the ecological situation.

Table 1. Spent gases from petrol engines.

Components	c_{max}, vol.%	Toxicity
N_2	74–77	Non-toxic
H_2O	3.0–5.5	»
O_2	0.2–5.0	»
CO_2	0.5–12	»
CO	0.2–5.0	Toxic
NO_x	0–0.8	»
SO_2	0.02–0.1	»
Paraffins	0–1.2	»
Olefins	0–1.6	»
Aromatic compounds	0–0.4	»
Soot	0–0.4 *	»
Benzopyrene	up to 20*	Carcinogenic

* The concentration is expressed in g m^{-3}.

Table 2. The norms for the emission of toxic products in the USA, Japan, and Western Europe.

Country	year	Norm, g km^{-1}		
		hydrocarbons	CO	NO_x
USA*	up to 1975	6.2	52	3.4
	1975	0.93	9	1.9
	1980	0.25	4.3	1.2
	1985	0.23	2.1	0.62
Japan	1988	0.25	2.1	0.25
Western Europe	1988	0.86	6.17	1.63

* In 1990, George Bush signed the law concerning the further increase in the strictness of emission norms (including that for CH_2O).

One should also note the well tried procedure for the introduction of standards in the West, the combined approach to their application, and also the provision for legal and economic sanctions as regards the quality of fuels and oils, the system of financial incentives for the low toxicity of exhausts, etc.

The adoption in the USSR of sufficiently strict standards has unfortunately not led to a significant improvement of the atmosphere, as regards risks to health, in large cities for a number of reasons. In the first place, one should note the considerable gap between the quality of the exhaust from an automobile leaving the conveyer belt and an autombile in normal use—the extremely low quality of technical servicing and the long operating life lead to a toxicity several times greater than the specified parameters. The norms are simply not fulfilled. There exist considerable reserves also in the design and in the technology of the manufacture of the engine and of the means of transportation—random tests have shown that even on delivery a considerable percentage of Soviet automobiles do not meet the requirements of the standards.

Table 3. The norms for the emission of toxic products in the USSR.

Year of introduction	Weight category of automobiles	Norms, g m^{-1}		
		hydrocarbons	CO	NO_x
Actual standard OST 37.001.054–86	1250 kg	5.06	14.8	–
	1450 kg	5.43	16.8	–
For engines with catalytic converters				
1991	h=1.4–2.0 litres	1.97	7.4	–
1988	h > 2.0 litres	1.97	7.4	–
1990	h > 2.0 litres	1.63	6.17	0.86
For engines without catalytic converters				
1991	h=1.4–2.0 litres	3.7	11.1	1.48
1990	h > 2.0 litres	4.19	11.1	1.48

Note. h = volume of cylinders.

Another cause is the structure of the standards in the USSR, which have separate norms for automobiles without converters and for automobiles with converters [the latter are close to Western European norms]. However, when there are two norms, nobody tries to satisfy the stricter one. In view of the fairly liberal interpretation of standards, it is difficult to expect a serious effort by industry and operating organisations to achieve a radical decrease in the toxicity of spent gases.

Finally one should emphasise that extremely strict norms as regards toxicity can be satisfied only by a combined approach to the problem, which presupposes a high level of organisation of the fuel combustion process in the engine cylinders, electronic control of the engine, the availability of lead-free fuel, and the appropriate level in the industrial manufacturing process, servicing, and the application of extremely effective devices such as catalytic converters.

II. Catalysts

In the practice followed in the leading foreign countries, the exhaust gases from internal combustion engines are purified in catalytic converters. A large number of catalytic reactions take place

on the detoxificiation catalysts for the exhaust gases from automobiles, for example:

$$CO + {}^1/_2O_2 \rightarrow CO_2, \quad (1)$$

$$C_nH_m + (n + m/4)O_2 \rightarrow nCO_2 + (m/2)H_2O, \quad (2)$$

$$H_2 + {}^1/_2O_2 \rightarrow H_2O, \quad (3)$$

$$CO + NO \rightarrow {}^1/_2N_2 + CO_2, \quad (4)$$

$$C_nH_m + 2\,(n + m/\Delta)NO \rightarrow (n + m/\Delta)N_2 + m/2H_2O + nCO_2, \quad (5)$$

$$H_2 + NO \rightarrow {}^1/_2N_2 + H_2O, \quad (6)$$

$${}^5/_2H_2 + NO \rightarrow NH_3 + H_2O, \quad (7)$$

$$2NO + 5CO + 3H_2O \rightarrow 2NH_3 + 5CO_2, \quad (8)$$

$$2NO + CO \rightarrow N_2O + CO_2, \quad (9)$$

$$CO + H_2O \rightarrow CO_2 + H_2, \quad (10)$$

$$CH_4 + 2H_2O \rightarrow CO_2 + 2H_2. \quad (11)$$

The key reactions among the processes listed above are the oxidation of CO [reaction (1)] and of hydrocarbons [reaction (2)] to CO_2 and the reduction of nitrogen oxides by carbon monoxide to molecular nitrogen [reaction (4)]. Under non-stationary conditions, where the temperature of the exhaust gases varies from 200 to 1000 °C and the mixture composition varies from an oxidising mixture (with an excess of O_2) to a reducing mixture (with a deficiency of O_2), the best and virtually the only catalysts available, despite their high cost, are noble metals: platinum, palladium, ruthenium, and rhodium. In terms of their activities in the three main reactions, they can be arranged in the following way:[3]

Reaction	Catalysts
$CO+O_2$	$Pd \approx Rh > Pt > Ru$
$C_nH_m+O_2$	$Pt > Pd,\ Rh > Ru,$
$NO+CO$	$Ru > Rh > Pt > Pd.$

In terms of the complete set of catalytic properties, rhodium occupies the first place. However, it is very expensive—not more than 2.5 tonnes of rhodium are produced annually throughout the world. For this reason, the main component of catalytic converters (after-burners) is platinum, more rarely palladium, their overall production exceeding 100 tonnes. For the majority of reactions, platinum is more active than palladium but it is approximately twice as expensive. The main exporters of platinum metals on the world market are the USSR and the Republic of South Africa.[2]

The active component (a noble metal) is deposited on the oxidant (aluminium oxide), while the latter is deposited on a ceramic block in an amount of approximately 0.1%. For an overall weight of the catalyst of about 1–2 kg in one converter, this entails the consumption of 1–2 g of platinum.

There are two main types of converters: the straight-flow converter in which the exhaust gas passes through thin (0.5–1 mm) straight channels in a catalytic block with the deposited catalyst and a Z-shaped converter in which the catalyst, in the form of spherical pellets coated by the active mass, is exposed to the exhaust gases. Catalysts of the first time are being developed, for example, by the Engelhard Company and are used by the Ford Automobile Company. Catalysts of the second type are manufactured by the UOP Company and are used by the General Motors autombobiles.

The overall cost of the catalysts used in automobile after-burners is at present about one-third of the total cost of the catalysts manufactured throughout the world. The sharp increase in the cost of catalysts for the purification of automobile exhaust gases which occurred in 1988 is noteworthy. New stricter norms for the emission of harmful waste were introduced in Western Europe in that year.

Cost of catalysts manufactured throughout the world

	1987	1988
Petrochemical industry	620 million dollars	650 million dollars
Chemical industry	570 million dollars	600 million dollars
Automobile industry	330 million dollars	485 million dollars
Total	1520 million dollars	1735 million dollars

About 4 billion dollars have been spent on the development of catalytic converters by U.S. firms. At the same time, in the USSR controversy has continued as to the desirability of using converters, which are fitted throughout the world to more than 100 million automobiles with appropriate systems, about half of the world's consumption of noble metals being consumed in their provision.

In the development of catalysts during the 1970s, attention was concentrated on the possibility of eliminating hydrocarbons and carbon monoxide from exhaust gases with their aid. To ensure the complete combustion of these impurities, the catalysts must operate in the presence of a slight excess of air in the so-called "lean" mixtures with the stoichiometric coefficient $\alpha = [O_2]/[\Sigma C_nH_m] = 1.0-1.05$. In "rich" mixtures ($\alpha < 1$), the degree of conversion of hydrocarbons and carbon monoxide is sharply reduced.

A similar study of the kinetics of the reduction of NO_x by carbon monoxide, carried out, in particular, at the Institute of Chemical Physics of the USSR Academy of Sciences[4] on platinum and rhodium catalysts, showed that the opposite behaviour is observed for reaction (4); complete conversion is ensured in "rich" mixtures with $\alpha < 1$, while with increase in the oxygen content in the mixture it falls sharply. Only within a narrow concentration range (near stoichiometry) is there a "window" in the vicinity of which it is possible to achieve with a high degree of completion both the oxidation of carbon monoxide and hydrocarbons and the reduction of nitric oxide. The width of the "window" has come to be characterised by the quantity Δ (Δ is the range of variation of the oxygen content in the products resulting from the mixture in which all three reactions can occur with a high degree of convesion). Data[5] for the width of the "window" for different catalysts are presented below:

Catalyst	Ru	Pd	Pd–Ru	Pt	Pt–Rh	Pt–Pd–Rh
Δ, %	0.08	0.1	0.13	0.20–0.26	0.32–0.4	0.44–0.5

As can be seen from these data, binary and ternary catalysts are more effective in the elimination of all impurities than monometallic catalysts. In practice Pt–Rh catalysts are most often employed. However, owing to the high cost of rhodium, attempts have been made to reduce its content, i.e. to create compositions made up of platinum and rhodium in which rhodium would continue to exhibit its promoting effect even though its amount has been reduced. It has been possible to obtain effective catalysts with the ratio Pt : Rh = 15 : 1.

The study of the mechanism of the NO + CO reaction by spectroscopic-kinetic methods *in situ* (during catalysis), carried out at the Institute of Chemical Physics of the USSR Academy of Sciences,[4,5] showed that CO_2 and NCO groups can be identified on the catalyst surface under the conditions of the catalytic reaction.

On the basis of these investigations, the following mechanism of the NO + CO reaction was proposed:

$$NO + M_1 \rightleftarrows M_1{-}NO,$$
$$CO + M_1 \rightleftarrows M_1{-}CO,$$
$$CO + M_2 \rightleftarrows M_2 - CO,$$
$$NO + M_2 \rightleftarrows M_2{-}NO,$$
$$M_2 + M_2{-}NO \rightarrow M_2{-}N + M_2{-}O,$$
$$M_2{-}N + M_2{-}CO \rightarrow M_2{-}NCO + M_2,$$
$$M_1 + M_2{-}NCO \rightleftarrows M_1{-}NCO + M_2,$$
$$M_1{-}NCO + M_1{-}NO \rightarrow M_1{-}CO + N_2 + M_1,$$
$$M_1{-}CO + M_2{-}O \rightarrow M_2{-}CO_2 + M_1,$$
$$M_2{-}CO_2 \rightarrow CO_2 + M_2,$$

where M_1 are metallic centres on which NO molecules are adsorbed in the undissociated form and M_2 are similar centres on which NO molecules are adsorbed in the dissociated form. The key intermediate species is in this instance apparently the isocyanate NCO which can be adsorbed both on the metal (2240 cm^{-1} IR band) and on the carrier (2260 cm^{-1} band). The NCO groups can diffuse from the metal to the carrier and back again. The decomposition of NCO results in the formation of N_2. In the steady (stationary) state, the concentration of NCO adsorbed on the carrier does not enter into the kinetic equation. However, the real process in catalytic after-burners is markedly non-stationary. In a non-stationary process it is in fact important to have reserves of NCO stored on the carrier, which diffuses to the active centres of the metal and ensures the continuous reduction of NO to N_2.

Catalysts ensuring the removal of all harmful impurities (CO, C_nH_m, and NO) are referred to as three-component catalysts (it would be more correct to call them three-pathway catalysts) or bifunctional catalysts. Their composition is as a rule more complex than that of the catalysts designed solely for oxidation. Furthermore, in automobiles fitted with catalytic converters there are special electronic devices regulating the composition of gases so that they are close to stoichiometry.

After a time, the efficiency of the catalyst falls. The principal causes of the deactivation of platinum and rhodium catalysts are as follows:

(1) sintering after prolonged operation whereupon the size of the platinum and rhodium single crystals increases from 10–50 to 1000–5000 Å.

(2) the formation of higher oxides in an oxidising atmosphere, for example of Rh_2O_3, which reacts with the carrier to form $RhAlO_3$;

(3) the separation of the catalyst into layers, which leads, in particular, to the concentration of rhodium in the surface layer;

(4) poisoning (Pb, S, Zn, and P poisons).

The most important factor in the USSR is de-activation as a result of poisoning by lead, which is present in ethylated petrol. Non-ethylated petrol is used only in several large cities (Moscow, Leningrad, Kiev, and Alma-Ata). However, even in these cities it is difficult to avoid filling car fuel tanks with ethylated petrol anywhere outside the cities and this results in the deposition of lead on the catalyst surface and puts the converter out of order.

As a result of much research carried out by a number of firms, it has been possible to reduce appreciably the content of noble metals in catalysts for the purification of exhaust gases by introducing various additives, in some cases up to 0.1–0.2 g. The following are the main stabilising additives: SiO_2, CeO_2, SnO_2, BaO, and Cr_2O_3, whose role is to prevent the sintering of metal particles, and also additives which provide oxygen (CeO_2, MoO_3, WO_3, etc.). It appears that additives of this type are especially important for the operation of the catalyst under non-stationary conditions. It has been shown at the Institute of Chemical Physics of the USSR Academy of Sciences[6] that, when the $Pt + V_2O_5$ system is used, it is possible to reduce appreciably the temperature of the onset of the oxidation of methane. Under these conditions, the non-equilibrium V_2O_5 oxide phase is produced and on it oxygen is rapidly transported to the hydrocarbon oxidation centres. Such systems are very important for initiating the operation of the catalyst at a low temperature. The composition of one of the catalysts used by the Ford Company is as follows: 19% Al_2O_3, 1.6% NiO, 0.7% CeO_2, 0.15 Pt, an 0.015% Rh. Here CeO_2 is apparently both a stabiliser and an oxygen supplying agent.

Silicate systems are usually employed as carriers in the catalyst: cordierite $Al_4Mg_2Si_5O_{18}$, mullite $3Al_2O_3.2SiO_2$, and spodumene $LiAl(SiO_3)_2$. Cordierite is most common. Aluminium oxide (corundum — α-Al_2O_3) is sometimes used directly without decomposition on a silicate support.

The ShPK-2, ShPAK-0,5, and other catalysts, developed at the Karpov Physicochemical Institute and the Institute of Organic Catalysis and Electrochemistry (IOCE) of the Academy of Sciences of the Kazakh SSR jointly with NAMI, are used in the Soviet Union. The active component of the catalyst is platinum and palladium deposited on Al_2O_3 spherical pellets thermostabilised by added silicon, calcium, lanthanum etc. oxides. Experimental-industrial batches of the catalysts are produced by the Redkinsk factory.

Catalysts on metallic block carriers with a honeycomb structure are also being developed. Work on catalysts of this group has been carried on at the IOKE of the Academy of Sciences of the Kazakh SSR. The production of laboratory batches of metalic block carriers has been initiated at this institute and methods for depositing the support on the walls of the block channels (to increase the specific surface) and of depositing the active component on the carriers prepared in this way have been developed.

At the Institute of Catalysis of the Siberian Division of the USSR Academy of Sciences, catalysts on ceramic block carriers (made of spodumene, cordierite, and silicon nitride) are being developed jointly with other organisations. The blocks have a high mechanical strength (resistance to wear) and a reduced hydrodynamic resistance.

Catalytic converters are being developed and are being tested in the USSR by the Central Institute of Motor Construction Engineering (for diesel engines) and by the Automobile Engine Research Institute (NAMI) for petrol engines. The tests are performed on engine stands, stands with revolving drums, and under operating conditions on automobiles themselves.

The mass production of catalytic converters in the USSR has not yet been initiated. Several years ago, an experiment was carried out in Moscow: 600 taxicabs were fitted with catalytic converters. The experiment failed completely; firstly, it was not possible to prevent the introduction of ethylated petrol into the fuel tanks, which resulted in the poisoning of the catalyst, and, secondly, fires were started because in a number of engines the ignition did not work properly. For this reason, the uncombusted fuel entered the after-burner, was ignited on the catalyst, spoilt the after-burner, and sometimes set the engine on fire as well.

Thus the necessary conditions for the successful operation of catalytic converters is a thoroughly tuned engine with properly functioning ignition and non-ethylated lead free petrol.

3. Diesel fuel

Despite the widely held view that the toxicity of the spent gases from diesel engines is low, the problem of the protection of the environment from this source of emission should apparently be assessed as at least comparable to the problem of the pollution of the atmosphere by the spent gases from carburettor (petrol) engines, and, as transport fleets are increasingly provided with diesel engines and the study of the composition of the products of the combustion of diesel fuel intensifies, the urgency of the problem of their detoxification is becoming increasingly more acute and self-evident. Indeed, the amount of waste comprising the incomplete combustion products for which norms have been specified—carbon monoxide and hydrocarbons—generated by diesel fuels is smaller by a factor of 5–10 than that generated by carburettor engines, while the amount of waste comprising nitrogen oxides is similar. However, diesel engines eject into the atmosphere considerable amounts (on average 0.3–0.5 g m^{-3}) of soot—disperse particles which contain biologically active and toxic components, among which there is a group of carcinogens (benzopyrene, fluoranthene, chrysene, etc.), aldehydes, sulphur, nitrogen-containing organic compounds, inorganic sulphur compounds, etc.[7]

Despite the ambiguity of the results obtained in the study of the emission of these compounds by engines of different types, the leading role of diesel engines in polluting the atmosphere by disperse particles is noteworthy. Thus, according to an estimate,[8] the contribution of diesel engines to the 24.6 million kg of disperse particles ejected annually into the atmosphere in Western Europe by automobile exhaust gases is 21.3 million kg. In addition to the enhanced biological activity and toxicity, the presence of suspended disperse particles in the atmosphere impairs visibility on motor roads, pollutes the regions adjoining the roads, etc. In estimating the overall balance in the pollution of the atmosphere by the exhaust gases from diesel engines, one should naturally take into account also the presence in the exhausts of components for which norms have been laid down—carbon monoxide and especially hydrocarbons. Finally, the increased emission by diesel engines of nitrogen oxides constitutes a serious danger to the environment and human health especially if one bears in mind the increased biological activity of carbon monoxide in the presence of nitric oxide. These considerations, combined with the well known tendency towards an increase in the fleet of diesel-engined motor cars, show that the purification of the exhaust gases from diesel engines constitutes a serious and extremely urgent problem whose solution would make it possible to improve significantly the ecological situation not only in sites with limited exchange of air—mine shafts, quarries, stores, ships' holds, etc.—but also in cities with intense motor traffic, where the fraction of automobiles and buses with engines of this type has been increasing steadily.

Neutralisation (conversion) in diesel engines can be achieved by catalytic oxidation, filtration, or a combination of both methods. In addition, the application of these processes to the diesel engine is complicated by a number of factors due to the specific features of the operation of the antitoxic devices in the exhaust tract of the diesel engine. Among them the following should be included:

the relatively low temperature of the spent gases, which usually does not exceed 300–400 °C even under supercharged conditions;

the presence in the gas stream of fairly high (0.2–0.6 vol.%) concentrations of sulphur oxide compounds (mainly sulphur dioxide) and nitric oxide (0.1–0.2 vol.%), which are comparable or actually higher than the concentration of carbon monoxide;

a very considerable (up to 0.5 g m^{-3}) content of disperse particles of diesel soot in a number of instances (when the quality of the tuning of the fuel injection is inadequate) supplemented by aerosols comprising uncombusted fuel;

an increased emission of the degradation products of motor fuels, including the additives introduced into the fuel (the loss of oil in diesel engines is about 0.5% of the consumption of the diesel fuel, which is approximately 1.5–2.0 times greater than in carburettor engines);

strict requirements as regards the resistance of the exhaust system in modern and especially turbocharged diesel engines (the pressure drop in the exhaust system is limited to 500 mm of water).

These features of the design and of the working process in diesel engines have a significant influence on oxidation catalytic processes as well as filtration processes and must be taken into account in selecting and assessing the components, especially catalysts, used to purify the exhaust gases from a diesel engine.

As regards the operating conditions of diesel engines in the USSR, sulphur creates the greatest problems. Here we may note that almost the entire petroleum extracted in the USSR contain considerable amounts of sulphur and our industry (as well as science) is concerned with the catalytic hydrodesulphurisation, which appreciably lags behind foreign countries. Admittedly, one should note that the sulphur dioxide emitted with fuel combustion products in diesel engines makes a relatively small contribution (1–3%) to the overall pollution of the atmosphere by sulphur dioxide (thermal electric power stations make the main contribution). However, the oxidation of sulphur dioxide on a catalyst results in the formation of the appreciably more toxic sulphur trioxide, whose reaction with Al_2O_3 converts the latter into the sulphate, which leads to rapid breakdown of the catalyst.

A large series of studies on the selection of active oxide catalysts for catalytic converters has been carried out at the Azizbekov Azerbaijan Petrochemical Institute.[9] Studies are also being prosecuted at the Institute of Catalysis of the Siberian Division of the USSR Academy of Sciences and at the Institute of Chemical Physics of the USSR Academy of Sciences. Sulphates leading to the breakdown of the catalyst are formed in almost all the oxide compositions. The development of oxide catalysts in Bulgaria has been reported.

It is noteworthy that the attempts to replace noble metals in converters in both petrol and diesel engines for the removal of harmful gases by a system comprising the oxides of transition metals or other elements have so far proved unsuccessful, mainly because of their being poisoned by the components of the exhaust gases and because of their low activity at low temperatures. The results in this field cannot nowadays be regarded as even hopeful to any extent.

In the USSR, catalytic converters for diesel engines are manufactured in small numbers using platinum and palladium catalysts (of the type ShPK and ShPAK). However, the Al_2O_3 forming part of their composition is rapidly converted into $Al_2(SO_4)_3$, which can be washed away by water on regeneration. After 2–3 regenerations, the converter becomes unsuitable. Despite their short lifetime, such converters are nevertheless used in highly gas-saturated closed spaces and in deep quarries.

There are certain prospects of being able to use aluminosilicates to create carriers with an increased resistance to sulphur oxides, but the choice of the optimum ratio of SiO_2 and Al_2O_3 makes it necessary to take into account, apart from the minimum capacity for conversion into sulphate, a number of other properties: strength, surface, resistance to water vapour, etc. It is possible to use other compounds, which do not interact with sulphur trioxide—phosphates, oxygen-free silicon compounds, etc.

The removal of soot is also a difficult problem. The planned standards for the emission of disperse soot particles are 0.16 g km^{-1} in 1989 and 0.12 g km^{-1} in 1992 for light automobiles and 0.6 g kW^{-1} h^{-1} in 1988 and 0.14 g kW^{-1} h^{-1} in 1994 for goods vehicles and buses with diesel engines.[10]

Taking into account the extremely high sensitivity of diesel engines to the resistance of the exhaust system and also the fairly strict requirements which must be met by the weight and size characteristics of the antitoxic devices, the creation of soot filtering systems for the latter presupposes the solution of a set of problems, including those concerning materials and catalysis:

(1) the choice of a material and of a technology for the construction of a filter from it subject to the permissible resistances, temperature, resistance to the action of the components of the spent gases, strength characteristics, porous structure, soot trapping efficiency, etc.;

(2) the search for catalysts capable of reducing by 200–300 °C the temperature of the combustion of the soot accumulated by the filter, ensuring thereby the regenation of the filter by means of the heat of the spent gases;

(3) the development of filter-catalytic devices ensuring in a single space the after-burning of the incomplete combustion products as well as the trapping of the soot.

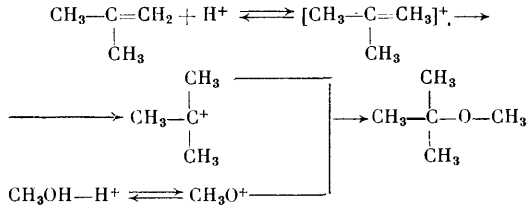
Apart from the problem of creating a filtering material, it is in this instance necessary to solve the problem of depositing a support (meeting the requirements as regards the pressure drop on the filter) and of the regulation of the soot regeneration (combustion) process in order to eliminate the superheating of the catalyst. It is also necessary to develop methods for increasing the useful lifetime of the catalyst and the filter in which provision is made for protection against the ash products of the combustion of soot.

4. Alternative fuels

Tetraethyl-lead, used as the antiknock additive, is a highly toxic component of petrol. One of the versions of the causes of the destruction of the Roman Empire is the poisoning by lead of its inhabitants who used water from lead pipes. This led to apathy of the inhabitants and the consequent destruction of the empire under the onslaught of barbarians. Lead acts on the human nervous system and is not eliminated from the organism. Furthermore, lead compounds have a destructive effect on nature in territories adjoining motor highways.

There exist two main ways of creating metal-free high-octane fuels: (1) by increasing the degree of catalytic processing of the products of the primary distillation of petroleum: cracking, reforming, etc.; (2) by using metal-free antiknock additives. In the USA, studies are being prosecuted mainly via the first route, whilst in Europe the second route is followed. Certain firms (for example, ENI—Italy) have carried out a wide scale screening of newly synthesised organic compounds as antiknock agents. In the USSR, studies on such a scale have not been performed.

The most widely used antiknock agent in the West is t-butyl methyl ether (TBME). It is synthesised using acid catalysts:



The side reactions accompanying the synthesis of TBME are as follows:

$$\text{iso-}C_4H_8 + H_2O \rightleftharpoons (CH_3)_3COH,$$
$$2CH_3OH \rightleftharpoons H_2O + CH_3OCH_3,$$
$$2\text{iso-}C_4H_8 \rightleftharpoons C_8H_{18} \longrightarrow \text{polyisobutenes},$$
$$CH_3OH + \text{iso-}C_4H_8 \rightleftharpoons CH_3OC_4H_9.$$

Catalysts of the synthesis of TBME include gel cation exchangers (KQ-2, FPP), heteropolyacids ($H_3PW_{12}O_{40}$/activated charcoal), H-acids [sulphonic acids, H_2SO_4, HCl, and HNO_3 (70–150 °C)], zeolites, Al_2O_3, $Al_2O_3.SiO_2$, and P_2O_5/Al_2O_3 (60–250 °C). In the presence of some of them, it is possible to achieve a selectivity close to 100%. Methods for the continuous catalytic synthesis of TBME using zeolites (Tseokar-2) or toluene-*p*-sulphonic acid have been developed at the Institute of Chemical Physics and at the Institute of Organic Chemistry at the USSR Academy of Sciences. Methods for the synthesis of TBME are being developed at the Institute of the Ministry of Petrochemical Industry. However, the large scale manufacture of TBME in the USSR is not planned to start until 2000–2005.

The decrease of the octane number of petrol, induced by the decrease in the content of lead and aromatic hydrocarbons, is fully compensated by the addition of 5–15% of TBME. The use of TBME also constitutes a very rational procedure for the indirect introduction of methanol into petrol. The problems of phase separation, occurring in petrol–methanol mixtures, do not then arise.

The manufacture of TBME in the USSR requires an increase in the manufacture of methanol. This can be achieved by using a new productive method of synthesis of methanol developed at the Institute of Petrochemical Synthesis of the USSR Academy of Sciences.[12]

Using a procedure similar to that for the synthesis of TBME, it is possible to obtain from tertiary C_5 olefins the tertiary methyl pentyl ether, which has certain advantages over TBME as an antiknock agent.

A disadvantage of such antiknock agents is the presence of oxygen atoms in their molecules. The combustion of the ethers results in the formation of toxic aldehydes.[13,14] In the norms for the emission of toxic products, aldehydes are so far in no way regulated and this also applies to carcinogens of the type of benzopyrene. This problem requires special study.

We are unable to consider here the problems of the toxicity of all types of automobile fuels. We may note that, whereas from the standpoint of economics this problem continues to be discussed, the systematic studies on fuels from the standpoint of ecology are clearly inadequate.

Studies on the use of light hydrocarbons as a petrol-substitute fuel have been expanded in recent years in many countries including the USSR. Thus an attempt has been made to use

propane–butane mixtures as a fuel. In recent press publications, it has been reported that the drivers and passengers of automobiles operating on the propane–butane mixture have been poisoned. This can apparently be accounted for by design faults and not by the higher toxicity of the combustion products. On combustion of the propane–butane fuel, the exhaust gases contain much less carbon monoxide and hydrocarbons, but the amount of NO_x is approximately the same as in the combustion of petrol.[13] However, it is hardly possible to supply the automobile fleet by large amounts of the propane–butane fuel. The situation is different as regards methane, the potential amount of which in the USSR is very great. At the present time methane is regarded as the No. 1 alternative fuel.

The combustion of light hydrocarbons in internal combustion engines is being investigated at the Institute of Chemical Physics of the USSR Academy of Sciences. It has been found that the emission of toxic products can be reduced by a suitable organisation of the combustion process in the engine.

The study of the ignition limits of ballast-containing hydrocarbon mixtures (containing combustion products and inert gases) demonstrated a distinct shift of the ignition region for hydrocarbons heavier than propane to richer compositions, while the ignition region for the only hydrocarbon lighter than oxygen (methane) was displaced towards leaner mixtures (although their composition is closer to stoichiometry). The study of the operation of a one-cylinder petrol engine with low filling (in reality the engine operates most of the time partial load conditions with low filling) also showed that stable operation with low filling (minimum scatter in pressure diagrams and the absence of missing in ignition) is recorded in the region of rich mixtures. These experiments indicate the influence of diffusion-thermal phenomena (roughly speaking the "selective" diffusion of the lighter, deficient mixture component) on the combustion process and that attempts to shift the range of stable operation to leaner composition in engines operating on petrol by increasing the energy of the discharge are doubtful. Studies prosecuted at the Institute of Chemical Physics of the USSR Academy of Sciences, using a discharge with additional charging, with plasma ignition, and using a "magnetic" spark plug led to the same result. Furthermore, the energy required to ignite rich propane mixtures is much lower than that required for the ignition of lean mixtures. Conversely, the energy is minimal for methane in lean mixtures. All this indicates the special role of methane as an engine fule. Methane has an octane number in excess of 100 and can be used for higher compressions (12–13 and above) and smaller cylinder diameters.

The possibility of the operation of engines on methane in lean mixtures eliminates the problem of the ignition of carbon monoxide and hydrocarbons. The problem of NO_x naturally remains. An important problem is the filling of cylinders and the storage of methane. The storage of methane in the compressed form in cylinders requires a large capital expenditure associated with the conversion of petrol filling stations into gas filling compressor stations. The use of compressed methane naturally limits the transportation distance. Experiments on the possibility of filling with methane cylinders containing an adsorbent—silica gel or activated charcoal—have been carried out at the Institute of Chemical Physics of the USSR Academy of Sciences.

The problem of the use of methane in internal combustion engines involves a number of questions associated directly with the engine. It is necessary to create an engine which operates on methane at a high compression. For this reason, it is impossible to employ the usual petrol engines. The use of methane at a low compression (7–8) is pointless. One can be satisfied with an intermediate version of the engine in which the compression is reduced from 12–13 to 7–8. It is possible to create a gas-diesel cycle at high compressions (>15–17) with injection of an igniting dose of fuel with a high octane number.

The opposite process is one involving the pre-chamber ignition of methane (a single fuel engine containing an injection apparatus only in the ignition system). It is also possible to introduce petrol and even heavy fuels (for example, with post-injection into a very lean methane–air mixture (for a coefficient of the excess of air of 5 and above, i.e. for a low consumption of methane).

Engines with precombustion chamber ignition, constructed at the Gorky Automobile Factory on the basis of designs developed at the Institute of Chemical Physics of the USSR Academy of Sciences, are used in the Volga motor cars. They achieve an appreciable reduction of the emission of carbon monoxide and hydrocarbons. For the wide scale introduction of high-octane fuels and catalytic converters, the manufacture of automobiles with precombustion chamber ignition may be a palliative solution. For this purpose, it is essential to continue the work at the Gorky Automobile Factory and the Institute of Chemical Physics of the USSR Academy of Sciences.

Hydrogen is an ecologically clean fuel. It can ignite over a wide range of concentrations and burns in very lean mixtures in the presence of a large excess of air. The maximum temperature developed in the engine and determining the formation of nitrogen oxides is therefore much lower than in the combustion of petrol and the oxides NO_x are hardly formed.[14] The exhaust gases contain no hydrocarbons and carbon monoxide. The only combustion product is water vapour.

The problem of hydrogen as a fuel for internal combustion engines has been widely discussed. At the end of the 1988, an international conference on hydrogen power engineering was held in Moscow.[15] At the present time, the remaining problem is the high cost of hydrogen and the difficulty of storing it. However, in the XXIst century the cost of hydrogen will be such that its use will become justified not only from the ecological but also from the economic point of view, especially bearing in mind the high cost of cleaning the environment when other fuels are employed. Together with the gasification of coal, the promising processes for the preparation of hydrogen are apparently those where hydrogen is produced from the biomass.[15] An interesting method is the preparation of hydrogen by decomposing hydrogen sulphide. Before the industrial development of such a process, one should abandon the development of the Astrakhan deposit of natural gas and other hydrogen-containing gases.

Hydrogen for use in internal combustion engines may be stored in compressed and liquefied forms and as part of hydrides. At the present time, liquid hydrogen is most promising, but there is as yet no final technical and economical solution.

In the USSR, the problem of using hydrogen as a fuel for internal combustion engines is a major concern of the Institute of the Problems of Machine Construction of the Academy of Sciences of the Ukrainian SSR (Kharkov). The involvement of specialists in catalysis in the problem of hydrogen power engineering is clearly inadequate.

A version of the use of hydrogen in internal combustion engines may involve the employment of fuels generating hydrogen on decomposition. For example, methanol produces the $CO+2H_2$ mixture on catalytic decomposition. This mixture burns at high rates for very lean compositions (the diffusion-thermal phenomena in hydrogen are especially pronounced for lean compositions) and for

this reason this version is also ecologically interesting. A catalytic reactor for the decomposition of methanol may be placed before the combustion chamber and can be heated by the combustion products.

An alternative to the proposed variants may be the abandonment of the automobile as a means of transport in the XXIst century.

For the successful prosecution of the relevant studies in the USSR, the following steps are necessary:

1. The creation of a qualifying commission made up of scientists and engineers of the USSR Academy of Sciences and government departments for the systematic examination of the prospects for the manufacture of automobile fuels from the standpint of ecology.

2. An appreciable expansion of theoretical studies at the Institutes of the USSR Academy of Sciences on catalytic conversion, particular attention being devoted to the mathematical modelling of non-stationary catalytic processes in engines, the study of elementary processes in the conversion of carbon monoxide, hydrocarbons, nitrogen oxides, and ammonia by physicochemical methods *in situ*, and the development of conversion processes in the presence of oxygen. It is necesary to devise a theory of the effect of additives increasing the efficiency of noble metals as oxidation catalysts.

3. The development of longer-lived catalysts resistant to the action of poisoning impurities (sulphur dioxide, lead, etc.) and further studies designed to reduce the content of noble metals in catalysts and their complete or partial replacement by oxide systems whilst retaining the required level of efficiency and useful life.

4. The development of catalyst carriers (monolithic and granular) with a required level of hydrodynamic, mechanical, and physico-chemical characteristics and resistant to the action of catalytic poisons. Their production in the USSR should be initiated.

5. The development of methods for the regeneration of catalysts containing noble metals.

6. The organisation of the industrial manufacture of catalysts to provide catalytic converters for petrol and diesel engines.

7. The improvement of the design of internal combustion engines and the introduction of oxygen sensors and electronic systems for the control and regulation of fuel compositions.

8. The provision of the promoter of catalysts with the necessary amount of compounds of precious metals. The limitations to the use of platinum should be removed.

9. The development of methods for the removal of disperse particles from exhaust gases, including catalytic methods for the after-burning of soot on filter elements.

10. An increase in the number and accessibility of tests of catalytic converters on automachines, including comparative tests; the provision of foreign currency for the purchase of the best foreign designs.

11. The creation of a program of toxicological tests on the products of the combustion of various fuels, including oxygen-containing fuels.

12. The achievement of the strict fulfilment of the standard norms of the UNO and the USSR as regards the emission of toxic substances. Economic measures stimulating the use of antitoxic devices (for example, penalities for harmful emissions, and conversely, a decrease in the price of automobiles fitted with a catalytic converter) should be introduced. The question of the introduction of norms for the emission of aldehydes and carcinogenic hydrocarbons should be raised.

13. The submission to the government of the USSR of the proposal to accelerate the large scale manufacture of methanol and TBME.

14. The organisation of the mass screening of organic compounds for the antiknock properties in order to replace tetraethyl-lead in petrol.

15. The expansion of theoretical studies on the combustion of various fuels in automobile engines. A well equipped centre for problems of combustion should be created.

16. The examination of the problem of the need to create a high-compression methane engine.

17. The expansion of the manufacture of engines with precombustion chamber flame ignition for the rapid solution of the problem of reducing harmful exhausts in the immediate future.

18. Theoretical and experimental study of the use of adsorbents to concentrate methane in cylinders.

19. An appreciable intensification of research into the combustion of hydrogen in engines and on catalytic, photochemical, electrochemical, thermal, and biological methods for the production of hydrogen and its storage in a liquefied or bound form. The prospects for using hydrogen in internal combustion engines should be widely discussed and the participation of catalytic laboratories in the solution of this problem should be increased.

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Translated from *Uspekhi Khimii* **60** 649–652 (1991)

Development and introduction of catalytic methods for the detoxification of industrial and automobile transport waste emissions

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New technologies based on the use of chemical catalysis should play an important role in the solution of acute ecological problems. Firstly, these are the catalytic technologies for the detoxification of the largest amounts of waste emissions from industry and automobile transport. Secondly, these are new technologies, producing little waste, for the manufacture of chemical products and based on the use of more selective catalysts.

The catalytic technologies for the detoxification of gases and liquid waste from various branches of industry and automobile transport, developed by the "Katalizator" Interbranch Scientific-Technical Complex, will be examined below. Their wide scale employment in the existing undertakings and in transport could even today improve significantly the ecological situation in our country.,

1. Elimination of sulphur dioxide from the waste gases in non-ferrous metallurgy

The emission of sulphur dioxide by non-ferrous metallurgical industries is one of the principal sources of the formation of acid rain. The "Katalizator" Scientific-Technical Complex is developing, jointly with the organisations of Ministry of Metallurgy of the USSR, several technologies for the removal of sulphur dioxide from such gaseous emissions with the simultaneous manufacture of valuable products—sulphuric acid or elemental sulphur. Some of these developments are significantly superior to those abroad as regards the level of their sophistication.

A non-stationary method (the flow reversal process) for the removal of sulphur dioxide with the simultaneous manufacture of sulphuric acid has been developed. This new technology is suitable for the majority of regions in the USSR. It is applied on an industrial scale in a number of factories. With the aid of this technology, more than 300 000 tonnes of sulphuric acid annually is already being produced† and is finding useful applications in the national economy. Licences for the flow reversal process for the oxidation of sulphur dioxide have been taken up by firms in Japan and Bulgaria.

Catalysts and processes for the conversion of sulphur dioxide into sulphur are being developed for the detoxification of the waste gases from the Noril'sk Mining-Metallurgical Industrial Unit. The conversion of sulphur dioxide into sulphuric acid under the conditions of the Noril'sk establishment is not appropriate because of the difficulties in transporting it away. Sulphur can be obtained by the partial reduction of sulphur dioxide to hydrogen sulphide, after which the catalytic Claus process is carried out. This process can be achieved in the presence of both heterogeneous and homogeneous catalysts. Both heterogeneous and homogeneous catalysts of the Claus process, specially developed for the Noril'sk Mining-Metallurgical Industrial Unit, have already been tested experimentally in the latter. The characteristic features of the new heterogeneous catalyst are improved activity (as a result of this, it is possible to reduce significantly the size of the catalytic apparatus) and also resistance to the oxygen present in the waste gases from the unit. The manufacture of a large batch of this catalyst for experimental-industrial tests is being prepared.

A method for the removal of sulphur dioxide from waste gases is being developed on the basis of the new homogeneous catalyst—the so called LES‡ (liquid-phase elimination of sulphur) process. At the present time this method is being tested on a large scale experimental apparatus in Noril'sk.

2. Elimination of nitrogen oxides from the waste gases from chemical industries and thermal electric power stations

A new catalytic method is being developed for the reduction of nitrogen oxides by ammonia under artificially created non-stationary conditions (a variant of the flow reversal process). An experimental-industrial apparatus with an output of 10 000 $m^3\ h^{-1}$ has been constructed and has been working successfully.

A variant of the flow reversal process for the selective catalytic reduction by ammonia of nitrogen oxides in the waste gases from thermal electric power stations is being developed.

3. Elimination of hydrogen sulphide from natural gas

The natural gas from a number of large deposits in the USSR contains considerable admixtures of hydrogen sulphide. The method for its elimination used at present is fairly complex. It is based on the partial oxidation of hydrogen sulphide to sulphur oxides followed by the multistage Claus process. The "Katalizator" Interbranch Scientific-Technical Complex has been developing jointly with the organisations of the Ministry of the Gas Industry of the USSR a fundamentally new single-stage purification technology involving the catalytic oxidation of hydrogen sulphide to elemental sulphur. The method has passed an experimental test in the detoxification of the so called blow-off gases from bore holes.

4. Elimination of carbon monoxide and organic substances from industrial waste gases

An appreciable amount of carbon monoxide and a wide variety of organic compounds is present in the waste gases from ferrous metallurgical and chemical industries. Harmful organic substances

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are also present in the emissions from a number of other undertakings employing solvents, varnishes, etc.

In order to achieve the detoxification of such emissions, the "Katalizator" Scientific-Technical Complex has proposed several technologies based on catalytic extensive oxidation reactions. The usefulness of a particular technology is determined by the nature and concentration of harmful impurities, the degree of saturation of the emission with dust, etc. For high concentrations of the substances being oxidised, one can employ the oxidation method in additional reactors with a stationary catalyst bed. At lower concentrations (down to 0.5–0.8 g m^{-3}), the flow reversal process is effective. This new energy-saving method has already been introduced in seven§ undertakings in different cities. At still lower concentrations, it is possible to use the adsorption-catalytic method. Finally, the method involving oxidation in a fluidised catalyst bed is promising for the detoxification of dust–gas mixtures. In particular, studies are being prosecuted on the introduction of this method for the purification of gaseous emissions from the Coke-Chemical Industry and plants for the dry quenching of coke.

5. Catalytic combustion of liquid organic waste

A method has been developed for the combustion of liquid organic waste in compact reactors with a fluidised catalyst bed (catalytic heat generators). The procedure makes it possible to burn the waste at comparatively low tempereatures, i.e. under conditions which rule out the formation of toxic nitrogen oxides, and at the same time it permits the utilisation of the heat evolved.

6. A catalytic method for the detoxification of waste water

This technology is also based on the use of catalytic heat generators. It has passed an experimental-industrial test and is applicable to the purification of salt-free waste waters containing organic substances at concentrations sufficient to vaporise water by the heat of their combustion.

A similar technology is being developed also for the detoxification of the solid waste present as admixtures in waste waters.

7. Block catalysts for the purification of the exhaust gases from internal combustion petrol engines

The exhaust gases from automobile transport constitute one of the main sources of the pollution of the atmosphere by carbon and nitrogen oxides. Specimens of block and granulated catalysts of different kinds have been produced for the elimination of these oxides from the exhaust gases. Experimental tests of catalysts based on metallic blocks and alumina grains have been carried out with positive results.

The data presented below concerning the catalytic technologies for the detoxification of the gaseous and liquid emissions from industry and automobile transport, being developed at the "Katalizator" Interbranch Scientific-Technical Complex, are summarised in Table 1, which also indicates the level (i.e. the degree of completion) of each development. About half of them have been introduced into industry or are at the stage of experimental-industrial tests.

Table 1. Catalytic technologies for the detoxification of the waste emissions from industry and automobile transport developed at the "Katalizator" Interbranch Scientific-Technical Complex.

Type of pollutant	Source of pollution	Type of development	Level of development
Sulphur dioxide	Waste gases from metallurgical and chemical industries; natural gases; concomitant gases in petroleum processes; gaseous emissions from heat and power generating plant	Non-stationary method for the processing of sulphur oxides with formation of sulphuric acid	Industrial apparatus
		Liquid-phase purification method with formation of commercial sulphur	Experimental-industrial apparatus
		New catalysts of the Claus process	Experimental apparatus
		Claus method in a non-stationary regime	Research stage
		Catalytic procedure for the purification of waste gases from the Claus process	Experimental apparatus
Hydrogen sulphide	Waste gases from metallurgical and chemical industries; concomitant gases in petroleum processing	Liquid-phase purification method with formation of commercial sulphur	Experimental-industrial apparatus
		New catalysts of the Claus process	Experimental apparatus
		Claus method in a non-stationary regime	Research stage
		Catalytic procedure for the purification of waste gases in the Claus process	Experimental apparatus
		Plants for the detoxification in a fluidised bed of the hydrogen sulphide-containing blow-off gases from bore holes	Experimental apparatus
Nitrogen oxides	Technological gases and gaseous emissions from industrial undertakings; spent gases from internal combustion engines; gaseous emissions from heat and power generating plant	Non-stationary purification method	Experimental-industrial apparatus
		Development of block catalysts for converters	Experimental-industrial apparatus
		Development of granulated catalysts for converters	Experimental-industrial apparatus
		Method of involving selective catalytic reduction by ammonia	Research stage
Carbon monoxide	Technological gases and gaseous emissions from industrial undertakings; spent gases from internal combustion engines	Non-stationary purification method	Experimental-industrial apparatus
		A fluidised bed catalytic purification method	Experimental apparatus
		Adsorption-catalytic purification method	Experimental-industrial apparatus
		Development of block catalysts for converters	Experimental apparatus
Organic compounds	Technological gases and gaseous emissions from industrial undertakings; waste water; products of the incomplete combustion of organic fuels	Non-stationary purification method	Industrial apparatus
		A fluidised bed catalytic purification method	Experimental apparatus
		Detoxification plant used on catalytic heat generators	Experimental-industrial apparatus
		The use of mixed catalytic air heaters for combustion	Experimental-industrial apparatus

However, the rate of introduction of the new developments is clearly unsatisfactory. They have been applied in a comparatively small number of undertakings and have not so far led to a

§ By February, 1989.

significant alteration of the ecological situation in our country. The main reason for this unsatisfactory situation is inadequate interest in industrial undertakings in measures for the protection of nature. In my view, there is only one solution to the problem which has arisen: the universal introduction of fines for exceeding the level of harmful emissions above the permitted limit. A reasonable approach is necessary both to the selection of the initial magnitude of the fines and to the dynamics of their increase as a function of time. Both these parameters must be chosen so that industrial undertakings are encouraged to introduce more rapidly nature-protecting technologies without going at the same time beyond the limits of realistic possibilities.

From statements made by the leaders of the State commission on Nature in the USSR, we known that the inevitable introduction of fines is expected at the beginning of the next five year plan and that proposals for the appropriate resolutions are being prepared. They suggest that it would be right to publish these proposals as quickly as possible, so that they can be discussed in good time and also to make sure that workers of the industrial undertakings and in transport should be convinced of the reality of the coming fines.

Translated from *Uspekhi Khimii* **60** 653–658 (1991)

Ecological aspects of the production and consumption of hydrogen

K N Semenenko
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The world annual production of hydrogen is about 50–60 million tonnes, including that of the USSR which is about 6 million tonnes. Natural gas is the major raw material for the production of commercial hydrogen; the amount of hydrogen obtained by electrochemical methods is not greater than 1–2% of the total.

Virtually all hydrogen produced is consumed within the chemical industry, in particular for the production of ammonia and nitrogeneous fertilisers. In the decades ahead, it is expected that not only will hydrogen production increase (to 80–100 million tonnes annually), but also the structure of its consumption will change. It is also predicted that the use of hydrogen in the national economy will increase in an effort to create ecologically clean power generation and fuel technology for transportation facilities, to increase substantially the efficiency of oil refining and to use coal as the raw material for the production of synthetic fuel. Even nowadays, a small admixture of hydrogen to motor fuels would assist in overcoming a number of regional environmental problems, primarily those of increasing pollution of the atmosphere by carbon monoxide and carcinogenic products from the combustion of organic fuels, prevalent in large cities and opencast mines, which produce ore, coal, and other minerals.

Hydrogen is assuming special importance in low-volume high-technology branches of industry, such as electronic and pharmaceutical, in the production of high-purity metals and alloys, composite materials, chemically highly active substances, catalysts, and the like.

In the mid-1970's, the possibilities of the widespread use of hydrogen in the national economy as an alternative fuel or energy carrier were considered in the context of the so-called "energy crisis". At that time, however, various approaches to energy problems, based on the concept of hydrogen energy system, despite its apparent logic and attraction, were not supported by the necessary volume of research and development work. What is more, in engineering and economical respects the above approaches lost the competition with alternative ideas for the development of power engineering complexes based on high-performance energy-saving technologies.

At present, owing to the worldwide deterioration of the ecological situation, hydrogen is again actively considered as an alternative fuel and hopes are being placed on it. This feeling was expressed by the US participant at the 7th International Conference on Hydrogen Energy Systems, held in Moscow in October 1988. The use of hydrogen "gives humanity a unique change to survive in the world, rescued from ecological and social disasters", he said in his concluding remarks.

It is worth quoting some figures which illustrate how acute is the ecological problem associated with the combustion of organic fuel. In recent years, the industrial emission of carbon dioxide has been in excess of 5 billion tonnes annually, while that of carbon monoxide was in the range of 100–200 million tonnes annually. The emissions increased by a factor of 3.5 compared with their level in the 1950's and the tendency to increase is continuing: by the year 2000, the amount of carbon dioxide entering the atmosphere will rise to 6.0–6.5 billion tonnes annually, whilst that of carbon monoxide will rise to 250–300 million tonnes annually. Motor transport is responsible for up to 20% of CO_2 and (depending on the region) for 60–90% of CO emissions. For example, during the period 1985–1988, 800 000 trucks and diesel buses, which formed part of the Moscow fleet, ejected into the atmosphere about 200–250 thousand tonnes of carbon monoxide annually, excluding carcinogenic smoke resulting from incomplete combustion and pyrolysis of organic fuels.

However, in order to pave the way for hydrogen energy systems, including ecologically clear transport, we must solve a number of complex technical problems, relating to chemistry and to hydrogen technology, or at least in the next few years get this process going.

The first problem is due to the fact that hydrogen is currently too expensive as a fuel and is produced in amounts that are too small to satisfy the demand for it in the new branches of the national economy, which include not only power generation, but also chemical technology and materials science applications mentioned earlier.

Furthermore, current production of hydrogen from natural gas is itself not ecologically clean and not only leads to the consumption of nonrenewable resources of this valuable raw material, but is also accompanied by the generation of a considerable amount of carbon dioxide as a by-product. In the USSR alone, the emission of carbon dioxide into the atmosphere caused by hydrogen production, is about 18–20 million tonnes annually.

In view of this, improvement of the existing processes for electrochemical production of hydrogen by the electrolysis of water and water vapour is acquiring paramount importance along with the reduction in the associated energy consumption which may be achieved through the use of radically new materials and nonconventional chemical processes, primarily those based on renewable energy sources, such as solar energy, wind power, geothermal and hydrothermal processes, etc.

In the late 1970's a concept was promoted which is currently acquiring practical importance, namely that not only water and

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The world annual production of hydrogen is about 50–60 million tonnes, including that of the USSR which is about 6 million tonnes. Natural gas is the major raw material for the production of commercial hydrogen; the amount of hydrogen obtained by electrochemical methods is not greater than 1–2% of the total.

Virtually all hydrogen produced is consumed within the chemical industry, in particular for the production of ammonia and nitrogeneous fertilisers. In the decades ahead, it is expected that not only will hydrogen production increase (to 80–100 million tonnes annually), but also the structure of its consumption will change. It is also predicted that the use of hydrogen in the national economy will increase in an effort to create ecologically clean power generation and fuel technology for transportation facilities, to increase substantially the efficiency of oil refining and to use coal as the raw material for the production of synthetic fuel. Even nowadays, a small admixture of hydrogen to motor fuels would assist in overcoming a number of regional environmental problems, primarily those of increasing pollution of the atmosphere by carbon monoxide and carcinogenic products from the combustion of organic fuels, prevalent in large cities and opencast mines, which produce ore, coal, and other minerals.

Hydrogen is assuming special importance in low-volume high-technology branches of industry, such as electronic and pharmaceutical, in the production of high-purity metals and alloys, composite materials, chemically highly active substances, catalysts, and the like.

In the mid-1970's, the possibilities of the widespread use of hydrogen in the national economy as an alternative fuel or energy carrier were considered in the context of the so-called "energy crisis". At that time, however, various approaches to energy problems, based on the concept of hydrogen energy system, despite its apparent logic and attraction, were not supported by the necessary volume of research and development work. What is more, in engineering and economical respects the above approaches lost the competition with alternative ideas for the development of power engineering complexes based on high-performance energy-saving technologies.

At present, owing to the worldwide deterioration of the ecological situation, hydrogen is again actively considered as an alternative fuel and hopes are being placed on it. This feeling was expressed by the US participant at the 7th International Conference on Hydrogen Energy Systems, held in Moscow in October 1988. The use of hydrogen "gives humanity a unique change to survive in the world, rescued from ecological and social disasters", he said in his concluding remarks.

It is worth quoting some figures which illustrate how acute is the ecological problem associated with the combustion of organic fuel. In recent years, the industrial emission of carbon dioxide has been in excess of 5 billion tonnes annually, while that of carbon monoxide was in the range of 100–200 million tonnes annually. The emissions increased by a factor of 3.5 compared with their level in the 1950's and the tendency to increase is continuing: by the year 2000, the amount of carbon dioxide entering the atmosphere will rise to 6.0–6.5 billion tonnes annually, whilst that of carbon monoxide will rise to 250–300 million tonnes annually. Motor transport is responsible for up to 20% of CO_2 and (depending on the region) for 60–90% of CO emissions. For example, during the period 1985–1988, 800 000 trucks and diesel buses, which formed part of the Moscow fleet, ejected into the atmosphere about 200–250 thousand tonnes of carbon monoxide annually, excluding carcinogenic smoke resulting from incomplete combustion and pyrolysis of organic fuels.

However, in order to pave the way for hydrogen energy systems, including ecologically clear transport, we must solve a number of complex technical problems, relating to chemistry and to hydrogen technology, or at least in the next few years get this process going.

The first problem is due to the fact that hydrogen is currently too expensive as a fuel and is produced in amounts that are too small to satisfy the demand for it in the new branches of the national economy, which include not only power generation, but also chemical technology and materials science applications mentioned earlier.

Furthermore, current production of hydrogen from natural gas is itself not ecologically clean and not only leads to the consumption of nonrenewable resources of this valuable raw material, but is also accompanied by the generation of a considerable amount of carbon dioxide as a by-product. In the USSR alone, the emission of carbon dioxide into the atmosphere caused by hydrogen production, is about 18–20 million tonnes annually.

In view of this, improvement of the existing processes for electrochemical production of hydrogen by the electrolysis of water and water vapour is acquiring paramount importance along with the reduction in the associated energy consumption which may be achieved through the use of radically new materials and nonconventional chemical processes, primarily those based on renewable energy sources, such as solar energy, wind power, geothermal and hydrothermal processes, etc.

In the late 1970's a concept was promoted which is currently acquiring practical importance, namely that not only water and

water vapour can be used as raw materials for the production of hydrogen, but also hydrogen sulphide, at first glance an exotic chemical compound. Its natural resources are very large and may in principle serve as the basis for the development of industrial technologies. A solution to this scientific and technological problem would increase the availability of raw materials for hydrogen energy systems and hydrogen technology. In actual fact, the above concept has more general ecological and economical character, since in the first place it involves purification of natural hydrocarbon raw materials from highly toxic hydrogen sulphide and the use of the latter in the production of hydrogen and such a valuable chemical product as free sulphur.

Another problem with hydrogen energy systems is that, even with abundant cheap fuels or energy carriers, any branch of power generation (including that based on hydrogen) will flourish only if facilities are available for the effective use of chemical energy contained in the fuel and its conversion into electrical energy, thermal energy, etc.

For hydrogen, considering its unique physicochemical properties, such as calorific value which exceeds that of organic fuels by a factor of 3.5 and its low activation energy barrier with respect to catalytic oxidation, one can regard electrochemical power generators, which have 2–2.5 times greater efficiency than heat engines, as such facilities.

However, as opposed to heat engines which can in principle run on 'dirty' commercial hydrogen containing carbon oxides, water vapour, hydrocarbons and other impurities, electrochemical power generators are "capricious" and can use only high-purity hydrogen with no contaminants, which cause poisoning of catalytic contacts and reduce the efficiency of electrochemical oxidation. The above-mentioned high-technology branches both of chemical industry and of materials science place equally stringent requirements upon the purity of hydrogen.

Therefore, industrial hydrogen technology that would be appropriate for hydrogen energy systems would consist not only of ecologically clean technology for hydrogen production, based on the renewable sources of initial materials and energy, but would also involve a technology for the separation of industrial gas mixtures containing hydrogen and a high degree of purification of the latter that would reduce the content of impurities to $10^{-3}-10^{-4}$ vol.%.

At present, the most effective procedure for the production of high-purity hydrogen from industrial gases involves their preliminary separation and enrichment with hydrogen as the main component followed by the use of membrane technology, with palladium alloys acting as the materials for the selective filtration of hydrogen.

As long as the use of high-purity hydrogen is confined to certain special branches of metallurgy and the production of materials for the microelectronics and pharmaceutical industries, and does not exceed several thousand tonnes annually, this need may well be met on the basis of the existing technology. However, the situation will drastically change when hydrogen will be looked at as a basis for the creation of ecologically clean power systems for the 21st century. In this case the required annual production of low-cost high-purity hydrogen will amount to hundreds of thousands rather than thousands of tonnes. This task cannot be fulfilled with filters, using palladium alloys, simply because the required amount of palladium is not and will never be available. Alternative materials are required, which would act in a way similar to palladium alloys but would essentially differ in cost and suitability for mass production and consumption.

The second of the above problems is formulated in much the same manner, i.e. the creation of catalysts for the oxidation of hydrogen in electrochemical power generators. Materials containing platinum and platinum group metals serve as catalysts in contemporary fuel cells which are widely used in space and other special applications†. The consumption of platinum for each fuel cell with an output of 1 kW is about 100–200 mg. Even if this amount were to come down by a factor of 100 through improvements in the technology of production of electrode materials, the consumption of platinum metals required to furnish a fleet of, say, 50 million vehicles with an average power of 100–150 kW, woud nevertheless amount to approximately 500–600 tonnes, which is substantially more than the world annual extraction of platinum (not counting the USSR) of about 80 tonnes. Therefore, the creation of an ecologically clean electric car is in principle highly improbable, unless platinum-free catalysts for 'cold' electrochemical oxidation of hydrogen which would be competitive or at least comparable to platinum-based ones, are produced.

Fundamental studies on the chemistry of the interaction of hydrogen with metals and intermetallic compounds, conducted in the USSR and abroad[1–5] since 1968, offer real prospects for a successful search for and creation of catalysts that could replace palladium and the metals of the platinum family.

The "hydride dispersion" technology, which emerged in 1980–1982 on the basis of the above studies, allows dispersed metallic powders to be produced that are functionally similar to palladium and platinum group metals.

This technology is based on the ability of a large group of alloys of rare-earth elements, titanium, zirconium calcium, and magnesium, with transition metals which possess appropriate crystalline and electronic structures to reversibly absorb up to 1000–1200 times their volume of hydrogen, with a relatively small thermal effect (~5000 kcal per 1 kg of H_2). This process is accompanied by spontaneous comminution and formation of fine powders without resource to any mechanical processing. The resulting powders are characterised by a narrow particle size distribution, which depends on the number of sorption–desorption cycles, and "sterile" unoxidised surfaces. The sorption of hydrogen is also accompanied by a 15–25% increase in the volume of the metallic phase, its structure remaining unaltered and having a very low activation energy barrier. It is remarkable that the density of hydrogen nuclei in the hydride phase exceeds that of liquid hydrogen by a factor of 1.5–2.0.

A sponge which can be used an unlimited number of times for soaking up and squeezing out a liquid may serve as a model for these alloys. In our case hydrogen takes the place of the liquid, being sorbed on cooling and released on heating. Technological potentialities of these alloys are very high, being in the range of 10–15 thousand cycles.

It is important that hydrogen can also be sorbed from gas mixtures that contain as much as 80–90% of nitrogen, methane, inert gases, water vapour, oxygen, and carbon dioxide.

Another interesting feature of this process is its high selectivity, i.e. only hydrogen is sorbed. Therefore, the purity of hydrogen desorbed during the thermal decomposition of the hydride phase, i.e. on 'squeezing out the sponge', is very high, in excess of 99.999%.

† We are referring here to 'low-temperature' fuel cells. In the USSR, the USA and a number of other countries, strenuous efforts are currently under way to create prototypes of industrial 'high-temperature' fuel cells based on ceramic oxide materials.

Table 1 also shows various areas of application of metallic powders produced by the hydride dispersion technique. One should take special note of two processes, directly related to the ecological aspects of hydrogen technology and power engineering.

Table 1. Applications of dispersed metallic powders produced by the chemical dispersion technique. The powders are characterised by "sterile" unoxidised surfaces; absence of cold hardening and mechanical contamination; and narrow particle size distribution, controllable over a required range.

1.	Absorbents of hydrogen from industrial gas mixtures.
2.	Components of platinum-free catalysts for the oxidation of hydrogen in electrochemical fuel cells.
3.	Reversible sources of high-purity hydrogen, containing up to 1200 volumes of hydrogen per unit volume of a solid phase.
4.	Magnetic materials produced by compacting dispersed powders with the composition RCO_5, R_2CO_{17}, where R = Fe, B, etc.
5.	"Working media" in thermalsorption equipment and mechanisms.
6.	Components of mateirals with a high density of hydrogen nuclei.
7.	Highly efficient catalysts for processes involving activation of molecular hydrogen.

Problems involved in producing high-purity hydrogen, including its extraction from gas mixtures with low hydrogen content, may be resolved through the creation of absorption units, wherein a mass of a dispersed powder, or compacted material produced from it, kept together by an organic or metallic binder, performs sequentially in a sorption–desorption mode. The gas mixtures may be quite poor in hydrogen, containing as little as 10–15 vol.%.

The viability analysis of the sorption method carried out independently by several organisations, showed its high efficiency: the cost of obtaining 1 tonne of high-purity hydrogen from industrial hydrogen-bearing gases was found to be 1000–1500 roubles, which is approximately 2–3 times less than the current price.

A more promising, although technologically more complicated technique, involves the use of filters produced from dispersed powders containing rare-earth metals and metals of the iron group, these powders having been obtained by the hydride dispersion method. Judging from preliminary data (referring to 1988), such materials may well compete with palladium–silver alloys.

The second task is to create new catalysts for the oxidation of hydrogen, based on dispersed powders containing nickel, manganese, zirconium, etc. Studies along these lines are being conducted in the Soviet Union—the Electrochemistry Institute of the USSR Academy of Sciences, the Moscow State University and other organisations—and abroad, and are particularly actively pursued in Japan, USA, and EEC countries. Considerable progress has already been made in this direction. Current densities in electrodes, manufactured from compressed powders are now as high as 200–300 mA cm^{-2}, comparable to those in contemporary small fuel cells in which platinum-containing catalytic contacts are used.

Abroad, the hydride dispersion technique forms the basis for one of the fastest developing high-technology branches of industry.

In the USA, Japan, and EEC countries the envisaged annual production of hydrogen-absorbing alloys is about 1000 tonnes. Production of such alloys is apparently carried on an industrial scale in China, where hydride technology is being actively applied in the electronic industry, in the chemical industry, and for the production of high-quality magnetic materials. The world market prices for dispersed powders capable of reversibly absorbing hydrogen are currently about 400–500 US dollars per kg. Japanese experts estimate that by the year 2000 the internal market alone for the materials and articles involving the use of hydride technology will reach about 500 million US dollars.

Let us take a brief look at the model of the interaction of hydrogen with alloys of rare-earth metals, titanium, zirconium, and magnesium with transition metals (iron, cobalt, nickel, copper, chromium and vanadium) which is used as the basis for predicting the nature of such interaction in relation to the crystalline structure, chemical composition, and thermodynamic properties of the alloys.[6–8]

If an alloy capable of absorbing hydrogen is regarded as a 'sponge', reversible sorption of hydrogen should be possible under the following conditions:

1. The energy of activation of chemisorption of hydrogen at active centres on the surface of the metallic phase should be small. This surface can be modified by introducing into the alloy small admixtures of other metals so as to influence the physicochemical properties of the hydride phase in the desired direction.

2. The structure of the alloy should have a crystal-chemical 'predisposition' to the sorption of hydrogen, this predisposition being characterised by the presence of cavities or voids of definite size and configuration.

3. For virtually all alloys that are potential hydrogen sorbents, a reaction alternative to the sorption of hydrogen is thermodynamically possible, for example, a chemical reaction of destruction yielding binary hydrides and free transition metals which do not absorb hydrogen. The probability or possibility of a reaction of this kind at a certain temperature and hydrogen pressure is predictable, given the main thermodynamic properties of the initial alloy. On this basis chemists may design and produce any alloy whose sorption parameters would be optimised to meet specific technical conditions required by chemical engineers and designs of equipment for various purposes.

This allows us to be optimistic about prospects of using the hydride technology for creating in the near future ecologically clean power engineering complexes, based on a wide use of hydrogen as the chemical raw material, energy carrier, and medium for conducting technological operations in sterile conditions.

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Brief communications

Translated from *Uspekhi Khimii* **60** 659–660 (1991)

Prospects and current problems in the reduction of emission from automobile transport

V Z Makhov
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The contribution to atmospheric pollution by automobile transport, which amounts to 15–25% relative to the overall pollution, increases to 75–80% (with respect to CO) when pollution in cities is considered.

Real tests have shown that the limiting permissible concentrations have been exceeded by a factor of 7–16 with respect to components for which norms have been laid down in relation to automobile transport, the factor increasing to 20–50 with respect to the overall emissions subject to norms let alone the presence of indirectly normalised and non-normalised components (lead and sulphur compounds, aldehydes, etc.) as well as the "background" (inadequate purification of water, contamination of food products). A similar situation is characteristic of at least 116 cities in the USSR. The possible measures for the planned reduction of emissions from transport, in Moscow for example, could actually prove ineffective because of the growth of the transport fleet and its long renewal cycle (up to 20 years).

The USSR tends to adopt the normalisation level established by the EEC and UNO rules, although the majority of the European countries are going over to the stricter U.S. norms. However, even the EEC and UNO norms presupposes the use of only non-ethylated (unleaded) petrol as the fuel and hence the catalytic purification of spent gases. In our country, the presence of norms for automobiles with catalytic converters (production for export with imported converters) is combined with "milder" norms for automobiles without converters (for internal use). Such "dual" normalisation reflects the situation in which there is a lack of material means for the fulfilment of stricter norms. Thus acording to EEC estimates, the changeover by 1991 to non-ethylated fuels will require 2.7–3.5 billion dollars in capital investment. One must recognise that, as a result, there has been no reduction in automobile transport emission in our cities. Therefore in the general prospective programme for the reduction of emissions from means of transportation, it is essential to concentrate on the rapid improvement of the ecological situation in cities.

The problem of developing promising means of transportation with improved economic parameters includes the search for ecologically acceptable energy carriers. The most promising of these (hydrogen) cannot be regarded as an "ecologically clean" fuel because of the formation, on its combustion in air, of NO and the thermal pollution common to all energy consuming devices. A real effect can be achieved even at the present time by using liquified and compressed gaseous fuels.

The use of gaseous fuels in engines with a homogeneous mixture makes it possible to go over to the combustion of leaner mixtures, taking into account the effect of the diffusional enrichment of the flame front in the lighter component. In diesel engines, the use of gaseous fuel involves the solution of the problem of the reliable ignition of the gaseous fuel stream.

The most effective and realistic procedure is the employment of soot filters in diesel engines and of controlled catalytic converters in petrol engines. However, such converters require an oxygen sensor, an electronic system for the control of fuel injection, and the use of a fuel without a lead antiknock agent. The same measures can be taken in the solution of urgent ecological problems in cities, including Moscow. Here one can assume that purely technical problems are not of decisive importance. In the first place, it is essential to solve the following main problems:

The specification of norms for harmful emissions by legal organs with an expert assessment by an independent competent organisation (the USSR Academy of Sciences) instead of normalisation by what is in fact a government department.

The establishment of the magnitude of fines on the grounds that it is preferable to finance nature-protecting measures rather than pay for the pollution of the atmosphere under conditions where industrial undertakings are economically truly independent.

Transition from financing the research programmes set up by the researchers themselves to the creation of a scientific-industrial association with target financing and the rights of the director (or general constructor) concerning its utilisation.

A combined approach to decreasing the contamination of a city with gases, the reconstruction of the network of highways, and the development of green zones and plantations (including for this purpose financial means received from the increased expenditure on transport).

Thus the current task of reducing sharply the level of contamination of cities by gases is organisational rather than technical in character, which should be taken into account in the development of an ecological programme.

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IV. ANALYSIS OF CHEMICAL CONTAMINANTS

Translated from *Uspekhi Khimii* **60** 661–666 (1991)

Physicochemical analysis of organic toxic substances in natural waters

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One of the most important problems in preserving the environment is the identification and quantitative determination of the contaminating substances passing into it. Upwards of 1000 organic compounds are included in the list of priority contaminants of the biosphere.[1] The main organic contaminating substances of natural waters are recognised to be phenols, lignins, pesticides and petrochemicals.

Investigations have been carried out by us recently with the aim of developing procedures for the qualitative and quantitative analysis of the various classes of contaminating substances, primarily hydrocarbons and phenols, using physicochemical methods such as capillary gas chromatography (CGC), gas chromatography-mass spectrometry (GCMS) and nuclear magnetic resonance spectroscopy (NMR).

Petrochemical hydrocarbons are some of the main and stable contaminants of aqueous media. As a result of human activity more than a million tons of petrochemicals pass into the oceans of the world every year, 90% entering with fresh water.[2] Such contamination of the oceans leads to a disturbance of the ecological balance, accumulation of petrochemicals in aqueous organisms and correspondingly in man.[3]

CGC and GCMS are universal methods of analysis of oil and petrochemicals in the environment. This is linked with the ability of chromatographic methods to resolve complex mixtures and with the high sensitivity of chromatographic and mass spectrometric detectors.

CGC was used for the determination of contamination by paraffin hydrocarbons of the western waters of the Black Sea.[4] Water was sampled at 25 points of the coastal waters to the west of longitude 32° E in April 1981. Samples of water were extracted with chloroform and the paraffin hydrocarbon fraction was separated from the extracts. The concentration of n-alkanes containing from 14 to 44 carbon atoms was determined by GLC.

In the region investigated the overall concentration of n-alkanes varied from 2 to 400 μg litre^{-1}. The coastal zone and also all the navigable region was characterised by an increased content of hydrocarbons (see Fig. 1). This may be explained by contamination of the Black Sea both by carry down from rivers and by means of transport.

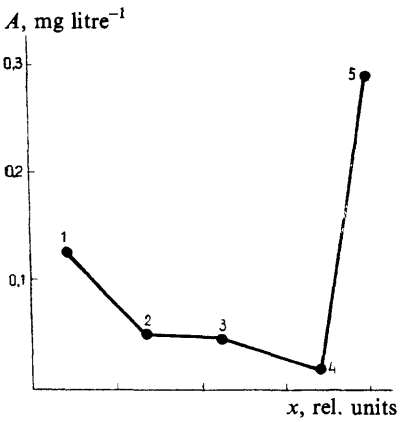


Figure 1. Dependence of the total content of n-alkanes (A) in water from the Black Sea on distance (x) from the coast: *1*, station 36; *2*, station 35; *3*, station 34; *4*, station 33; *5*, station 31.

An important question linked with contamination of the world's oceans by petrochemicals is the solution of the arbitrary problem of the search for the culprits of petroleum contamination.

A complex approach to the solution of this problem was used by us in several cases when determining culprits for the catastrophic oil spills in the Baltic Sea. In this case CGC was used for determining the ratios of quantities of isoprenoid and normal hydrocarbons Ph/C_n and Pr/Ph, where $n > 18$, Ph is phytane and Pr is pristane, from which the culprits of the spills were identified.

It was established previously,[5-7] that NMR spectroscopy enables analysis of both crude petroleum and its refined products including heavy fractions not yielding to chromatography. This method is used together with other physicochemical methods for the estimation of structure-group parameters of petroleum. The main parameters determined by NMR are the relative content of aromatic protons H_a (contribution of the integrated intensity of signals for aromatic protons in the ^1H NMR spectrum to the total integrated signal intensity) and the relative content of aromatic hydrocarbons C_a (contribution of the integrated intensity of signals for aromatic carbons in the ^{13}C NMR spectrum to the total integrated signal intensity). It was shown that it was necessary to use a relaxant such as chromium(III) acetylacetonate for the quantitive determination of the C_a parameter and a method for decoupling the spin-spin interaction of ^{13}C nuclei with protons. The decoupling unit was switched on during the time for sensing the impulse of the radiofrequency field and was switched off during the time for sensing the free induction signal. This led to the quenching of the nuclear Overhauser effect.

Analysis of specimens of petroleum spills showed that depending on the weathering of the petrochemicals, H_a may vary several fold while the C_a parameter was practically unchanged. In addition data from the analysis of numerous oilfields of the Soviet Union showed[7] that the range of change of C_a was wider than that of H_a and was 9–23%. Consequently the C_a parameter, together with the overall shape of the ^{13}C NMR spectrum, which enabled determination of the oil type, paraffinic or napthenic, was used to determine the source of origin of the oil spill into the sea.

Table 1. Results of analyses of contamination of the Baltic Sea by hydrocarbons.

Parameter	Sample				
	Control oil		Oil I, weathered	Contamination samples taken from the sea	
	I	II		I	II
H_a, %	4.0	0	2.2	2.3	1.5
C_a, %	18	14	20	18	19
Pr/C_{17}	0.59	0.98	0.50	0.49	0.52
Ph/C_{18}	0.78	0.56	0.72	0.71	0.72
Pr/Ph	0.75	1.75	0.70	0.69	0.72

Data shown in Table 1 of CGC and NMR which were used for determining the culprit for a catastrophic oil spill in the Baltic Sea. Samples presented for analysis were from two assumed sources of the spill (oils I and II), an oil sample subjected to 40 days weathering under laboratory conditions (oil I, weathered) and samples of contamination taken from the sea (I and II). NMR data and the ratios of isoprenoid hydrocarbons Pr/Ph showed that oil from the first source had spilled into the sea.

The procedure for determining the culprit for the contamination by GCMS was based on the detection of aromatic compounds of the homologous series benzene, naphthalene, anthracene and phenanthrene. Since polynuclear aromatic hydrocarbons are less subject to weathering and biodegradation in water in comparison with aliphatic hydrocarbons for example[8,9] the probability of correctly identifying the culprit of a spill by detection of these compounds is high. It appeared possible to analyse petrochemicals which had been in the sea for several days (their composition was very different from that initially).

In the case of water with little contamination, i.e. when the sensitivity of the gas chromatograph-mass spectrometer was inadequate to carry out an analysis in the field scanning mode, monitoring of definite ions from aromatic hydrocarbons of the series indicated was used. To detect homologues of benzene the instrument was adjusted to record ions of mass m/z 77, 91 and 105, of naphthalene 127, 141 and 155 and of anthracene and phenanthrene 177, 191 and 205. Such a procedure enabled the sensitivity of determining aromatic hydrocarbons to be increase 100–1000 times. The culprit of the contamination was determined fairly simply from the chromatogram drawn from the current of the indicated ions.

Table 2. Content of some organic contaminants in test samples of snow and water in Kemerovo.

Compound	Concentration (μg litre^{-1})	
	snow	water
Hexadecane	112.0	2.9
Pentadecane	151.0	2.8
Octadecane	75.4	3.9
Nonadecane	70.0	9.0
Tricosane	98.0	4.4
Octacosane	98.0	2.0
Nonacosane	279.0	traces (<0.5)
Triacontane	70.5	traces (<0.5)
Untriacontane	184.5	—
Dotriacontane	112.0	—
Tritriacontane	80.0	—
Tetratriacontane	37.1	—
Naphthalene	5.7	3.0
Methylnaphthalenes	0.4	—
Acenaphthene	10.0	traces (<0.1)
Anthracene	1.5	traces (<0.1)
Pyrene	traces	traces
Dibenz[*a*,*c*]anthracene	8.1	0.5
Phenol	0.7	traces (<0.5)
Dimethylphenols	traces (<0.5)	0.9
4-Chlorophenol	—	1.0
4-Chloro-*m*-cresol	—	4.8
2,6-Di-t-butylphenol	—	
4-Methylphenol	3.0	
Oct-2-ene (isomers)	—	112.0
t-Butylmethylcarbinol	—	10.1
iso-Butylmethyl carbinol	—	13.7
Bis(2-chloroethyl) ether	—	65.0
Bis(2-chloropropyl) ether	—	63.1
Bis(2-chloroisopropyl) ether	—	30.0

Contamination of surface waters may also occur from the atmosphere since[10] on going from alkanes to a polynuclear aromatic hydrocarbon the size of the contribution of this contamination to the total contamination of water increases from 1–2 to 25%. Gas chromatographic analysis of samples of snow taken in March 1988 near Kemerovo showed that alkanes and aromatic hydrocarbons

were the principal organic contaminants of snow. For example, the content of individual n-alkanes was 100–200 μg litre^{-1} and their total content exceeded 3 mg litre^{-1} which was approximately 10–100 times greater than their content in water samples from the same region. An analogous result was observed for aromatic hydrocarbons. On the other hand phenols, widely represented in water, were practically absent from snow samples with the exception of phenol itself and dimethylphenols. Data on the content of certain organic compounds present at the highest concentrations in snow and water samples are given in Table 2.

It is possible to explain the similar character of the distribution of contamination in the given region by the theory of the adsorption of organic compounds by dust particles suspended in the atmosphere.[10] The process for the transfer of organochlorine pesticides, polychlorinated biphenyls and polynucler aromatic hydrocarbons, which occurs in this way, has been studied previously.[10] Carbon dust, present in the atmosphere of Kemerovo, adsorbs organic compounds to a significant extent, having higher values of adsorption coefficients than activated carbon k_c. The value of $\lg k_c$ for higher alkanes and aromatic hydrocarbons is appreciably greater than for phenols, alcohols and ethers.[1]

Phenols, like hydrocarbons, belong to the group of widely distributed and highly toxic contaminants of natural waters. Chlorophenols are formed on chlorination of water, and their toxicity and ability to accumulate in organisms grows with increasing content of chlorine atoms in the aromatic ring.[1,11] Many phenols are detected in water by taste and smell at concentrations less than 0.1 μg litre^{-1}.[1]

From our data the detection limit for phenols when using CGC with a flame-ionisation detector was from 0.4–1.8 μg litre^{-1}, and by HPLC was several μg litre^{-1}, which frequently does not meet modern nature conservation requirements. It is possible to increase the sensitivity and selectivity of determining phenols by chromatographic methods if phenols are converted into various derivatives.[12] Thus the combined use of acetylation and pentafluorobenzoylation of chlorophenols and the use of an electron capture detector enables the quantitative determination of phenol in water at concentrations of 0.2–0.4 μg litre^{-1}.[13] With the aim of improving and clarifying the actual possibilities of the highly sensitive quantitative analysis of phenols in natural waters at the background level by CGC and HPLC, we have carried out a qualitative and quantitative determination of phenols as pentafluorobenzyl ethers (I), pentafluorobenzoyl (II) and dabsyl (III) esters.

$$C_6F_5CH_2Br + ArOH \longrightarrow C_6F_5CH_2OAr, \quad (I)$$

$$C_6F_5COCl + ArOH \longrightarrow C_6F_5COOAr, \quad (II)$$



(III)

Various esters and ethers of types (I)–(III) were synthesised and obtained in the pure state for the first time for this purpose. Their structures were demonstrated by elemental analysis, IR and NMR spectroscopy and mass spectroscopy.

It was established that the limits of detection of derivatives of types (I) and (II) by CGC using an electron capture detector were 1–2 mg and of derivatives (III) by HPLC 1–2 ng. For the quantitative determination of phenols as derivatives (I)–(III) we determined values of the relative factors for the detector signal in relation to the phenol derivatives and also established the so-called degree of detectability of phenols (i.e. the degree of conversion of phenols by the method). Limits of detection of phenols in natural waters were 10–100 ng litre^{-1}.

For the qualitative determination of phenols as derivatives (I)–(III) we studied their mass spectral decomposition by electron impact and for derivatives (I) by chemical ionisation with isobutane recording both the positive and negative ions. It was established that mass spectrometry enabled identification of phenols in nautral waters with a high degree of reliability.

The method of determining phenols as ethers of type (I) was tested by us when investigating water from the Moscow River in the spring of 1987 for the presence of phenols (Table 3).

Table 3. Content of phenols in water samples from the Moscow River.

Compound	LPC, μg litre^{-1}	Concentration in water, μg litre^{-1}
Phenol	1	2.9
4-Chlorophenol	1	7.7
4-Nitrophenol	20	1.4
Pentachlorophenol	10	103.9
2,4-Dinitrophenol	30	10.7

Identification of derivatives of phenols was carried out by comparing retention times of standards (pentafluorobenzyl ethers of phenols) at various temperature modes of chromatography and was confirmed by gas chromatography-mass spectrometry. As follows from the data of Table 3 the content of chlorophenols in the Moscow River exceeded the values of the limiting permissible concentrations (LPC) by 3–10 times. The contents of nitrophenols were somewhat lower than the LPC values.

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Translated from *Uspekhi Khimii* **60** 667–672 (1991)

Problems of the development of ecological instrument making

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The attention devoted to the development of new analytical methods and instruments for ecology has been aroused by the appearance in the waste from economic activity of a large amount of highly toxic pollutants, which are dangerous to man and the environment even in very small amounts. The detection of these substances at the level of limiting permissible concentrations against the background of interfering substances is a very complex scientific and technical task. Bearing in mind that about 70 000 organic compounds are being used throughout the world and are therefore present in the environment and that their number increases by 1–2000 annually,[1] the necessity for newer modern approaches to ecological analyses becomes evident. For such studies, it is essential to have at one's disposal a set of fairly universal methods and instruments with a high sensitivity and selectivity. The results should be interpreted on a computer. Furthermore, it is essential to possess a data bank for the identification of substances.

The development of analytical methods in ecology has been stimulated by a series of accidents in chemical undertakings and by the results of their investigation. The results of a study of the accident in Seveso (Italy) in 1976,[2,3] where the latest advances in chromatography and mass spectrometry had to be used in order to detect traces of dioxins, which poison human beings and pollute the locality, have appeared in print to the greatest extent. The consequences of the agricultural pollution and of the use of chemicals (herbicides) during most recent wars have also served as stimuli.[4] All these major catastrophic pollutions have led to a sharp increase in the number of scientific publications on the development of analytical methods using the latest instruments: highly effective gas and liquid chromatograph and mass spectrometers, which are used in more than half the instances where analytical methods are needed.[5]

The increasing complexity of the ecological situation and frequent accidents in chemical undertakings have induced a rapid growth of the industrial manufacture of analytical apparatus in various countries. The quality of the apparatus has been increasing significantly as a result of a large number of service devices: devices for sampling and preparation of samples and a sophisticated system for the interpretation of data on computers with extensive program libraries, data bands, and systems for the identification of substances.

The achievements in instrument making and electronics enabled a number of firms to develop mobile laboratories equipped with chromatographs and mass spectrometers. The best known of these is the TAGA-3000 Laboratory (Canada). It uses as the detector a mass spectrometer with a device for the automatic injection of samples from the atmosphere, which ensures a high sensitivity (10^{-15} g cm^{-3}). The presence of a navigating device makes it possible to plot maps of contamination in the given locality. The MM-1 mobile laboratory of the Bruker Company (Federal Republic of Germany) has effective analytical characteristics. It uses as the detector a quadrupole mass spectrometer with sample injection through a capillary column and with heating at the sampling site. This laboratory is designed for the rapid identification and estimation of the amount of organic substances in water, air, and on the surface. It can be used to analyse the distribution of dioxins.[6]

The use of modern analytical methods and apparatus combined with well thought out organisational measures is undoubtedly the most promising trend in ecology, which has already frequently led to positive results, and not only in the case of industrial accidents already mentioned. The significant improvement of the ecological situation in the region of the Greak Lakes (USA) and the Mississippi River may serve as an example. The combination of modern physicochemical and biological analytical methods and international cooperation has made it possible to investigate fairly rapidly the causes of the death of seals in Lake Baikal.[7]

The use in ecology of the majority of analytical instruments is limited by their high cost, the need for special accommodation, and the unduly laboratory-oriented design of the instruments as well as the need for highly qualified specialists to carry out the analyses. For the mass application of analytical instruments in ecology, the designers must significantly reduce the cost of the apparatus without loss of their quality, reduce their weight and size, and expand their operating conditions.

The small batches of chromatographs and mass spectrometers produced by Soviet industry do not satisfy the requirements of ecologists either as regards their functional possibilities or their operating characteristics. Essential instruments such as chromatograph-linked mass spectrometers and quadrupole mass spectrometers are not produced at all. There is a particularly serious lack in the field of assembly and interpretation of data on the basis of modern advances in computer techniques. Devices for continuous monitoring based on laser techniques and small cheap and selective sensors of different types are completely lacking.

One of the main reasons why Soviet industry lags behind in ecological instrument making is the absence of a scientific-technical base and of permanent specific organisational stimuli, which, on the one hand, would stimulate the demand for ecological instruments because of the need to carry out measures to protect nature and, on the other hand, would stimulate the manufacture and improvement of their quality.

The Siberian Division of the USSR Academy of Sciences prepared the program "Development of Methods, Instruments, and Mobile Laboratories for the Analysis of the Pollution of the Environment", which can be regarded as the first stage of work designed to create a

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The Siberian Division of the USSR Academy of Sciences prepared the program "Development of Methods, Instruments, and Mobile Laboratories for the Analysis of the Pollution of the Environment", which can be regarded as the first stage of work designed to create a

base for ecological instrument making. The program included 34 research and experimental-design studies which are planned for 1989–1991. The program of the development of studies in the subsequent period will be prepared in 1990 using the experience gained.

The main executor of the program is the Limnological Institute of the Siberian Division of the USSR Academy of Sciences. The overall cost of the studies is 23 million roubles (7.7 million roubles annually). The main bulk of the studies are being performed by members of the Institute of the Siberian Division of the USSR Academy of Sciences, the Geophysical Instrument Making Division of the Tochnash Design Bureau at the Institute of Geology and Geophysics of the Siberian Division of the USSR Academy of Sciences, the EKOTEK Company, and the experimental factory of the Irkutsk Scientific Centre.

It is proposed initially to set up and standardise a limited list of toxicants, each of which will represent a specific group of ecological toxicants of prime importance, classified in relation to the analytical methods and instruments. Such a list is necessary for laboratory tests of instruments and should be reduced to a minimum in order to diminish the cost of the development of the metrological aspect of the work.

In addition, it is necessary to set up an information data bank for the study of the advances in the field of ecological instrument making and for the refinement of different aspects of the research. In the course of the studies, it is proposed to develop a packet of programs for personal computers, to carry out bibliographic and patent searches, and to introduce the information into the data base and analyse it.

The next group of studies is designed to create instruments for the analysis and monitoring of prime toxicants in the gas phase.

In order to construct the gas chromatographs, it is essential to employ the experience gained in the development of the "Ekho" gas analyser-identifier, whose design is so advanced that it can become the basis for a series of universal an specialised chromatographs which are not inferior to the best devices throughout the world. The design of the "Ekho" gas analyser is protected by a patent.[8] The instrument employs novel units: a device for sample injection from a concentrator, polycapillary columns, an improved electron capture microdetector, and a microprocessor device for controlling the apparatus and for interpretation of data, which are also protected by patents. Further improvements to the design of the apparatus will make it possible to extend the range of substances analysed and to improve the sensitivity of the determination of impurities in the atmosphere to 10^{-15} g cm^{-3} (combined with a resolving capacity ranging from thousands of plates in portable versions of the apparatus to tens of thousands of plates in stationary designs). The detector being developed on the basis of molecular condensation nuclei possesses unique sensitivity and is capable of detecting a wide range of substances. The set of existing technical solutions, the degree of elaboration of the components of the apparatus, and the design as a whole make it possible to create an instrument which will not be inferior to the best devices available throughout the world as regards its characteristics.

Rapid performance (a fraction of a second for the entire range of substances detected) and a high sensitivity (10^{-13} g cm^{-3}) are combined in the novel instrument called "drift spectrometer", where the substances are separated on the basis of the non-linear dependence of the mobilities of their ions in specially generated electric field pulses.[9,10] The instrument operates with air being continuously pumped through it and is designed to analyse the composition of the air on board moving carriers. The studies being performed should lead to the construction and tests of a prototype of the instrument. The instrument has no analogues abroad.

For remote-control analyses, it is proposed to construct a batch of atomic-absorption mercury Zeeman analysers in air which have proved very satisfactory in a whole series of tests on the detection of mercury vapour in the atmosphere performed on an aeroplane (developed by the Institute of the Optics of the Atmosphere, Siberian Division of the USSR Academy of Sciences, Tomsk).

Members of the Krasnoyarsk Scientific Centre of the Siberian Division of the USSR Academy of Sciences have been investigating new principles of the analysis of air and liquid media using the resonance effects in laser spectroscopy and microwave spectroscopy. It is proposed to construct analysers with a very simple design and easy to operate.

It is proposed to construct several prototypes of a lidar for remote-control measurements of the amounts of sulphur dioxide, nitrogen oxides, and aerosols in the atmosphere and to test them in Tomsk, Novosibirsk, and Irkutsk. The instrument has been developed by the Institute of the Optics of the Atmosphere of the Siberian Division of the USSR Academy of Sciences and is designed to monitor the state of the atmosphere in the vicinity of major industrial undertakings, heat and power generating plant and urban regions.

Yet another group of studies has been devoted to the development of means for the analysis of liquids. These studies should result in the modernisation of the electronic units of the "Milikhrom" liquid chromatograph, the development of which led to the award of the USSR State Prize. The novel units and blocks of the chromatograph, patented in major capitalist countries[12–18] and protected by USSR patents, ensure effective characteristics of the instrument: sensitivity down to 10^{-9} g with respect to nucleotides, duration of analysis from 2 to 20 min, and selectivity equivalent to 4000 plates.[11] After modernisation, the instrument should be produced commercially.

It is also proposed to use the best advances in the development of the units of the "Milikhrom" chromatograph to improve the efficiency of the ionic chromatograph in a flow-injection analyser. By virtue of the employment of the principle of microcolumn chromtography, a tenfold saving has been achieved in the reagents and sorbents in the ionic chromatograph compared with the best foreign analogues. The flow-injection analyser is based on the detector of the "Milikhrom" chromatograph incorporating a 2:μl cell and a small-size system for the supply of the solution of the solvent and for injection.

An attempt has been made to devise an apparatus for the neutron-activation analysis of admixtures of chemical elements in water under field operating conditions. For this purpose, one uses small neutron generators with a flux $>10^8$ neutron s^{-1}. Similar generators are used for the neutron bore hole logging. In the above study a novel design of a generator with a gas-filled tube was employed. The study led to the creation of a mock-up of the apparatus.

The most complex problems have to be solved in the studies designed to devise different types of mass spectrometers. The principal difficulties arise in the creation of transportable versions of the apparatus for mobile ecological laboratories and in the development of devices for the introduction of samples. It is proposed that both direct sample injection from the atmosphere and sample injection via chromatographic columns be employed, as well

as a novel hydrodynamic procedure for the introduction of liquid samples into the mass spectrometer.

The possibility of devising a Soviet-produced transportable quadrupole mass spectrometer has been investigated. The MM-1 mass spectrometer, developed by the Bruker Company (Federal Republic of Germany), may serve as a model.

It is proposed to develop an analytical system based on a static mass spectrometer with a samarium magnet, which is equipped with a device for the introduction of samples from the atmosphere, a line of receivers for the simultaneous recording of the mass spectra, a device for coupling to a personal computer in order to interpret the information and identify the substances, and a vacuum system capable of working as a part of the equipment of a mobile ecological laboratory. The study should be completed by the construction and test of the system as part of an ecological laboratory. The system is designed for the analysis of toxicants of prime importance in the gas and liquid phases.

The problems concerning the testing and calibration of instruments for the analysis of traces of substances in the gas phase are being solved. Generators of standard concentrations of prime toxicants, based on the constancy of the concentration of the vapour of a solution at a given temperature, are being developed for the purpose of the tests. The solution is deposited on a large surface,[19] in the given instance on the channels of a polycapillary plate. The generators are first calibrated against a radioactive label. A calibration table, indicating the concentration of the toxicant vapour at a specified temperature to within $\pm 10\%$, is assigned to each generator. It is possible to construct in this way generators for the determination of the concentrations of substances down to 10^{-14} g cm^{-3} in air. Sets of such generators, designed for different concentrations, make it possible to test the linearity and sensitivity of instruments over a wide dynamic range.

Fluorine-graphite matrices, maintaining a constant flux of an evaporating substance for up to 6 months, are prepared by a special technology and are used for the sorption of volatile substances. The advantages of the sorption generators of standard concentrations are their small size and ease of operation, which makes it possible to incorporate them directly into the automatic calibration apparatus.

In the course of these studies, measures will be taken to ensure the metrological certification of the generators and sets of generators in the required numbers will be constructed.

A large series of studies is being performed on the creation of chromatographic phases and different types of capillary and polycapillary columns for gas chromatography. The results obtained at the Institute of Organic Chemistry of the Siberian Division of the USSR Academy of Sciences in the synthesis of polysiloxane liquid phases, reagents in the deactivation of the surfaces of glass and quartz using a specially developed technology for the deposition and stabilisation of phases, made it possible to set up the manufacture of columns which are not inferior to the best foreign examples either as regards selectivity or as regards the range of working temperatures (from -60 to 320 °C). The principal task at the present stage is to ensure the provision of highly effective chromatographic columns in all the developments involved in the given programme.

In order to improve the characteristics of a traditional analytical instrument—the emission spectrometer—a study has been undertaken to construct a mock-up of such a spectrometer in which all the latest advances in this field are employed: holographic grids, a recorder with a line of photodiodes for the simultaneous recording of the MASI spectra, and the assembly and interpretation of information with the aid of microprocessor computers. The size of the apparatus is significantly reduced and the requirements as regards vibration stability are less stringent, which makes it possible to employ the device in mobile laboratories.

A large series of studies has to be carried out on the development of methods for the analysis of toxicants of prime importance (it is proposed to involve in this investigation a large team of members of the Institutes of the Novosibirsk, Krasnoyarsk, and Tomsk Scientific Centres). The analytical methods should be based on the devices developed in accordance with the given programme and should employ the latest advances in the computer interpretation of information. A data bank should be set up for use in personal computers in order to identify the substances analysed. In the first stage of the investigation, it is proposed to create data banks and systems for the identification of substances against the background of impurities.

Two studies are designed to develop hydroacoustic devices for hydrobiological studies and for the estimation of the stock of fish and the state of water-containing areas.

The development of a mobile ecological laboratory is the most complex component among those planned in the programme "development of methods, instruments, and mobile laboratories for the analysis and monitoring of pollutants in the environment". The laboratory should be placed in a specially equipped automobile (bus). In the first stage of the development, it is proposed that the laboratory should incorporate (after structural modification) the following instruments: a modernised Ekho-M gas chromatograph, a modernised Millikhrom liquid chromatograph, a drift spectrometer, a mass spectrometer with sample injection from the atmosphere, a bioluminometer, an aerosol counter, devices for the selection and preparation of samples, and a set of personal computers within the automobile. The laboratory is designed for the operational analysis of the state of the environment. In the first stage of these studies, it is also necessary to revise the necessary set of apparatus, to specify the unsolved problems, and to formulate the task for the next stage.

The programme is completed by a series of studies designed to prepare for the construction of a scientific-industrial base for ecological instrument making at the Irkutsk Scientific Centre. In accordance with the resolutions of the Praesidium of the Siberian Division of the USSR Academy of Sciences, it is proposed to create the Irkutsk Engineering-Ecological Centre, in which the total number of engineers and other workers employed will be up to 1000. The tasks in the Centre are the development of modern methods for the analysis and monitoring of the state of the environment, the coordination of the work of the organisations participating in the execution of the programmes, the construction and testing of prototypes of the apparatus, the incorporation in commercial production of the developments achieved at the Centre, and cooperation in the practical employment of such developments by the monitoring organisations.

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Brief communications

Translated from *Uspekhi Khimii* **60** 673 (1991)

Chromatography in ecology

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The solution of the problem of ecology in all countries, namely the creation of waste-free technologies the utilisation of the materials obtained, the study of their metabolism under operating conditions, their regeneration, and their disposal, is impossible without chemical analysis of complex organic mixtures, which permits not only the determination of the overall content of the organic substance but also the establishment of the presence and the determination of the concentrations of specific mixture components. Chromatography combined with mass spectrometry, IR Fourier spectroscopy, UV spectroscopy, etc. has become such an analytical procedure.

Chromatography makes possible the selective determination of microimpurities at virtually any level, which is especially important in the solution of ecological problems. As a result of the chromatography of a mixture, the separated individual components pass to the instrument for their determination (mass spectrometer, IR Fourier spectrometer, etc.) and are then identified by spectroscopic methods. At the present time, all the leading and the majority of ordinary analytical laboratories abroad, engaged in the analysis of objects in the environment, are equipped with chromatograph-linked mass spectrometers and a large number of gas and liquid chromatographs.

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Translated from *Uspekhi Khimii* **60** 674–675 (1991)

Electrochemistry and protection of the environment

V E Kazarinov
Frumkin Institute of Electrochemistry, USSR Academy of Sciences

There are many electrochemical aspects of the solution of ecological problems. In the first place, these include the creation of new industrial technologies, procedures for the purification of waste waters, and the development of sensors for the monitoring of the environment. Electrochemistry can also make a serious contribution to the creation of ecologically clean transport and power engineering.

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2. W Forth *Deut. Arztbelatt*, 1977, **74** 2617
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4. V I Vysochin *Dioksin i Rodstvennye Soedineniya: Kratkii Literaturnyi Obzor* (Dioxin and Related Compounds: A Brief Survey of Literature), Izd. NIBKh Akad. Nauk SSSR, Novosibirsk, 1988, pp 13–42
5. K Bayerman *Determination of Traces of Organic Substances* (Translated into Russian), Mir, Moscow, 1987, p. 21
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Brief communications

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O G Larionov
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The scientific principles of a low-waste industrial technology for the electrosynthesis of chemical additives to polymers are being developed. In particular, processes for the electrochchemical synthesis of sulphenamide M (a thiazole vulcanisation accelerator) and benazole P (a benzotriazole photostabiliser for polymers) have been developed. These make it possible to obtain high-quality products, to abandon the use of chemical oxidants, and to reduce sharply the amount of industrial waste. Both developments are being tested on an experimental-industrial plant at NIIKhIMPOLIMER (in Tambov).

On the basis of the results of fundamental research into electrocatalysis, a highly sensitive and rapid method for the analysis of organic impurities and heavy metals in water, which has no analogues in world practice, has been devised. The method is protected by USSR and Swiss patents. On the basis of this method, our Institute devised and constructed jointly with NIIKhIMMASh a series of analysers (AKVEL) which have been highly approved by specialists at International and All-Union Expositions. Their sensitivity is 0.01 mg litre^{-1} with respect to total organic carbon and 0.001 mg litre^{-1} with respect to heavy metals. The duration of analysis is 3–15 min. The weight of the apparatus is 1.5 kg and its size is 19 × 28 × 20 cm. the AKVEL analyser is not inferior to the best western analysers for total organic carbon as regards sensitivity and speed of action. At the same time, it is distinguished by simplicity of design, small size, and low cost.

An experimental batch of AKVEL analysers, used for the monitoring of especially pure deionised water and for the analysis of natural waters, has been produced recently. Studies are being prosecuted on the creation of a sensor for organic impurities which is extremely small and works in a stream of water using an ion-exchange membrane as the electrolyte.

Sensors for oxygen in liquid media, carbon dioxide, hydrogen sulphide, carbon monoxide, and hydrogen have been developed. The electrochemical sensors designed to determine the concentrations of sulphur dioxide and hydrogen sulphide, constructed jointly with the Automation Experimental Design Bureau "Khimavtomatika", have no analogues in world practice as regards electrochemical instrument making. Models of sensors for low and high concentrations have been developed. The nominal time for the establishment of readings is 30–40 s. The sensors are distinguished by a low level of the background signal and a high stability of the output signal and contain no precious metals. It is proposed that the sensors be used to monitor the atmosphere in sulphuric acid and other industries.

Several types of sensors for oxygen have been developed: amperometric sensors of the Clark type and sensors based on a new adsorption kinetic principle. The Clark type sensor with a membrane, for artificial blood circulation apparatus, is distinguished by the rapidity of response, high stability of readings, and very small size (miniaturisation). An experimental batch of such sensors has been produced recently by the Institute of Experimental and Clinical Surgery of the Ministry of Health of the Georgian SSR. Clinical tests have been carried out under operating conditions and permission for clinical application has been received. These sensors can be used successfully also for ecological purposes.

Studies are being prosecuted on an oxygen sensor of the open type (without a membrane) for use in liquid and gaseous media with a carbon material as the indicator electrode. The response requires several seconds. The range of pressures determined is 0–760 mmHg.

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A selective catalyst for a carbon monoxide sensor, permitting the determination of CO concentrations in the presence of hydrogen, has been developed. The sensors, with an improved selectivity, have been constructed jointly with the Chirchiksk Automation Experimental Design Bureau and have been introduced at the Novo-Dzhambul'sk Phosphorus Works.

It is noteworthy that the electrochmeical methods are extremely effective in the creation of sensors for different individual substances. They are highly sensitive, respond rapidly, and can be used in automatic monitoring systems.

Translated from *Uspekhi Khimii* **60** 676–678 (1991)

Local monitoring. Organic materials — new possibilities for ecological monitoring

A A Ovchinnikov, L M Khidekel', V N Spektor
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The principal argument used by opponents of giving immediate priority to ecological problems is the lack of reliable quantitative data on the state and quality of the environment and about the immediate and remote ecological consequences (including man) of deviations from the ecological norm and concerning the very concept of the ecological norm. The primary aspect of the answers to all these questions is provided by the measurement of the set of parameters of the environment which is as complete as possible.

Ecological monitoring is divided into global, regional (at the level of continents, sub-continents, and countries and the trans-border transport of pollutants), territorial (industrial regions, cities, large agricultural-industrial complexes, dissipation of pollutants), and local (the vicinity of individual undertakings, emissions, waste, discharges, and the technosphere).

Each of the above types of monitoring has its own main task and its own set of measuring devices. However, the optimum provision of information-gathering devices for the control system at all the hierarchical levels can be achieved only by employing the entire set of data obtained by all types of monitoring, i.e. by means of a systemic approach.

Global, regional and territorial monitoring are carried out mainly by remote control methods — aerocosmic, laser, etc. The main limitation of the remote control methods is the generation of averaged information and appreciable difficulties in establishing a specific source of pollution of the environment or, more precisely, the determination of the centres of ecological breakdowns. However, the devices for remote control monitoring have been thoroughly developed during the last decades, a system of exchange of information within the limits of individual countries has been set up, and a system of international links is being gradually established.

The principal cause of the breakdown of ecological equilibrium is human activity, as a result of which local monitoring comes to the fore in the solution of problems of the rational control of ecological processes. However, local monitoring is in fact least adequately

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provided with measuring devices. The existing measuring devices and sensors, mainly from the range of analytical instruments which were not initially designed for ecological purposes, are too cumbersome, expensive, and insufficiently selective for wide scale employment in practice. Furthermore, it is virtually impossible to achieve their unification as regards the output signal and thus to create an information-measuring system on their basis.

The creation of monitoring-measuring apparatus for local monitoring of the environment requires the involvement of devices produced by microelectronic instrument making, involving the use of adequate materials for the sensitive elements of sensors.

During the last decade, data have appeared in the scientific and patent literature concerning the effective use of organic semiconductors as materials for the sensitive elements of sensors designed to determine the composition of complex gas mixtures, including the real atmosphere.

The advantages of organic semiconductors are their high sensitivity and selectivity combined with a high resistance to breakdown including the poisoning effect of the accompanying impurities. Sensors for ammonia, phosphine, arsine, hydrogen sulphide, oxygen, and sulphur dioxide have already been developed on the basis of organic semiconductors (molecular charge-transfer complexes and conducting polymers as materials of the sensitive elements) and the possibility of constructing sensors for a number of other gaseous atmospheric pollutants has been investigated. The use of metal-containing phthalocyanines for the detection of hydrogen sulphide yielded best results, superior to the current world level.

These sensors, which operate even in a direct resistive regime, are distinguished by their small size, reliability, stability of operation under natural conditions, and the possibility of being manufactured by means of a standard planar microelectronic technology. Their main disadvantage is an inadequately rapid cyclic response in the interrogatory (discrete) regime of the operation of information-measuring systems incorporating such sensors. A further increase in the rapidity of response, the expansion of the range of measurement using a single sensor, miniaturisation, and the generation of a voltage signal without an intermediate amplifier involve the use of integrated hybrid sensitive elements combining in a single planar structure a transistor based on the traditional semiconductors and a sensor based on organic semiconductors.

One of the important conclusions reached in a theoretical study of the relation between the sensitivity and selectivity of the sensitive elements and the electronic structure of organic materials has been the conclusion that extensive purification or purification with subsequent deliberate doping of the materials of the detecting media is necessary, since the presence of non-controlled impurities makes the semiconductor non-intrinsic and always reduces the sensitivity and the threshold of the determination and frequently also the selectivity of the material of the sensitive element. Methods for the purification of organic semiconductors have now been developed at the Gorky State University. For the practical purpose of constructing information-measuring systems for local atmospheric monitoring, one of the consequences of this systemic approach is most important, namely, when two sensitive elements based on organic semiconductors have comparable but different sensitivities with respect to two atmospheric components being determined, the concentration and temperature dependences of their sensitivities are different for the two elements, which makes it possible to increase their selectivity appreciably by purely computer methods. This property of the sensitive elements in the sensors of the multiparameter system permits a reduction of the requirements which must be met by the material of each element and an increase in their effectiveness in the system. The earlier sensors are amplitude-modulated detectors. Their great advantage is their low intrinsic cost and ready susceptibility to technological operations, while their disadvantage is the need for additional schematic and technical solutions in computer systems for the collection and processing of information.

The enormous advantages of large information-measuring systems constructed using modern facilities provided by the computer technique arise from the application of frequency-modulated sensors. Thus an instrument for the measurement of the concentrations of atmospheric and technological oxygen has been developed on the basis of the long-lived diphenylpicrylhydrazyl radical in the core of a superheterodyne receiver exposed to the stream of gas.

Thus the materials developed within the framework of studies on the electronics of organic materials can provide a new elementary base for ecological instrument making, which will in its turn make it possible to create an effective local monitoring system. The creation of such a system will permit the adoption of well-founded solutions in controlling the operation of undertakings in order to rule out the pollution of the environment, and in the first place the atmosphere, on the state of which depends human health and man's very life.

Translated from *Uspekhi Khimii* **60** 689–713 (1991) U.D.C. 541.128

Strong metal–carrier interaction and its role in catalysis

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ABSTRACT. The present state of the problem of the strong interaction of a metal with the carrier is analysed and the main causes responsible for the appearance of this effect are considered. Data demonstrating the influence of the strong interaction of a metal with the carrier on the absorption and catalytic properties of deposited metallic catalysts are presented.

The bibliography includes 175 references.

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II. The sources of the effect of the strong interaction of a metal with the carrier 331
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I. Introduction

The term "strong metal–carrier interaction", which is so widely used nowadays to describe a wide variety of effects in reduced deposited metallic catalysts, was introduced by Tauster[1] to designate interactions whose essential feature involves the formation of a covalent bond between the atoms of the deposited metal and the cations of carriers such as TiO_2 [1] and vanadium, manganese, niobium, and tantalum oxides.[2]

A classification of metal–carrier interactions has been proposed;[3,4] a weak interaction (on non-reducible oxides of the type SiO_2, Al_2O_3, etc.), a moderately strong interaction (in zeolites), and a strong interaction (on oxides capable of being reduced at elevated temperatures). Without going into the details of the mechanisms, one can give the following phenomenological definition of the effect of the strong interaction of a metal with the carrier (SIMC): the SIMC effect is the term applied to the group of phenomena leading to the alteration of the electronic and structural properties of deposited metallic particles, which is accompanied by the corresponding changes in the absorption and catalytic (rate of reaction, selectivity) properties.

During the years which have elapsed since the publication of Tauster's study, a large number of studies devoted to the nature of the SIMC effect have been published. It was found that the phenomenon is much more complex than was suggested in the first investigations and the aim of the present review is therefore to compare the earlier data with the results published recently in order to understand more clearly the nature of the effect and the direction which will be taken by further studies.

II. Sources of the effect of the strong interaction of a metal with the carrier

In modern literature, the following sources of the SIMC effect have been specified:[3,5–10] electronic (collective and local) interactions, migration of the carrier on to the surface of the metallic particles and encapsulation of the metal in the carrier, the formation of alloys and intermetallic compounds, and thermodynamic factors.

1. Electronic interactions

The explanation of the SIMC effect in terms of collective electronic phenomena is based on Schwab's idea[11] that the Schottky theory is applicable to the metal–carrier interface in catalytic systems. If the catalyst contains an *n*-type semiconductor with an electron work function φ_n (on reduction, TiO_2 actually becomes precisely such a semiconductor) and a metal with a work function φ_m, where $\varphi_n < \varphi_m$, then electrons will migrate from the semiconductor to the metal until the chemical potentials of both solids (Fermi levels) are equalised. Under these conditions, the layer of the semiconductor adjoining the metal is depleted in current carriers and becomes positively charged, while the layer of the metal becomes negatively charged. A potential barrier, called the Schottky barrier, arises at the interface. If the Schottky theory is applicable to deposited metallic catalysts, then the change in the concentration of conductivity electrons does indeed influence the catalytic and adsorption properties, and this constitutes one way of explaining the SIMC effect, which has in fact been used in some studies.[12] However, the question arises of the meaning of the change in the concentration of conductivity electrons in the metal if their number in the latter is 10^{23} per cm^3. In order to determine from experimental data[13] the real concentration of electrons migrating from the carrier to the metal in conformity with the Schottky theory, the potential difference at the nickel–germanium interface was calculated. It was found that one electron is transferred from the conductivity band of germanium per 10^4 atoms. Evidently such a transition cannot alter in any way significantly either the concentration of conductivity electrons or the nature of the filling of the *d* band and it cannot influence greatly the adsorption and catalytic properties [of the metal]. This proof has been quoted also in other communications[14,15] in which deposited palladium catalysts were considered. Many investigators altogether cast doubt on such an approach, in which conductivity electrons are regarded as being responsible for the catalytic and adsorption properties of the metal. Furthermore, there is no certainty that the Schottky theory is applicable to the metal–carrier interface in real catalysts, because the potential jump at the interface may be due to the presence of extraneous poorly conducting layers between the metal and the semiconductors, for example layers of oxides as well as chemical impurities or lattice defects on the surface. Nevertheless, despite the clear deficiencies of the collective approach, some investigators[16,17] attempted in recent

years to use it to account for the mechanism of the influence of the carrier on the catalytic and adsorption properties of the deposited metal. For platinum deposited on TiO_2 to which Ta^{5+}, Sb^{5+}, or W^{6+} had been added to increase the electronic conductivity of the carrier, a model has been proposed,[18] according to which a platinum particle 20 Å in diameter creates on the carrier an electron-depleted semispherical zone with the radius r = 640 Å (Fig. 1). The authors suggest that electron transfer to platinum reaches an extent sufficient to alter the properties of the deposited metal compared with platinum on a non-doped TiO_2 after reduction at 473 K.

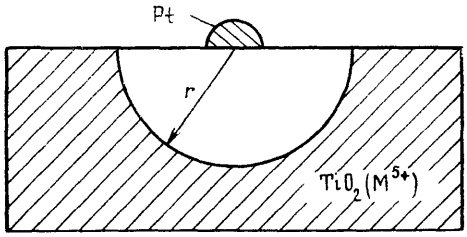


Figure 1. Model of the location of platinum crystals on the surface of modified TiO_2.[18]

Explanations associated with the local interaction of the metal atoms with a definite centre on the carrier surface are better founded.

TiO_2, which is reduced, losing O_2 on heating *in vacuo*, is the most typical carrier for the SIMC effect.[5] Hydrogen, dissociatively adsorbed on the deposited metal is capable of reducing TiO_2 at elevated temperatures. According to EPR spectroscopic data,[19] the deposited Ti/TiO_2 catalyst contains about 0.3% of Ti^{3+} ions after reduction in H_2 at 573 K. The ions are formed by the reaction

$$Ti^{4+} + O^{2-} + H = Ti^{3+} + OH^-.$$

Four different forms of Ti^{3+} have been observed for the same system,[20] two of which are on the surface and are sensitive to the adsorption of CO and H_2 and one form, with $g_\perp$ = 1.969 and $g_\parallel$ = 1.936, is present only on Pt/TiO_2 and is absent from reduced TiO_2. Reduction at 773 K leads also to the formation of anionic vacancies (Y) on the carrier surface:

$$2Ti^{4+} + 2O^{2-} + 2H = 2Ti^{3+} + O^{2-} + H_2O + Y.$$

Further, it has been noted in a review[5] and in a later study[20] that it is by no means always possible to detect the signal due to Ti^{3+} in the EPR spectra. Moreover, the ease of the migration of the anionic vacancies from the surface into the bulk of the carrier has been emphasised.[21] Thus reduced TiO_2 constitutes a mobile system with surface and bulk-phase anionic vacancies, OH^- anions, and Ti^{3+} cations in a state of dynamic equilibrium. We may note that, apart from isolated Ti^{3+}, the appearance of conducting Magneli phases (Ti_nO_{2n-1}) has been observed in deposited metallic catalysts reduced at 743 and 773 K.[22,23] The deposition of the metal (in the given instance Pd) reduces the electron work function of the Magneli phases and prevents their oxidation in O_2 at 300 K.[22]

Experiments using XPS, ^1H NMR, EPR, and the adsorption of H_2 demonstrated that at temperatures above 573 K the hydrogen adsorbed on the metal (Ni, Pt, Rh) spills over into the oxygen vacancies of the reduced TiO_2 with formation of the hydride-like forms $Ti-H^{3+}$.[24]

It is noteworthy that the relation between the SIMC effect and the anatase–rutile transition in deposited metallic catalysts reduced at 643–873 K has been emphasised in a number of recent studies.[25–27]

In the definition of the term SIMC,[1] it was postulated that a covalent bond is formed between the metal atom and the Ti^{3+} cation formed on reduction of the carrier. Quantum-chemical calculations for the interaction of platinum and TiO_2 using two cluster models (Fig. 2)[28] confirmed the validity of this hypothesis. The model (II) in which platinum atoms are inserted in the oxygen vacancies of the carrier with formation of a bond between Pt and Ti^{3+}, is more convenient. Not only a covalent interaction but also an ionic interaction involving the transfer of an electron from Ti^{3+} to a Pt atom takes place in this model. The disposition of the metal atoms outside the TiO_6 octahedron gives rise to only weak interaction as a consequence of the repulsion between Pt and the nearest O^{2-} ions. Indirect evidence for the metal–carrier interaction in highly disperse metallic systems has been obtained by spectroscopic methods. Thus it has been shown by the XPS method[29] that, after the reduction in H_2 at 773 K, the binding energy of the $4f_{7/2}$ level of Pt in the 5% Pt/TiO_2 system diminishes by 9.4 eV compared with the same specimen reduced at 473 K. Electron transfer from TiO_2 to Ni atoms has been observed by the XPS and AES methods in the Ni/TiO_2 system in which nickel was deposited in a thin layer on TiO_2 subjected to a preliminary vacuum treatment at 673 K.[30] The degree of electron transfer is 0.1 of an electron per Ni atom.[30] An increase in electron density on the Rh and Pt clusters as a result of their interaction with Ti^{3+} cations after high-temperature reduction has been observed by the XPS, AES, SIMS, and ISS methods.[31] Within the framework of this model, it is easy to explain the disruption of the SIMC effect by O_2, which leads to the disappearance of oxygen vacancies in the carrier and hence of Ti^{3+} cations.

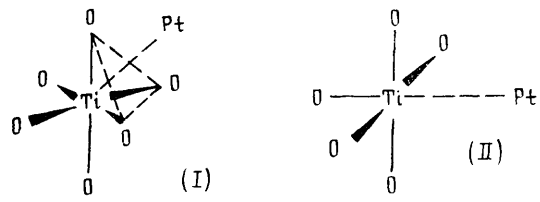


Figure 2. Cluster models for quantum-chemical calculations for the local interaction of a Pt atom with TiO_2.[28]

Direct evidence for the formation of a direct $Rh-Ti^{n+}$ chemical bond in the Rh/TiO_2 catalyst after reduction at 773 K[32] and of the $Rh-Ta^{n+}$ bond in the Rh/Ta_2O_5 catalyst after reduction at 858 K[33] has been obtained recently by the EXAFS method, the cation of the carrier being located in the first coordination sphere of Rh with a radius of 2.55 Å (2.68 Å in the Rh–Ti alloy) and about 1.7 Å

(2.73 Å in the Rh–Ta alloy) respectively. On the other hand, if the Rh/TiO_2 catalyst is obtained not by impregnation with a $RhCl_3$ solution but by the reaction of $Rh(\eta^3\text{-}C_3H_5)_3$ with the OH groups on the TiO_2 surface and subsequent reduction, then according to the EXAFS and electron microscopic data, thin three-layer positively charged Rh clusters are formed on the TiO_2 surface (Fig. 3) and interact strongly with the surface oxygen which remains in the catalyst even after reduction in H_2 at 773 K.[34]

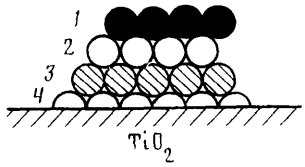


Figure 3. The structure of a Rh cluster fixed on the surface of TiO_2: *1–3*, upper, second, and first layers of rhodium atoms respectively; *4*, layer of oxygen ions of the carrier.[34]

An interesting approach to demonstrating the interaction of the Ni clusters with Ti^{3+} in the Ni/TiO_2 system has been used in a study[35] where the properties of the nickel deposited on the SiO_2 surface, modified by Ti^{3+} cations as a result of the attachment of $Ti(BH_4)_3$ and subsequent removal of the ligands *in vacuo* at 423 K, proved to be close to those of the Ni/TiO_2 catalyst reduced at 773 K. A similar result was obtained for palladium deposited on the SiO_2 surface and the surface of carbon doped with Pr^{3+} cations via organometallic precursors.[36] However, the SIMC mechanism examined above is not apparently the only one.

The possibility of a strong interaction of the deposited metal with the acid centres of the carrier has been frequently pointed out in the literature. For example, Zur Loye et al.[37] investigated the magnetic properties of the 1% Ni/TiO_2 catalyst prepared in different ways. It was then found that extrapolation to zero field of the specific magnetisation (σ) of the catalyst obtained by ion exchange and reduced at 773 K yields a value close to σ for the metallic nickel powder, while σ for the catalyst obtained by the impregnation method is diminished after reduction under the same conditions and corresponds to the reaction of 36% of the nickel with TiO_2. It has been suggested that the difference in the behaviour of the given system is due to the difference in the concentration of the surface OH groups, which is greatly reduced in the specimen obtained by ion exchange.

If one postulates the interaction of the metal with the acid centres, then the SIMC effect should be manifested on zeolites, aluminosilicates, Al_2O_3, ZrO_2, modified SiO_2, and other carriers with acid properties. The occurrence of electronic interaction between Ru clusters and Lewis and Brønsted acid centres has been demonstrated by IR spectroscopy and the thermoprogrammed reduction method in a study[38] of a series of ruthenium catalysts deposited on SiO_2, Al_2O_3, $SiO_2.Al_2O_3$, and an HY zeolite. The increase in acidity in the sequence $SiO_2 < Al_2O_3 < SiO_2.Al_2O_3 < HY$ is correlated with the increase in the electron deficiency on the Ru centres for the adsorption of CO. An XPS study of Ni, Pd, Re, Rh, Ru, and Pt, deposited on SiO_2, $\gamma\text{-}Al_2O_3$, and zeolites established that the metals interact to the maximum extent with zeolites, which is probably due to the presence in the latter of the strongest acid centres.[39] According to XPS, EXFAS, and electron microscopic data, the 6–7 and 11–13 Å Pt_{18} and Pt_{45} clusters located within the structure of the H-ZSM-5 zeolite are coordinated to the skeletal oxygen even after reduction at 773 K and exhibit an appreciable electron deficiency.[40] The interactions of platinum with the acid centres of L-zeolites modified by alkali and alkaline earth metal cations, after reduction at 623 K as a result of charge transfer, have been reported in a study[41] where the catalytic activity of the Pt/L-zeolite system was investigated in the hydrogenation of benzene and toluene.

Another example of the interaction of a metal with definite centres on the carrier is provided by the formation of paramagnetic Pt^{3+} cations on heating in O_2 of ammineplatinum deposited on Al_2O_3, which apparently takes place in the presence of a Lewis acid centre on the carrier surface:[42]

$$O^{2-}\text{—}Pt^{4+}\text{—}O^{2-} \xrightarrow{\text{reduction}} \square\, Pt^{2+}\text{—}O^{2-} + {}^1/_2O_2,$$
$$\square\, Pt^{2+}\text{—}O^{2-} + L\text{—}Al_2O_3 \xrightarrow{\text{heating}} \square\, Pt^{3+}\text{—}O^{2-} + L^-\text{—}Al_2O_3.$$

In general, the question of the relation between the SIMC and the acid properties requires a serious systematic study, which may yield interesting results when the acid carriers investigated in recent years (such as TiO_2, modified Al^{3+},[43] $\gamma\text{-}Al_2O_3$ treated with $SiCl_4$ [44] and tetraethoxysilane[45] vapours, the chemically mixed $TiO_2\text{–}SiO_2$, $TiO_2\text{–}Al_2O_3$, $Al_2O_3\text{–}SiO_2$, and $ZrO_2\text{–}SiO_2$ carriers,[46–48] and SiO_2 modified by the Sc^{3+}, Mg^{2+}, Fe^{2+}, Zn^{2+}, Al^{3+}, and Ga^{3+} cations[49]) are used for the preparation of deposited metallic catalysts.

Thus the explanations of the SIMC effect within the framework of local ideas reduce to a change in the electronic state of the metal atom and hence of the catalytic and adsorption properties under the influence of some kind of centre on the carrier surface. This is apparently true of an atomically disperse metal and small two-dimensional crystals and also of the atoms in larger metallic particles at the metal–carrier interface.[8]

2. Migration of the carrier onto the surface of metallic particles and encapsulation of the metal in the carrier

The appreciable changes in the properties of metallic particles whose size is 50 Å and more after high-temperature reduction cannot be explained solely by electronic effects. Several groups of investigators[50,51] put forward a hypothesis according to which part of the surface of metallic crystallites is shielded by the partially reduced TiO_2. A series of careful experiments carried out in 1984 confirmed the validity of this hypothesis.[52–54] It was found that TiO_x (where $x < 2$) has the surprising ability to migrate over considerable distances in a short time. For example, in an H_2 atmosphere at 698 K, TiO_x fragments appear on the surface of 120 Å thick nickel film deposited on TiO_2 after only 10 min, including the time necessary for the reduction of the TiO_2 surface.[54] The surface of platinum or rhodium film 30 Å thick on TiO_2 reduced beforehand are half-coated by a TiO_x monolayer after keeping the specimens in H_2 at 673 K for 2 min.[9] The mechanism of the migration of TiO_x is nevertheless not clear. On the one hand, in certain studies[54,55] the diffusion of TiO_x within the crystallites of the deposited metal has been demonstrated and, on the other, since the migration is frequently rapid it is logical to postulate that the carrier penetrates between the grains of the metal.[56] At any rate, the migration requires the dissociation of bonds in the crystal lattice of the carrier

and this can occur when the loss of the Madelung energy is made good by the stronger TiO_x–metal interaction. Thus the appearance of a TiO_x layer on the surfae of the metal supports the SIMC. We may note that not only the TiO_x phase can shield the surface of the deposited metallic particles. On the basis of the results of studies of the adsorption of H_2 and O_2, XPS, and electrical conductivity of the Ni/TiO_2 catalysts reduced at 623 and 773 K and having a nickel particle size of 100–200 Å, the following picture of the phase distribution has been put forward[57] (Fig. 4). Depending on the NiO content, on the surface of the initial catalyst there is either the nickel titanate phase (at a NiO concentration $\leqslant$ 35 mol%) or a mixture of nickel titanate and the NiO phase (at a NiO concentration > 35 mol%).[58] The reduction of 623 K is accompanied by the appearance of Ni crystals stabilised on the surface layer of the $Ni_\delta Ti_{1-\delta}O_2$ solid solution, which partly shields the Ni surface, and of the TiO_x bulk phase. The increase in temperature to 773 K leads to the decomposition of the $Ni_\delta Ti_{1-\delta}O_2$ solid solution and the formation on the surface of the conducting TiO_x of large nickel crystals, whose surface is shielded by the same TiO_x phase.

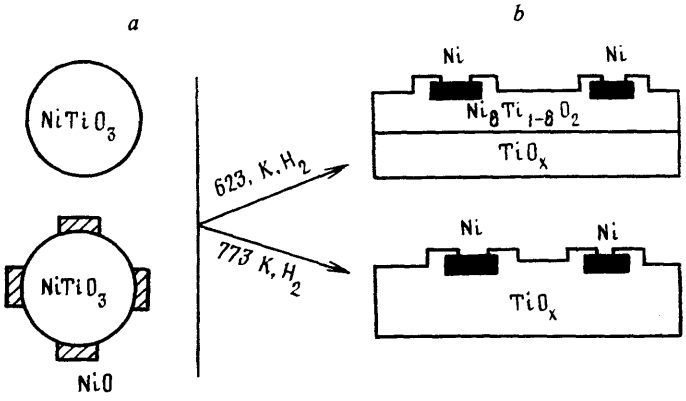


Figure 4. Distribution of the phases on the surfaces of initial (*a*) and reduced (*b*) nickel catalysts deposited on TiO_2.[57,58]

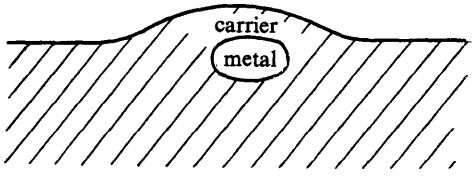


Figure 5. Model of a fully encapsulated metal particle.

The effect involving the spreading of the carrier on the metal surface during reduction is observed not only in metal–TiO_2 catalysts but also in the systems Ni/Nb_2O_5 at 773 K,[59] Ni/CeO_2 at 673 K,[60] and Pt and Rh/V_2O_3 at 773 K [61] and also for carriers which are difficult to reduce such as La_2O_3 in the Pd/La_2O_3 catalysts at 573 K,[29] ZrO_2 in the Rh/ZrO_2 catalysts at 873 K,[62] and SiO_2 modified with WO_3 in the Pt/WO_3–SiO_2 catalysts at 673 K.[29] In the last instances, the spill-over of hydrogen plays a major role in the reduction of the carriers to ZrO_x (with $x < 2$) and WO_2. Apparently even SiO_2 and Al_2O_3 exhibit some mobility in H_2 at high temperatures (about 1200–1300 K) and are capable of partially shielding the surface of the deposited metal.[4] On the other hand, there are carriers which migrate at an even higher rate than TiO_x. Thus an appreciable amount of MnO_x has been detected after heating for only 100 s *in vacuo* at 503 K on nickel films 150 Å thick deposited on MnO.[63]

We may note that the term "encapsulation", which means the immersion of the metallic particle in the carrier, is used fairly frequently in the literature.[64,65] Ultimately, the total encapsulation of the metal (Fig. 5) differs from the total shielding of the metal surface by the carrier perhaps only by the fact that the encapsulated metal does not recover its properties after oxidative treatment,[66] while in the case of the shielded metal in O_2 the carrier film becomes segregated and the metal surface is significantly freed with partial or complete removal of the SIMC effect after further mild reduction (Fig. 6).

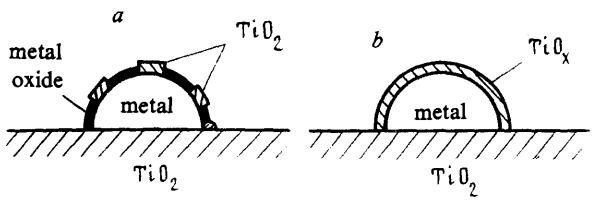


Figure 6. Model of the shielding of the metal surface by the carrier for different types of treatment: *a*, O_2, 673 K; *b*, H_2, 773 K.

Tauster, Vannice, Haller, Dumesic and over investigators,[9,24,29,31,67,68] who studied in detail the SIMC effect, frequently drew attention to the fact that often the carrier does not simply creep mechanically onto the metal, diminishing its surface area, but enters into electronic interactions with it, altering its properties. This can be seen particularly clearly in the study of metals coated by an incomplete TiO_x monolayer.[53,67]

The shielding of the metal surface by TiO_x combined with the electronic interaction is also observed when the metal is deposited on a support modified by TiO_2. Thus the study by XPS and Auger spectroscopic methods of platinum deposited on SiO_2 coated by 1–2 monolayers of TiO_2 showed that, apart from the partial shielding of the metal surface by the TiO_x oxide at high reduction temperatures, anionic vacancies and Ti^{3+} ions are formed and the platinum atoms interact with Ti^{3+}.[69] Admittedly, in contrast to the Pt/TiO_2 catalysts, in the Pt–TiO_2–NiO_2 system the TiO_2 phase exhibits a lower mobility and is more difficult to reduce as a consequence of the formation of strong linkages of the type Si–O–Ti.

3. Thermodynamic factors

In this section we shall consider the thermodynamic aspect of the SIMC effect. Theoretical calculations for the interaction of platinum with TiO_2 have led to the conclusion that, on strong interaction after the high-temperature reduction, the platinum crystallites should become lamellar.[16] This was indeed observed in an electron microscopic study of the Pt/TiO_2 catalyst in an H_2 atmosphere at 1075 K (Fig. 7), TiO_2 being reduced under these conditions to

Ti_4O_7, while the platinum particles on SiO_2 have a spherical shape.[70] Baker[71] showed that in H_2 at 875 K the spreading of platinum takes place after 10 s. Subsequent treatment in O_2 at 875 K of the Pt/TiO_2 catalyst reduced at a high temperature alters reversibly the morphology of the platinum crystals to the spherical form (Fig. 7).[71] From the thermodynamic point of view, this effect can be explained by the fact that platinum wets the surface of the reduced carrier phase more effectively than platinum oxide wets the TiO_2 surface.

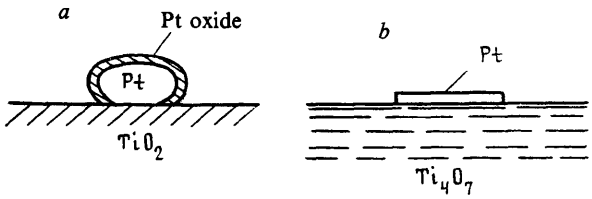


Figure 7. The change in the form of the Pt crystals deposited on TiO_2 and treated in a O_2 atmosphere at 875 K (*a*) and in a H_2 atmosphere at 1075 K (*b*).[70,71]

The spreading of the metal on the surface of the reduced TiO_2 has also been observed for nickel[72] and iron[73] but not for palladium[74] and rhodium.[75]

The existence of lamellar metal crystals is not an unambiguous demonstration of the SIMC. Firstly, this is associated with the experimental difficulty of identifying low-contrast images and, secondly, lamellar crystals have been observed on Ni/SiO_2,[76] Ru/SiO_2,[77] and Ru/Al_2O_3 [78] catalysts where there is apparently no SIMC effect. Evidently in certain systems weak physical forces are insufficient to alter the degree of wetting of the oxide surface by the metal.

The thermodynamic approach can explain also the high mobility of certain carriers coating the metal surface. Ko and Gorte[79] showed that TiO_x and NbO_x wet the platinum surface 5 times more effectively than Al_2O_3 and SiO_2. A comparative study of sorbed TiO_2 and Al_2O_3 layers on nickel yielded similar results. Under these conditions, the TiO_x monolayer occupying 0.1 of the nickel surface alters the catalytic and adsorption properties of the metal to the same extent as for coating by 0.7 of a Al_2O_3 monolayer.[67]

Finally, a thermodynamic model has also been developed for the encapsulation of the metal, according to which the free energy of the deposited system diminishes when the metallic particle is immersed in the carrier provided that the surface energy of the metal exceeds significantly the energy at the metal–carrier interface.[65]

4. The formation of alloys and intermetallic compounds

It was already noted above that the SIMC effect can be manifested also when a metal is deposited on SiO_2 and Al_2O_3. The reduction of the Pt/Al_2O_3 catalyst can be represented by Eqns. (1) and (2). It has been suggested[80] that the formation of a surface alloy via reaction (2) is a more realistic process:

$$Pt + Al_2O_3 \underset{\frac{1}{2}O_2,\ 723\ K}{\overset{H_2,\ 773\ K}{\rightleftharpoons}} Pt \cdot Al_2O_3, \qquad (1)$$

$$Pt + {}^1/_3Al_2O_3 \underset{\frac{1}{2}O_2,\ 723\ K}{\overset{H_2,\ 773\ K}{\rightleftharpoons}} Pt \cdot Al_{2/3}. \qquad (2)$$

The formation of the intermetallic compounds Pt_xAl_y has been observed for a platinum film 200 nm thick deposited on Al_2O_3 after reduction in H_2 at 1200 K [81] and also in a study of the Pt/Al_2O_3 catalyst under an electron microscope at a high temperature under the influence of an electron beam.[82] Magnetic measurements for the Ni/SiO_2 catalyst reduced at about 1180 K demonstrated the presence of the Ni–Si alloy.[83] If such surface alloys and compounds are formed, they can indeed explain the change in the adsorption and catalytic properties of deposited metals.

The change in the properties of the Pt/TiO_2 system can also be due to the formation of surface intermetallic compounds because the reaction

$$TiO_2 + 2H_2 + 3Pt \rightarrow TiPt_3 + 2H_2O$$

is thermodynamically feasible at 773 K.[84] However, in this case it is not possible to observe a shift of the binding energy of the $4d_{5/2}$ level of platinum.[80] The formation of an alloy between a metal and titanium has been observed[1] at temperatures above 1120 K. In general, for metals deposited on TiO_2 the SIMC state is induced by reduction at lower temperatures than are required for the formation of intermetallic compounds such as Pt_3Ti, Ir_3Ti, and Ni_3Ti and, furthermore, metallic titanium could not be identified under any conditions.[85,86] Nevertheless, the presence of two types of Ni–Ti(Ni–Nb) distances has been established by the EXAFS method for the Ni/TiO_2 and Ni/Nb_2O_5 catalysts reduced at 773 K, the shorter distance of 2.62 Å (2.65 Å) being comparable to the distance characteristic of the corresponding alloys.[87] The structure of the carrier is apparently reorganised in the vicinity of the nickel particles. In a recent study[88] using high-resolution electron microscopy and Pt/TiO_2 and Pt/ZnO catalysts reduced at 773 K and above, the intermetallic compounds Pt_3Ti, PtTi, and PtZn were detected. Direct evidence for the formation of RhTi and especially Rh_3Ti after the reduction of Rh/TiO_2 catalysts at temperatures above 623 K has been obtained by the XANES method.[89]

Thus the question of the formation of alloys and intermetallic compounds and of their influence on catalytic and adsorption properties, especially at reduction temperatures in the range 700 to 900 K, remains controversial. However, for certain catalytic systems one must consider the possibility of the extensive reduction of the carrier. For example, the reduction of the Pt/GeO_2 catalyst even at 573 K is accompanied by the formation of the intermetallic compounds Pt_5Ge,[90] while in the case of the Pt–ZnO system, the compound PtZn appears at the metal–carrier interface after treatment in H_2 above 573 K.[91]

III. Manifestations of the effect in deposited metallic catalysts

1. The influence of the SIMC on chemisorption properties

A typical external manifestation of the SIMC effect is the suppression of the chemisorption of H_2 and CO after the high-temperature reduction of metallic catalysts deposited on TiO_2 with retention of the dissociative character of the chemisorption of H_2. Table 1 presents the literature data for the chemisorption of H_2 and O on various metals deposited on TiO_2. After reduction at 473 K, the ratio of the adsorbed H atoms or CO molecules to the total number of metal atoms characterises the dispersity of the metal on the carrier for Ir, Pt, Ru, Rh, and Pd. This ratio decreases sharply

by a factor of 4–7 and more if the catalysts are reduced in H_2 at 773 K. In the latter case, the metal particle size, calculated from the degree of chemisorption of H_2 or CO, does not correspond to the real particle size determined by the X-ray diffraction and electron microscopic methods. Consequently, the decrease in the degree of chemisorption of H_2 and CO is not associated with the increase in the size of the metal crystals during the high-temperature treatment.

Table 1. Chemisorption of H_2 and CO on metals (M) deposited on TiO_2 (50 $m^2\ g^{-1}$).

Metal	T_{red}, K	H/M	CO/M	Refs.
2% Ir	473	1.60	1.19	[1,92]
	773	0.00	0.00	
2% Os	473	0.21	—	[1,92]
	773	0.11	—	
2% Pt	473	0.88	0.65	[1,92]
	773	0.00	0.03	
2% Ru	473	0.23	0.64	[1,92]
	773	0.06	0.11	
2% Rh	473	0.71	1.15	[1,92]
	773	0.01	0.02	
2% Pd	448	0.93	0.53	[1,92]
	773	0.05	0.02	
1.01% Ni	573	0.102	—	[5]
	723	0.064	—	
4.67% Ni	573	0.086	—	[5]
	723	0.055	—	
10% Ni	573	0.099	—	[93]
	773	0.025	—	
15% Ni	725	0.043	—	[76]
	1023	0.001	—	
6.3% Fe	673	—	0.043	[94]
	723	—	0.026	
	773	—	0.012	
	873	—	0.002	
5.0% Fe	723	0.014	0.014	[95]

* T_{red} = reduction temperature.

Similar effects have been observed also for Ni, Fe, and Co deposited on TiO_2. However, a number of features should be noted. Firstly the dispersity of these metals on TiO_2 is usually low (5–10%). Secondly, the extent to which the degree of chemisorption of H_2 diminishes (by a factor of 1.5–2) after the high-temperature reduction is smaller. The clear effect for the 15% Ni/TiO_2 catalyst after reduction at 1023 K (Table 1) is evidently associated with the encapsulation of nickel in the carrier.

The adsorption of H_2 is suppressed after the high-temperature reduction of metals, which may also be deposited on carriers other than TiO_2. The chemisorption of H_2 on iridium-containing catalysts has been investigated.[2] The results are compiled in Table 2.

Tauster emphasised the correlation between the reduction temperature required for the appearance of the SIMC effect and the susceptibility of the oxide carriers to reduction. For the iridium systems, the following series of carriers can be formulated in terms of the decrease in the reduction temperature required to suppress the chemisorption of H_2: $ZrO_2 > Ta_2O_5 > TiO_2, V_2O_3 > Nb_2O_5$,[2,92] although the H/Ir ratios after reduction at 774 K are similar for all the catalysts, except Ir/ZrO_2, and are in the range 0.06–0.01.

Table 2. Chemisorption of H_2 on deposited Ir catalysts.[2]

Metal content, %	Carrier (S_{sp}^*, $m^2\ g^{-1}$)	T_{red}, K	H/Ir
2	TiO_2 (145)	393	1.17
		523	0.32
		774	0.02
1	V_2O_3 (11)	476	0.84
		624	0.11
		774	0.046
1	Ta_2O_5 (135)	573	1.01
		774	0.06
		976	0.015
1	Nb_2O_5 (26)	476	0.67
		724	0.04
		774	0.01

* S_{sp} = specific surface.

It is possible to quote examples also of other deposited metals. Thus the chemisorption of H_2 on 7.5% Ni/CeO_2 diminishes by a factor of 20 on raising the reduction temperature from 523 to 673 K, on the 3% Rh/Ta_2O_5 catalyst the decrease is by a factor greater than 15 after reduction of 858 K,[33] and on the 15% $Ni/TaO_2–ZrO_2$ catalyst the decrease is by a factor of approximately 8 after raising the reduction temperature from 573 to 793 K.[96]

The decrease in the capacity for chemisorption is frequently accompanied by qualitative changes. The decrease in the initial heats of adsorption of H_2 on the Pt/TiO_2 catalyst from 22.2 to 19.1 kcal mol^{-1} and in the average heats of adsorption from 14.9 to 12.9 kcal mol^{-1} on raising the reduction temperature from 523 to 773 K has been reported.[97] Using the thermoprogrammed desorption method and IR spectroscopy, Raupp and Dumesic[67] showed that, when TiO_x flows onto the nickel surface, the strong centres for the adsorption of CO (apical nickel atoms) with a desorption activation energy of about 134 kJ mol^{-1} are blocked and CO is then sorbed on weaker centres which are not occupied in adsorption on a clean nickel surface owing to the appreciable repulsion between the CO molecules. The long-range electronic influence of TiO_x is believed to be responsible for the decrease by 6 kJ mol^{-1} in the strength of the bonding CO for a degree of surface coverage of nickel by TiO_x of 0.1. The slow absorption of H_2 after the high-temperature reduction of the Ni/TiO_2 and Pt/TiO_2 catalysts, accompanied by a decrease in the strength of adsorption, has been observed.[98] The authors explain this by the slow binding of hydrogen at the metal–carrier interface or on the TiO_x coating of the surface of the metallic particles.

In a study of the states of adsorbed CO on the Ni/TiO_2 surface (film 120 Å thick on a thin layer of TiO_2), reduced at 700 K, and on the surface of nickel single crystals, the high-resolution spectra of the

electron energy losses for the deposited nickel showed a faster decrease in the intensity of the 1910 cm^{-1} band (bridging form of CO) as a function of the duration of the treatment of the specimen in H_2 compared with the intensity of the 2020 cm^{-1} band (linear form) owing to the blocking of the surface nickel centres by the TiO_x phase similar to the cluster effect in the alloys.[54] A similar blocking of the nickel centres by the oxide MnO_x (where $x = 0.2-0.5$), whereupon the amount of chemisorbed CO decreases linearly with increase in the area of the shielded metal surface, has been observed after the reduction of Ni(III) single crystals coated by MnO_2.[99] In addition, the appearance of new forms of CO adsorbed at the sites of contact between the nickel particles and the MnO_x "islands", to which corresponds a peak at 305 K in the thermal desorption spectrum and a 1620 cm^{-1} band in the high-resolution electron energy loss spectra has been noted. Vannice et al.[68] state that the band in the IR spectra of CO adsorbed on the Pt/TiO_2 catalyst shifts from 2050 cm^{-1} to 2070 or 2080 cm^{-1} after high-temperature reduction and explains this by the weakening of the Pt–C bond as a consequence of the increase in the filling of the *d* orbitals of platinum in the SIMC state.

As a rule, in the SIMC state the CO/H ratio increases for platinum group metals approximately from 1 to 2 –3,[5] while for Ni, Fe, and CO the ratio CO/H usually changes to a lesser extent.

In the joint adsorption of H_2 and CO on the nickel surface partly coated by TiO_x, the bond between CO and nickel is weakened and the concentration of the strongly bound hydrogen increases by 1–2 orders of magnitude compared with the clean nickel surface, i.e. in this case hydrogen competes successfully with CO for the adsorption centres on nickel.[72]

One of the features of the SIMC effect is its partial or complete reversibility after treatment in O_2 at 673 K [100,101] and after the adsorption of O_2 at 298 K [5] with subsequent mild reduction in H_2 (Fig. 5), which leads to the recovery by the deposited metal of its normal adsorption capacity in relation to H_2 and CO.

At the end of the 1970s, it was believed that the chemisorption of H_2 and CO is not suppressed on metals deposited on SiO_2, Al_2O_3, and certain other non-reducible carriers. However, subsequent experiments showed a decrease in the degree of chemisorption of H_2 on Ni/SiO_2 (reduction temperature 1120–1180 K) by a factor of 3–7 compared with Ni/SiO_2 (920 K) [83] and on Pt/Al_2O_3 reduced at 773 K (the extent to which the degree of chemisorption diminishes depends on the form of Al_2O_3).[102] For the Ni/Al_2O_3 catalyst (873 K), the nickel particle size, determined from the degree of chemisorption of H_2, is greater than the value estimated from electron microscopic data and the strength of the adsorption of H_2 on nickel is diminished owing to the interaction of the metal with the carrier, while the CO/H ratio reaches 4.4.[103]

The introduction into SiO_2 of the TiO_2 or Nb_2O_5 additives in an amount corresponding to one monolayer leads to the SIMC effect in the Ni/TiO_2 (Nb_2O_5)–SiO_2 catalysts reduced at 673 K. In this case, the catalysts can be arranged in the following sequence in terms of the degree of suppression of the chemisorption of H_2: Ni/TiO_2 (Ni/Nb_2O_5) > Ni/TiO_2-SiO_2 ($Ni/Nb_2O_5-SiO_2$) > Ni/SiO_2.[104,105] A similar result has been observed of 1% Pt/Al_2O_3 after the introduction of 4% of Ti into the carrier.[106] In contrast to CO and H_2, the chemisorption of O_2 on deposited metallic catalysts, calculated per m^2 of the metal surface, does not change on raising the reduction temperature of the catalyst, while the size of the metal particles, determined from the degree of chemisorption of O_2 and X-ray diffraction and electron microscopic data, remains unaltered. A change in the stoichiometry of the adsorption of O_2 at room temperature on the Ni/TiO_2 catalyst prepared by impregnating TiO_2 with nickel(II) chloride (O/Ni_{surf} = 1),† compared with Ni/SiO_2 and Ni/Al_2O_3 (O/Ni_{surf} = 2) reduced as 773 and 573 K, and also on the Ni/TiO_2 obtained by impregnating TiO_2 with nickel(II) nitrate, has been noted[107] on raising the reduction temperature from 573 K (O/Ni_{surf} = 2) to 773 and 973 K (O/Ni_{sur} = 1). This conclusion is based on the comparison of the nickel particle sizes estimated from the degree of chemisorption of O_2 and X-ray and magnetic measurements. For the stoichiometries presented above, these dimensions agree satisfactorily. It is noteworthy that the nature of the carrier can influence not only the stoichiometry of the adsorption of O_2 but also the strength of its bond with the deposited metal. For example, the Ir–O bond strength is greater when iridium is deposited on the highly basic MgO surface than on deposition on $Al_2O_3-SiO_2$.[108]

Additional information about the SIMC states can be extracted with the aid of the adsorption of N_2. Resasco and Haller[109] reported that, on reducing the reduction temperature of the 2% Rh/TiO_2 catalyst, the degree of adsorption of N_2 at 523 K increases, while the degree of adsorption of CO at 298 K is suppressed (Table 3). These effects were not observed on the 2% Rh/Al_2O_3 catalyst.

Table 3. The influence of the catalyst reduction temperature on the adsorption of N_2 at 523 K and of CO at 298 K on the 2% Rh/TiO_2 catalyst.[109]

T_{red}, K	CO/Rh	N_2/Rh	N_2/CO
773*	0.01	0.023	0.032
473*	0.7	0.01	0.01
773*	0.01	0.024	0.034

* Repeated reduction after treatment in O_2 at 673 K.

Although Burch and Flambard[110] did observe an increase in the degree of adsorption of N_2 at 273 K on the 1% Ni/TiO_2 and 5% Ni/TiO_2 catalysts reduced at 723 K compared with the 1% Ni/SiO_2 and 5% Ni/SiO_2 catalysts, they concluded that the adsorption centres are the Ti^{3+} cations located next to the oxygen vacancies because reduced TiO_2 adsorbed more N_2 per unit carrier surface than the Ni/SiO_2 catalysts, while non-reduced TiO_2 altogether failed to adsorb N_2. In the presence of nickel, the adsorption capacity of TiO_2 increased by virtue of the ready reduction of TiO_2 by the atomic hydrogen formed on nickel. Thus the increase in the amount of N_2 adsorbed on deposited metallic catalysts with increase in the preliminary reduction temperature can be regarded as one of the signs of the occurrence of the SIMC, although its interpretation is controversial.

† Ni_{surf} represents nickel atoms on the surface.

2. Catalytic properties and the strong interaction of metal with the carrier

The SIMC effect is manifested not only in the adsorption properties but also in the catalytic properties of deposited systems. With increase in the temperature of the reduction of metals deposited on TiO_2, a decrease in their activity is observed in the hydrogenolysis of hydrocarbons, the hydrogenation of benzene, the dehydrogenation of cyclohexane, and the isomerisation of methylpentanes. On the other hand, an increase in activity in the D_2-H_2O exchange and in the H_2 + CO and NO + CO reactions as well as the change in selectivity in the CO + H_2 reaction had been observed compared with metals deposited on SiO_2 and Al_2O_3 or on non-deposited metals.

We shall consider initially the structure-sensitive (in terms of Boudart's classification[111]) reactions of hydrocarbons such as hydrogenation, dehydrogenation, and isomerisation.

The experimental data for the benzene hydrogenation and cyclohexane dehydrogenation reactions on Rh, Ir, and Pt deposited on TiO_2 (Table 4) indicate a decrease in the activity of the Ir and Pt catalysts by an order of magnitude with increase in their reduction temperature.

Table 4. The influence of the reduction temperature of the metals deposited on TiO_2 on their activity in hydrogenation and dehydrogenation reactions.

M, %	T_{red}, K	10^{-2} W*, molecules M_{surf}^{-1} s^{-1}	Initial reactants	Refs.
3.2% Rh	473	3.0	$C_6H_6 + H_2$	[112]
	793	2.4		
2% Rh	573	6.0	C_6H_{12}	[100]
	773	4.7		
2.7% Ir	473	1.2	$C_6H_6 + H_2$	[112]
	793	0.1		
6.8% Pt	473	3.68	C_6H_{12}	[113]
	793	0.24		
4.8% Pt	473	1**	$C_6H_6 + H_2$	[90]
	773	0.08**		

* W is the catalyst activity.

** Relative to the activity of the specimen reduced at 473 K.

For the hydrogenation of benzene at 403 K, the activity of the 9.8% Ni/TiO_2 catalyst, reduced at 723 K, is 44 × 10^3 molecules s^{-1} Ni^{-1}, which is smaller by a factor of 4.75 than the activity of the same catalyst reduced at 523 K and by a factor of 3.61 than the activity of the 9.8% Ni/SiO_2 catalyst reduced at 723 K.[114] The decrease in the degree of conversion of benzene in hydrogenation at 393 K from 83 to 30% with increase in the catalyst reduction temperature from 673 to 793 K respectively has been observed on a catalyst containing 15% of nickel and deposited on a TiO_2-ZrO_2 mixed carrier (TiO_2/ZrO_2 = 1/1),[96] the SIMC state being abolished after the subsquent oxidation and reduction of the specimen at 573 K.

The relative probabilities of desorption and hydrogenation in the reaction of ethylene with deuterium have been determined.[115] It was found that the probability of the desorption of ethylene from Pt/TiO_2 is six times greater than from Pt/SiO_2. The authors explain this by the decrease in the strength in the absorption of ethylene on Pt/TiO_2 as a result of electron transfer from the carrier to the metal, although one should note that the catalyst was reduced at 573 K.

In the isomerisation of methylpentanes on the Pt/TiO_2 catalyst, the specific activity was smaller by a factor of 50 than on the Pt/Al_2O_3 catalyst, while the adsorption of hydrogen was suppressed slightly.[116] The isomers are formed mainly via the mechanism involving the migration of bonds in intermediate compounds.

The structure-sensitive hydrogenolysis reactions of saturated hydrocarbons and the interactions in the CO + H_2 reaction constitute a good test of the change in catalytic properties under the influence of the SIMC.

Table 5 presents data obtained[117] for the hydrogenolysis of ethane at 478 K on metals deposited on TiO_2 and SiO_2, reduced at 773 K for 16 h. It is noteworthy that the specific activity was calculated assuming 100% dispersity of the metal on TiO_2, which does not introduce serious errors for noble metals. However, this hypothesis is incorrect for Fe, Ni, and Co, because their dispersity is usually in the range 5–10%. Thus the real relative decrease in activity is greater by a factor of 10–20 than the values quoted in Table 5. Furthermore, iron in the SIMC state is almost inactive probably owing to the encapsulation effect. In terms of the decrease in the activity of the metal by the SIMC in the hydrogenolysis of ethane compared with the activity in the state of a weak interaction (M/SiO_2), the Group VIII noble metals can be arranged in the following sequence: Pt > Pd > Os, Ir > Rh > Ru, the activity of Ru remaining unchanged.

Table 5. The activities of deposited Group VIII metals, reduced at 773 K, in the hydrogenolysis of ethane at 478 K.[117]

M	W, mol h^{-1} m^{-2}		Relative specific activity of SiO_2/TiO_2
	SiO_2	TiO_2	
Fe	$1.2\cdot10^{-5}$	$<10^{-13}$	$>10^8$
Co	$3.4\cdot10^{-5}$	$1.0\cdot10^{-9}$	$3.4\cdot10^4$
Ni	$8.0\cdot10^{-4}$	$8.0\cdot10^{-7}$	10^3
Ru	$1.8\cdot10^{-3}$	$1.4\cdot10^{-3}$	1.3
Rh	$2.2\cdot10^{-4}$	$2.9\cdot10^{-5}$	7.6
Pd	$6.7\cdot10^{-10}$	$2.6\cdot10^{-13}$	$2.6\cdot10^3$
Os	$4.2\cdot10^{-2}$	$9.6\cdot10^{-5}$	$4.4\cdot10^2$
Ir	$1.1\cdot10^{-4}$	$3.0\cdot10^{-7}$	$3.7\cdot10^2$
Pt	$7.2\cdot10^{-10}$	$<10^{-13}$	$>7\cdot10^3$

A sharp decrease in the activity in the hydrogenolysis of n-butane and neopentane in the presence of Ir/TiO_2 in the SIMC state,[118] in the hydrogenolysis of n-hexane in the presence of Pt/TiO_2 [90] and Ni/TiO_2,[114] and in the hydrogenolysis of n-heptane in the presence of Ru/TiO_2 [119] has been noted.

On deposition of 9% of nickel on SiO_2 coated by a monolayer of TiO_2, the activity of nickel in the hydrogenolysis of ethane falls by 2–3 orders of magnitude compared with its activity on SiO_2.[104] A decrease in the activity of the 9% Ni/SiO_2-TiO_2 system from 5.6 × 10^{-5} to 9.5 × 10^{-6} molecules s^{-1} Ni_{surf}^{-1} with increase in the

specimen reduction temperature from 573 to 773 K has also been noted.

Such effects are not characteristic of catalysts with a TiO_2 carrier alone. Thus, on raising the reduction temperature of the 10% Ni/Nb_2O_5 system from 573 to 773 K, its activity in the hydrogenolysis of ethane falls by a factor of 35,[120] while the activity of the 9% $Ni/Nb_2O_5-SiO_2$ catalyst (Nb_2O_5 monolayer on a SiO_2 surface) diminishes under similar conditions by a factor of 14.[105]

The catalytic properties of deposited metals in the SIMC state have been studied in greatest detail in the CO + H_2 reaction, their activity being significantly higher than that of the metal single crystals and metals deposited on Al_2O_3 and SiO_2. Table 6 presents the activities for the Ru, Rh, Pt, and Ir catalysts.

Table 6. Specific activities of deposited Group VIII noble metals in the CO + H_2 reaction at 548 K and for the ratio CO/H_2 = 3.

M, %	T_{red}, K	$10^3 W$, $M_{surf}^{-1} s^{-1}$	Relative activity		Refs.
			$\frac{M/TiO_2}{M/Al_2O_3}$	$\frac{M/TiO_2}{M/SiO_2}$	
2% Ru	723	320	1	1	[95]
1% Rh	673	321	8.2	57	[121]
2% Rh	723	430	25	36	[95]
1.86% Pt	448	5.5	1	25	[122]
1.86% Pt	773	40	7	200	[122]
2% Pt	723	130	38	65	[95]
2% Ir	723	45	17	45	[95]

Evidently the specific activity of the M/Al_2O_3 catalyst is higher than that of the M/SiO_2 catalyst (the activity of the latter is comparable to that of the non-deposited metals). This is usually explained by the greater extent of the interaction of the metal with the carrier for the M/Al_2O_3 systems.[5] A strong interaction of the metal with the carrier does not affect the activity of Ru, which is correlated with the ease of the spreading of Ru on the surfaces of different carriers.[77,78] However, the selectivity of Ru/TiO_2 in relation to C_2 hydrocarbons and hydrocarbons with higher molecular weights is appreciably higher.[123] The specific activity of Rh, Ir, and Pt deposited on TiO_2 is higher approximately by 1 and 2 orders of magnitude than the corresponding values for catalysts deposited on Al_2O_3 and SiO_2, the fact that the activity of Rh/TiO_2 is highest being correlated with the highest reactivity of the CO adsorbed on it.[124] As regards selectivity, the latter does not change appreciably for Ir and Pt, whereas on Rh/TiO_2 and Rh/Al_2O_3 the main reaction product is methane and on Rh/SiO_2 it is methanol.[121,125] The data obtained by Japanese workers for the Rh/TiO_2 and Ir/TiO_2 catalysts[126] conflict with the above results, since the rate constants for the conversion of CO into methane hardly change on transition to the SIMC state. On the other hand, for Pt and Pd in the SIMC state, the rate constant is 10 times smaller than in the "normal" state.[127]

Deposited Fe, Co, and Ni apparently behave differently in the CO + H_2 reaction. Owing to the Fe encapsulation effect, it is difficult to observe the changes in catalytic properties on different carriers. Cobalt deposited on TiO_2, SiO_2, and Al_2O_3 has comparable activities.[4] On the other hand, the SIMC exerts an appreciable influence on the catalytic properties of the Ni/TiO_2 system. This system therefore merits greater attention.

Vannice[95] noted that the activities of various Ni/TiO_2 catalyst specimens, reduced at 723 K, in the CO + H_2 reaction at 548 K exceeds by a factor of 2–37 the activity of Ni/Al_2O_3 and Ni/SiO_2. In another study,[128] the ratio of the activities of the 5% Ni/TiO_2 and 5% Ni/SiO_2 catalysts, reduced at 723 K, was 33.8 at a reaction temperature of 553 K. The change in the activity of Ti in the SIMC state is as a rule accompanied by an improvement of selectivity in relation to higher hydrocarbons. Thus, whereas the selectivity of 9.8% Ni/SiO_2 (reduction temperature 723 K) was 9.3%, for 9.8% Ni/TiO_2 (723 K) it amounted to 27.7%.[114] At a reaction temperature of 600 K, the selectivity in relation to methane reached 99.82% for 9% Ni/Al_2O_3 (700 K), 54.6% for 13% Ni/TiO_2, and 68.1% for 12.5% Ni/Nb_2O_5 (700 K) (reaction temperature 503 K).[129]

The rate-limiting stage in the CO + H_2 reaction in the presence of deposited nickel catalysts is known to be either the dissociation of the adsorbed CO [130] or the hydrogenation of surface carbon.[131] A series of kinetic models have been proposed for the Ni/TiO_2 catalysts in the SIMC state,[132,133] according to which an increase in the fraction of hydrogen adsorbed on the surface, the weakening of the bond between CO and the metal, and other factors examined in detail above increase the rate of the rate-limiting stage. These conclusions have been confirmed by kinetic experiments on the hydrogenation of atomic carbon and the dissociation of CO on nickel-containing catalysts reduced in H_2 at 723 K. It was found that, while the activation energy remains unchanged, the specific rates of hydrogenation of carbon in the presence of nickel on different carriers differ by more than an order of magnitude, diminishing in the sequence Ni/TiO_2 > Ni/Al_2O_3 > Ni/SiO_2.[134] In addition, the order of the reaction with respect to H_2 is twice as great for Ni/TiO_2 as for other catalysts. The dissociation of CO on Ni/TiO_2 is also much faster.

A model has been proposed[114] for the Ni/TiO_2 system containing large nickel particles in which the specific influence of the carrier is restricted to the interface between the metal and the carrier. The increased activity of Ni/TiO_2 in the CO + H_2 reaction can be explained by the appearance of specific centres at the interface on which CO molecules are activated (Fig. 8*a*).

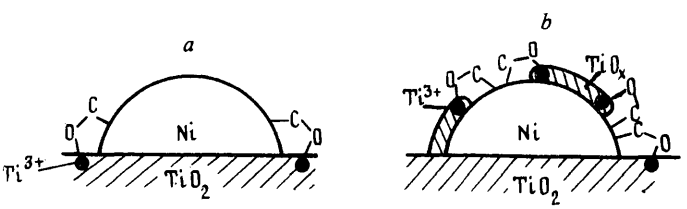


Figure 8. Model of the active centre in the CO + H_2 reaction at the interface between the Ni particle and the surface of the carrier after reduction at 573 K (*a*) and 773 K (*b*).[114]

Ponec[8] and Takatani and Chung[54] hold a similar view. In later investigations,[135] where an increase in activity in the CO + H_2 reaction was not observed for Ni, Pd, and Ir (deposited on TiO_2) in the SIMC state (suppression of the chemisorption of H_2 and of

activity in the hydrogenolysis of ethane), the model taking into account the phenomena at the interface was developed further (Fig. 8*b*). According to the authors,[135] the reduction of the catalyst at temperatures of about 723 K leads to the migration of TiO_2 onto the surfaces of metallic particles and the creation of new superactive centres at the interface. A significant proportion of the less active metallic centres are then shielded and ultimately the overall activity remains almost unaltered.

Chung et al.[136] rejected the model of Burch and Flambard on the grounds of data obtained for sputtered Ni/TiO_2 (100) specimens and for Ni (111) partly coated by TiO_2. They were treated in H_2 at 773 K. The authors believe that, if the active centres were located on the periphery of the nickel "islands", then the maximum concentration of such centres and hence their activity would have been observed for coverages corresponding to 0.6 of a nickel monolayer on TiO_2 or 0.6 of a TiO_2 monolayer on nickel. On the other hand, the highest experimental activity was shown by specimens containing three nickel monolayers on TiO_2 (100) and 8% TiO_x on Ni (111). Furthermore, their catalytic properties proved to be similar. It was concluded that the TiO_x diffusing onto the catalyst surface exerts a decisive influence on the activity of nickel. Similar conclusions (diffusion of CeO_x) have been reported[60] for the Ni/CeO_2 system.

In a number of studies,[129,137,138] the hypothesis was put forward that the changes in activity and selectivity following a change of carrier are associated with the presence of Ni^{n+} in Ni/Al_2O_3 and Ni/SiO_2 and its interaction with Ni^0. It has been suggested that the electron transfer from Ni^0 to Ni^{n+} increases the strength of the C–O bond in the adsorbed state, diminishing the probability of its dissociation. Thus the following series of specific activities (per m^2 Ni) in the CO + H_2 reaction on nickel in the "normal state", expressed in arbitrary units relative to Ni/SiO_2, has been explained[138] by precisely this factor: 14% Ni/TiO_2 (15) > 24% Ni/ZrO_2 (8) > 21% Ni/Al_2O_3 (2) > 24% Ni/SiO_2 (1); the same explanation was also used to account for the selectivity of the Ni/TiO_2 and Ni/ZrO_2 catalysts being higher by factors of 2 and 3 respectively compared with Ni/SiO_2. A decrease in the activity of nickel in the SIMC state has been noted for Ni/TiO_2 and Ni/ZrO_2. Treatment with O_2 and subsequent low-temperature reduction restore the initial activity to these catalysts.

Thus the question of the unique catalytic properties of metals deposited on TiO_2, Nb_2O_5, ZrO_2, and certain other carriers in the CO + H_2 reaction remains open and requires further studies.

Examples of other reactions in which the influence of the SIMC on the catalytic properties of deposited metals was investigated are fairly rarely encountered in the literature. These exist data on the catalytic activity of platinum deposited on TiO_2 doped with the Ta^{5+}, Sb^{5+}, and W^{6+} cations (to test the hypothesis concerning the nature of the SIMC involving electron transfer) in the CO + O_2 and CO + H_2O reactions.[139] Under these conditions, the activity of the doped catalysts in the first reaction is reduced by a factor of 3–5 and the activation energy is increased by 45%, while in the second reaction the activity falls by a factor of 80. An increase in the activity of the Rh/TiO_2 and Pt/TiO_2 catalysts in the SIMC state has been noted[140,141] in the CO + NO reaction. There are contradictory data for the acetone hydrogenation reaction as regards the SIMC effect. Thus a sharp decrease in the activity of the Rh/CeO_2 catalyst has been observed[142] after its reduction at 653 K, while the activity of Pt/TiO_2 in the SIMC state increased appreciably.[143] An elegant study of the catalytic properties of the Ir/Nb_2O_5 system reduced at 473 K ("normal" state) and at 773 K (SIMC state) in the acroleine hydrogenation and deuteriation reactions has been carried out by Japanese workers,[144] who established that mainly allyl alcohol is formed on the catalyst in the SIMC state at 353 K, and not propanol as on the catalyst reduced at 473 K. The activation energy for the formation of the main product falls from 12 kJ mol^{-1} (for the normal state) to 5 kJ mol^{-1}, while the activation energy for the formation of propanol increases from 12 to 35 kJ mol^{-1} respectively. Active centres of two types were identified with the aid of a kinetic study of the rate of formation of each product as a function of the catalyst reduction time in combination with the study of the distribution of the hydrogen isotopes in acroleine, allyl alcohol, and propanal. The formation of propanal, CH_2 = CDCHO, and of part of allyl alcohol and the dissociation of D_2 takes place on purely metallic centres, while CHD = CHCHO and the remainder of the allyl alcohol are formed on metallic centres adjoining the boundary of the NbO_x "islands", which appear on the catalysts reduced at 773 K.

IV. The apparent effects of the strong interaction of a metal with the carrier

It is frequently assumed nowadays that the change in the catalytic properties of deposited metals combined with the loss of ability to absorb H_2 and CO constitutes convincing evidence for the existence of the SIMC. It is therefore useful to examine certain effects erroneously interpreted as true manifestations of the SIMC.

In the first place, the sintering of metallic particles at elevated reduction temperature lowers the activity of the metal surface and hence diminishes its chemisorption capacity and alters the activity and selectivity of the catalyst. It is therefore essential to monitor the metal particle size at different reduction temperatures. Furthermore, the active surface of the metal can decrease as a result of the migration of the metal into the carrier, as in the case of the Fe/TiO_2 system. In this instance, comparison of the specific activities per gramme of the metal with those of other catalysts yields undistorted information only when additional data are secured by adsorption, X-ray diffraction, X-ray photoelectron spectroscopy, analysis of the extended fine structure of the X-ray absorption spectra, etc.

One must not forget that the surface of the metal contaminated in some way (poisoned, for example, by sulphur or iron impurities which may be present in the carrier[145] or the Cl^- anions remaining after the preparation of the catalyst from metal chlorides[107]) is incapable of adsorbing H_2 and CO or can adsorb them to a much lesser extent than the clean surface, and has significantly different catalytic properties. When catalysts consisting of a metal deposited on SiO_2 and especially on Al_2O_3 are obtained by impregnation with acid solutions, a very small proportion of the carrier can dissolve and ultimately, after reduction at elevated temperatures, can form a film or "islands" of oxygen-deficient SiO_x and Al_2O_x on the surface of the metallic particles, as a result of which the properties of the catalyst change qualitatively, as in the metal–TiO_2 system in the SIMC state.[146,147] Thus, on raising the reduction temperature of the Pt/Al_2O_3 and Pd/Al_2O_3 catalysts from 523 to 773 K, their activity in the CO + H_2 reaction at 498 K increases by factors of 5.1 and 1.8 respectively.[146]

It is essential to recall that Group VIII metal cations exhibit a certain tendency to react with aluminium and silicon oxides to form aluminates and silicates, which are difficult to reduce, or solid solutions which are also not easy to reduce on heating.[137,148,149]

If the active specific surface of the metal and the degree of its reduction are known, this does not create serious difficulties in the study of the SIMC. However, account must be taken of the influence of the non-reduced cations on the behaviour of the reduced metal in view of the possible electron transfer.[138,150] There are data showing that certain carriers, especially alumina, can stabilise the metal in intermediate states such as Rh^+, Pt^{3+}, Re^{4+}, and Ni^+ and can thus inhibit their reduction.[151–153]

The energetic, electronic, and geometrical properties of deposited metallic particles can be simultaneously modified by the metal–carrier interactions and by changes in the properties of the metal—both bulk-phase and atomic. Both effects become very important when the size of the metallic particles is reduced and, as noted by Bond[4] and Ponec,[8] it is not always easy to separate the contributions of these two effects to the adsorption and catalytic properties of metals.

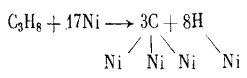
In the analysis of the dependence of the catalytic properties of deposited metallic crystals on their structure, it has been suggested[154] that three cases of structure-sensitive reactions be distinguished: (a) structural sensitivity for which the rate of reaction depends on the dispersity of the crystals which influences the number of specific centres in them (for example B_5 centres) is referred to as the primary structural sensitivity; (b) cases where the rate of reaction is independent of dispersity when the reaction is carried out under "clean" conditions but becomes structure-sensitive on partial poisoning of the surface of the catalyst (as already mentioned above) constitute a group of phenomena which are referred to as secondary structural sensitivity: (c) finally the third type of structural sensitivity may be due to the change in the electronic properties of crystals when their size is altered.

We shall now quote several examples. A study has been made[155] of the influence of the nickel particle size in the range 22–100 Å on selectivity of the propanol hydrogenation reaction at 473 K in the presence of Ni/SiO_2 catalyst. A sharp increase in selectivity with respect to propanol for a nickel particle size less than 50 Å was established. Taking into account the increase in the fraction of apical and edge atoms relative to the total number of surface atoms with decrease in crystal size, the authors concluded that the aldehyde is hydrogenated on edge and apical nickel atoms, while decomposition takes place on the planar surface of the crystal.

Apart from the number of edge and apical atoms and specific centres whose concentration is determined by the dispersity of the crystal, the ratio of different faces, whose activities in relation to the given reaction sometimes differ greatly, may vary on the surface of the crystal.[156] Thus, in order to account for the change in selectivity in the reaction of neopentane on platinum, it has been suggested[157] that neopentane isomerises via its three-point adsorption on atomic triplets located in the (111) plane and that the contribution of the isomerisation reaction increases with increase in the concentration of these faces on the surface. This result was confirmed in other studies.[158,159]

The Ni/SiO_2 catalyst containing nickel crystals oriented along the (111) plane and non-oriented crystals[160] exhibited different catalytic properties in the benzene hydrogenation and cyclohexene disproportionation reactions.[161] Whereas the rates of the first reaction were virtually the same on both catalysts, the second reaction was faster on the oriented crystals.

Analysis of the mechanism of the structure-sensitive and insensitive reaction involves directly the elucidation of the structure of the catalytically active centre, which may consist of a group of several atoms. Thus the hydrogenolysis of C_3H_8 can proceed on an assembly of 17 nickel atoms in accordance with the scheme[162]



A decrease in the rate of reaction is then observed for small nickel particles as their size diminishes further.

The influence of dispersity on the catalytic properties is manifested not only by a change in the rate and selectivity of the reaction but also by a change in the nature of the chemisorption bond in the adsorption stage as a function of the size of the crystals. For example, in a study of the adsorption of H_2 on nickel microcrystals deposited on SiO_2,[163] it was shown that the fraction of the irreversibly chemisorbed H_2 is related to the fraction of surface nickel atoms located on the edges and on the apices of the crystals. The different coordinative states of the surface metal atoms, which depend on the dispersity, influence significantly the form of the adsorption of CO, which was demonstrated[164] in relation to the Ni/SiO_2 and Ni/Al_2O_3 catalysts over a wide range of nickel crystal sizes and in another study[165] of the interaction of CO and H_2 on Ni/SiO_2 catalysts. It has been noted[166] that the form of the platinum particles themselves can change in the course of the adsorption of H_2 and CO on Pt/SiO_2 catalysts and hence their catalytic properties are also altered.

In a study of the adsorption of H_2 and CO on highly dispersed iridium deposited on Al_2O_3, it was shown that the H/Ir and CO/Ir ratios approach two and that this is not associated with the spill-over effect.[167] It has been established that such a high H/M ratio is characteristic of adsorption on atomically dispersed iridium and not on corner and edge atoms of small crystals because the stoichiometric adsorption on iridium crystallites smaller than 6 Å is approximately unity.

We shall now turn our attention to the electronic properties of the metallic crystals and clusters themselves as a function of their size without taking into account with the influence of the carrier. The general postulates concerning this problem have been described in another review:[10]

1. Depending on the number of atoms (n) in the cluster, the latter can have different structures (linear, two-dimensional, three-dimensional) and for $n > 10$ the three-dimensional crystals are probably more stable than the linear and two-dimensional structures. According to the results of calculations, among three-dimensional structures there may be a tetrahedron, a square pyramid, a pentagonal pyramid, a trigonal bipyramid, a triangular prism, or an icosahedron, i.e. structures which are not characteristic of massive metals. The icosahedral structures of small palladium and nickel clusters are apparently more stable than the face-centred cubic structures, which are in their turn preferred for copper and silver clusters.

2. The bond energy in the cluster calculated per atom is smaller than in the crystal, but increases with increase in n. The average bond energy in cubic and octahedral crystals with $n > 50$ does not differ very greatly from the energy of macrocrystals. In many cases, the equilibrium distances between atoms in the cluster are greater than in the metal lattice.

3. The ionisation potential of the cluster is greater than the electronic work function of the metal and diminishes with increase in the size of the cluster, approaching the electronic work function of the massive metal. Thus the electronic work function depends on the dispersity of the metal.

4. In the copper, silver, gold, and nickel clusters, the population of the *d* atomic orbitals is increased by virtue of the *p* atomic orbital [sic] compared with the $d^8s^1p^2$ configuration (the Engel-Brewer rule), while for the palladium cluster the population of thd *d* atomic orbitals increases with increase in *n*, approaching the value for the massive metal, i.e. the *d* character depends on the dispersity of the metal. It has been shown that for nickel the average magnetic moment per atom diminishes with decrease in *n*, amounting to 0.46 μ_B for Ni_{13} and 0.25 μ_B for Ni_8 compared with 0.54 μ_B for crystalline nickel.

5. With increase in the size of the cluster, the levels of the individual atoms are grouped into bands and the width of the *d* band increases with increase in the size of the cluster. The width of the forbidden gap then diminishes. It is of interest to note that all the possible features of the bulk-phase band structure are observed for the cubooctahedral Ni_{13} and Pt_{13} clusters.

In conclusion of this chapter, one should also mention a series of important factors which complicate the study of the SIMC effect. These are the reversibility of the SIMC as a function of the reaction conditions,[168,169] its sensitivity to the presence of water[169,170] and its relation with the spill-over of hydrogen,[171–173] the dependence on the way in which the catalyst is obtained,[34,37,174] and the presence of strongly retained forms of hydrogen.[175]

* * *

Summarising briefly the data presented above, one may note that the attention devoted by many investigators to the experimental and theoretical study of the SIMC effect has led to a sharp increase in the number of studies designed to elucidate the physicochemical and catalytic properties of deposited metallic catalysts. This fact is itself important because the above group of catalysts is of significant interest for industry. However, here one should note that the SIMC effect is frequently used to explain changes in adsorption and catalytic properties induced by completely different causes, for example by a change in the dispersity of the deposited metallic particles as a function of the nature of the carrier and the amount of the deposited metal, the complete encapsulation of the metal particles in the bulk of the carrier on sintering, the spill-over phenomena, etc.

Such a broad treatment of the phenomenon hinders to some extent its objective study and analysis and it is therefore useful, in our view, to restrict the consideration of the SIMC effect to the following phenomena, which influence the adsorption and catalytic properties: (a) the change in the electronic structure of the metal atoms or clusters located on the carrier and also in the electronic structure of the atoms at the metallic crystal–carrier interface; (b) the formation, as a consequence of the reduction of the carrier, of metal atoms doping the deposited crystals of the catalytically active metal; (c) partial shielding of the surface of the deposited crystals by a creeping film of the carrier accompanied by a change in the energetic, structural, and electronic properties of the surface.

Naturally, it is sometimes difficult to isolate these phenomena in a pure form and the application of a set of modern physicochemical methods and a wide variation of the procedures used to prepare the given deposited metallic catalysts are essential conditions for the understanding of the mechanism of the SIMC effect and for the synthesis of new effective catalytic systems.

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Translated from *Uspekhi Khimii* **60** 714–735 (1991) U.D.C. 541.128.4:[66.097.8+620.192.32]

Inhibition and synergism in phase transfer catalysis

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ABSTRACT. Questions concerning inhibition and synergism in phase transfer catalytic reactions in various systems are examined. Effects induced by the decomposition of the catalyst during the reaction and also by the introduction of various reagents and additives are analysed. Factors giving rise to synergistic and inhibition phenomena are considered.

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I. Introduction

The phenomenon of the synergism and inhibition of catalysts is well known in homogeneous and heterogeneous catalysis. In some cases, the mechanism of the action of promoting agents and catalytic poisons has been investigated and catalytic systems ensuring a high selectivity of reactions have been created. There are numerous patents devoted to the use of the synergistic effect in industrial processes.

The same effects involving the synergism and inhibition of catalysts have been observed also in phase transfer catalytic reactions. However, in this field synergism has been studied to an extremely slight extent. Whereas inhibition, albeit induced by different causes, is encountered fairly frequently, synergism is manifested much more rarely and to date it is generally considered to be a kind of exotic phenomenon. It is therefore useful to consider initially inhibition, since this effect has been better investigated and is more common.

The inhibition of a phase transfer catalytic reaction, understood in a broad sense, can be induced by a whole series of factors which will be considered below.

For the benefit of readers who are not familiar with the details of the problem, it is useful to explain briefly the essential features of phase transfer catalysis itself before considering specific effects. It consists in the fact that contact between two reactants in immiscible phases (a liquid–liquid or a liquid–solid system) is possible by virtue of the presence of a transferring substance — the phase transfer catalyst. Such transferring agents are as a rule quaternary onium salts. These substances effect either the transfer of a reactant into one of the phases (for reactions in a liquid–liquid system with a neutral aqueous phase) or the removal of the product from the reaction zone (for reactions involving concentrated solutions of alkalis). It is hardly possible within the framework of a single review to consider in detail the principles of phase transfer catalysis.

A number of designations have been adopted in the literature on phase transfer catalysis. The quaternary onium salt is usually designated by QX or Q^+X^-, where $Q(Q^+)$ is the quaternary onium cation and $X(X^-)$ is the anion (usually inorganic) or by the term "quat" from the word "quaternary". The subscripts "wph" and "oph" or "w" and "org" refer to the reagents and the catalyst in the aqueous and organic phases respectively. The symbol $MY(M^+Y^-)$ is understood as the inorganic reagent, where M is the metal cation and Y the anion. Subsequently this notation will be used without further explanation.

II. Inhibition in a liquid–liquid system

1. Inhibition as a result of the poisoning of the catalyst by extraneous anions

This type of effect was first observed by Starks and Owens.[1] It was noted that the interphase reaction of alkyl iodides with sodium cyanide, i.e.

$$RI + NaCN \xrightarrow{quat} RCN + NaI,$$

ceases after the attainment of 15–25% conversion.[1] It is usual to explain this by differences between the mutual extractabilities of the reactant ion (Y^-) and the departing ion (X^-) or the catalyst counterion (Z^-).

Such a difference in the reaction of the type

$$RX + M^+Y^- \xrightarrow{quat} RY + M^+X^- \qquad (1)$$

can be described with the aid of the ion-selective equilibrium constant $K^{sel}_{Y/X}$ (Gordon and Kutina[2]):

$$K^{sel}_{Y/X} = (C^{X^-}_{wph} \cdot C^{QY}_{oph})/(C^{Y^-}_{wph} \cdot C^{QX}_{oph}),$$

where $C^{Y^-}_{wph}$ and $C^{X^-}_{wph}$ are the concentrations of the reactant anion and the leaving anion respectively and C^{QY}_{oph} and C^{QX}_{oph} are the concentrations of different forms of the catalyst. The above constant determines the effectiveness of the catalyst in reaction (1).

$K^{sel}_{Y/X} < 0.1$ corresponds to the "poisoning" of the catalyst. Reaction profiles corresponding to different values of $K^{sel}_{Y/X}$, which makes it possible to select approximately a catalyst effective in the given system, have been published.[2] However, the special case where the catalysts 'own' counterion Z^- differs from both the reactant ion (Y^-) and the ion of the leaving group (X^-), i.e. in the system where there are three different anions, was not considered in the above studies. Theoretical examination of this version[3] showed that, even for $K^{sel}_{Z/X} \leqslant 10$, the "poisoning" effect can be avoided by taking a

tenfold excess of the inorganic reagent (M^+Y^-) relative to the substrate (RX). If $K^{sel}_{Z/X} \leqslant 1$, there is no poisoning even for a stoichiometric ratio of the reactant and the substrate. Hence it was concluded that the catalyst should be introduced into the reaction in the form Q^+X^-, i.e. when its counterion is identical with the leaving group. For $K^{sel}_{Z/Y} < 1$, the initial rate is higher if the catalyst is added in the form Q^+Z^- and not Q^+Y^-. The opposite effect is manifested for $K^{sel}_{Z/Y} > 1$.

The study of the "poisoning" of the catalyst by extraneous anions in processes occurring in the presence of alkalis, which is associated with the presence of an admixture of chlorates in technical alkali,[4] is very important. The quantity $\lg K^{sel}_{ClO_3/OH}$ is approximately 2. This means that chlorate is a powerful catalytic poison in reactions involving the hydroxide ion. Other lipophilic anions are inhibitors in reactions of this kind. For example, in the alkylation of acetone by alkyl halides in an alkali–organic phase system (catalyst—quaternary ammonium salt), the addition of sodium tetraphenylborate to the system stopped the process as a result of the removal of the catalyst from the reaction zone.[5]

The study of the inhibiting effect of extraneous anions by chemical kinetic methods[6] in relation to alkaline dehydrochlorination of 3,4-dichlorobut-1-ene made it possible to determine the corresponding inhibition constants. For this purpose, a series of inorganic salts were added to the reaction system. The familiar reversible inhibition model was used for the description of the results.[7] The dependence of the rate of reaction on the substrate concentration was expressed in a linear form in terms of double reciprocal variables (the Lineweaver–Burke plot), the effective rate constant was then determined. The following series based on the decrease in the inhibiting capacity of the anions was obtained: ClO_3^- (1) > NO_3^- (0.6) ≃ Cl^- (0.64) ⩾ SO_4^{2-} (0.24), where the inhibition constants are given in brackets. This sequence agrees quite well with the available data[8] for the relative lipophilicities of these anions.

Table 1. The influence of the catalyst counterion on the rate constant k_{obs} in the isomerisation of allylbenzene.[9]

Catalyst	$10^3 k_{obs}$, s^{-1}	Induction period, min	e_{QZ}*
MBu_4HSO_4	114	<0.1	$5.75 \cdot 10^{-2}$
NBu_4Cl	24	1.3	0.35
NBu_4Br	2.4	10	17

Note. Reaction conditions: 40% NaOH, catalyst—5 mol%, temperature 75 °C.
* The Brandstrom extraction constants e_{QZ} were taken from Ref. 11 for the water–methylene chloride system.

The influence of the catalyst's "own" counterion on the rates of different reactions occurring in the presence of alkalis has been examined.[9,10] In the study of the isomerisation of allylbenzene under the influence of an aqueous NaOH solution to a mixture of (*Z*)- and (*E*)-β-methylstyrenes,[9] the dependence of the rate constant and the induction period of this reaction on the catalyst counterion was found (Table 1). In this case, there is no departing group, i.e. the system contains only the Y^- (in the given instance OH^-) and Z^- anions. The dependence of $\lg k_{obs}$ on $\lg e_{QZ}$ (where e_{QZ} is the Brandstrom extraction constant[11]) is linear with a correlation coefficient of 0.995. However, since these data were obtained for only three catalyst, it is difficult to make any broad generalisations.

A similar influence of the catalyst counterion on the rates of dehydrochlorination of *m*-bis(α, β-dichloromethyl)benzene and *m*-bis-(α-chlorovinyl)benzene in the presence of tetrabutylammonium salts has been noted.[10] The usual extraction system was used to describe the reaction kinetics. The catalysts were the following tetrabutylammonium salts: the bromide, chloride, sulphate, and hydroxide. The activities of the sulphate and the hydroxide were virtually identical while on passing to the chloride and even more so to the bromide the rate of reaction fell appreciably, particularly in the initial period. Thus the lipophilic properties of the leaving anion and the catalyst counterion play a significant role in reactions involving not only neutral salts but also alkalis. However, the data obtained recently show that not everything proceeds quite so simply and smoothly. If in the estimation of the influence of the anions one is guided solely by the lipophilicity, one may conclude that quaternary ammonium iodides are in general ineffective in any phase transfer catalytic reactions. This has indeed been confirmed in a number of studies[1,11] and has led to the creation of the fairly well established view that these salts have no potential as catalysts.

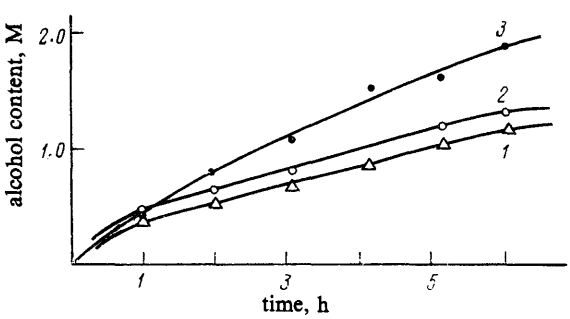


Figure 1. Hydrolysis of 2,3-dichloropropene using different phase transfer catalysts;[13] *1*, catamine; *2*, NBu_4Nr; *3*, NBu_4I. The amount of catalyst used was 10 mol% relative to the initial compound.

However the thesis that the activity of quaternary ammonium iodide is low in any phase transfer catalytic reactions is disproved both by data[12] on the alkylation of 2-methylacetoacetic ester (MAAE) and by the results of a study of the hydrolysis of 2,3-dichloroprop-1-ene to β-chloroallyl alcohol.[13] In the latter case, quaternary ammonium iodides proved to be appreciably more active as catalysis of the hydrolysis than the chlorides (Fig. 1). It was suggested[13] that the reaction proceeds via the mechanism

$$CH_2{=}CHCl{-}CH_2Cl + Q^+I^- \rightarrow [CH_2{=}CHCl{-}CH_2I],$$

$$CH_2{=}CHCl{-}CH_2I + NaOH \rightarrow CH_2{=}CHCl{-}CH_2OH,$$

which includes the intermediate formation of 2-chloro-3-iodoprop-1-ene, which should be hydrolysed much more readily than the initial compound (although the results of chromatographic analysis of the reaction mixture did not provide grounds for hypotheses of this kind). However, bearing in mind the fact that in the alkylation of MAAE by prenyl chloride in the presence of KF the exchange of chlorine for iodine does not occur when quaternary ammonium iodides are used as catalysts[12] and their increased catalytic activity is caused by the nucleophilic catalysis by the iodide anion, one may confidently postulate that the role of the iodide anion is similar also in the hydrolysis of 2,3-dichloropropene.

Table 2. The half-lives of quaternary ammonium salts in the chlorobenzene–50% NaOH two-phase system in the presence (A) and absence (B) of a molar excess of the salt NaY with a like counterion.

R_4M^+	Y^-	T, °C	ΔE^*_{act}, kJ mol^{-1}	$\tau_{1/2}$, h	
				A	B
$(C_6H_{13})_4N^+$	Cl^-	25		35	(4% after 6 days)
	Cl^-	60		0.4	8
	Cl^-	60		0.7 **	1.5 **
	Br^-	25	120	(8% after 6 days)	stable
	Br^-	60		13	stable
	Br^-	60		45 **	
	Br^-	80		1	272
	I^-	25		stable	
	I^-	60		stable	
	I^-	80		136	stable
$(C_8H_{17})_4N^+$	Cl^-	60		0.25	
	Br^-	60		3.5	stable
Bu_4N^+	Cl^-	25		18	
$C_6H_5CH_2N^+Et_3$	Cl^-	25		6.7 ***	127 ***
	Br^-	25	66	240 ***	stable***
	Br^-	35		96 ***	
$C_6H_5CH_2N^+(C_6H_{13})_3$	Cl^-	25	120	13	
	Cl^-	60		0.05	
	Br^-	25	120	432	
	Br^-	60		2.3	
$(C_8H_{17})_3N^+Me$	Cl^-	25	85	32	
	Cl^-	60		0.7	
Bu_4P^+	Cl^-	25		0.03	0.3
	Br^-	25	85	3.5	220
	Br^-	60		0.6	5.5
$Bu_3P^+C_{16}H_{33}$	Cl^-	25		0.03	0.8
	Br^-	25	68	2	220
	Br^-	60		0.25	
	Br^-	60		1.5 **	
	I^-	25		(8% after 3 days)	stable

* The quantity ΔE_{act} was estimated approximately on the basis of two temperatures.

** The reaction takes place in the solid NaOH–PhCl system.

*** The reaction takes place in the CH_2Cl_2–50% NaOH two-phase system.

In all probability, the directly opposed effects induced by the presence in the system of highly lipophilic anions such as the bromide and the iodide, i.e., on the one hand, the inhibition of the reaction, observed in a number of studies,[1,5,9,11] and, on the other hand, the acceleration of the reaction under the influence of the same iodide anion, established in other investigations,[12,13] are induced by the difference between the mechanisms of the reactions investigated.

The dehydrochlorination of chlorohydrocarbons and the isomerisation of allylbenzene take place in liquid–liquid systems and have a common rate-limiting stage—the deprotonation of the substrate by QOH at the interface between the phases or in the bulk of the organic phase. Naturally, anions more lipophilic than OH^- effectively inhibit this process. The hydrolysis of 2,3-dichloropropene is a substitution reaction of the S_N2 type and I^-, which is more nucleophilic than OH^-, catalyses it. The somewhat greater effectiveness of iodides in the alkylation of MAAE on solid KF, where deprotonation takes place on a solid surface, is believed[12] to be caused by the smaller Q^+-X^- bond energy.

These results show that, in estimating the influence of the counterion, one cannot use as a basis solely its lipophilicity without taking into account the mechanism of the main reaction.

A phenomenon of a similar nature—nucleophilic catalysis by an extraneous ion—has been observed in the alkaline hydrolysis of n-BuBr and benzoyl chloride.[14] In the presence of 60% NaOH solution, aliquat 336, NBu_4HSO_4 (or NBu_4Br), both hydrolysis and the formation of an ether are very slow: the degree of conversion of benzyl chloride into dibenzyl ether after 24 h at 100 °C is 71%. The addition of 10 mol% of sodium acetate to the solution leads to the full termination of the reaction after 3 h. In contrast to the alkylation of MAAE,[12] where there was no exchange of the halogen between the alkyl halide and the extraneous anion (I^-), the intermediate formation of acetates, which undergo alkaline hydrolysis to a much greater extent, was noted in the given instance. The alcohol formed as the alkoxide is transferred by the quaternary salt to the organic phase where an ether is formed. The ratio of the products obtained on hydrolysis makes it possible to establish the sequence based on the relative extractabilities of the ions: $OR^- > AcO^- > OH^-$.

2. Inhibition as a consequence of the decomposition of the catalyst

This version of the inhibition occurs in catalysis by the ammonium salts of reactions which take place in the presence of alkalis at a high temperature. The quaternary ammonium base decomposes via the Hofmann reaction or the Menshutkin retroreaction or via both processes simultaneously. Thus, benzoyl alcohol, dibenzyl ether, hexadecane, dimethylhexadecylamine, and dimethylbenzylamine were detected among the decomposition products of the catalyst $[C_6H_5CH_2N(CH_3)_2C_{16}H_{33}]^+Cl^-$ used to generate dichlorocarbene.[15] The decomposition products of triethylbenzylammonium chloride (TEBA) under the conditions of the acetone alkylation reaction were benzyl chloride, benzyl alcohol, and dibenzyl ether,[5] i.e. the catalyst decomposed via the Menshutkin retroreaction. The decomposition of a whole series of quaternary ammonium and phosphonium salts has been investigated semiquantitatively[16] in the chlorobenzene–50% NaOH two-phase system and the stability of the salts was estimated from the half-life.

The ammonium salt decomposed in the general case in accordance with the equation

$$RN^+R_3'Y^- + NaOH \rightarrow R_3'N + R_2'NR + R''CH{=}CH_2 + \\ + R_2O + NaY + H_2O.$$

Symmetrical and asymmetric tetraalkyl derivatives decompose mainly via the Hofmann reaction while benzyl-substituted salts decompose via the Menshutkin retroreaction. Similar data have been obtained also by other workers.[5,15] Factors such as the nature of the heteroatom and the counterion, the structure of the alkyl chain, the reaction temperature, and the presence of a salt with a like counterion were investigated. The results are presented in Table 2.

Although it has been stated in the early and familiar monograph of Weber and Gokel[17] with a reference to Herriott and Picker[18] that phosphonium ions are more thermally stable than the corresponding ammonium catalysts, the results of Landini et al.[16] contradict this view which is in general widely held. It is essential to note that in the original study of Herriott and Picker[18] it is also claimed that, although phosphonium salts are more active than ammonium salts, they undergo thermal decomposition and side reactions to a much greater extent. Thus according to the data of Herriott and Picker[18] benzyltriphenylphosphonium chloride decomposes even under mild conditions 30 °C, 2 N NaOH). It is therefore incomprehensible whence arose the idea that quaternary phosphonium salts are more stable in the presence of alkalis. This has also been repeated in the monograph of Dehmlow and Dehmlow.[19] As can be seen from Table 2, all ammonium salts are appreciably more stable than the phosphonium salts. The high stability of the symmetrical tetraalkylammonium salts falls after the introduction of the benzyl substituent and increases in the sequence chlorides $\ll$ bromides $<$ iodides. Interpretation of data [16] on the influence of the concentration of alkali on the decomposition of a quaternary salt (Table 3) showed that the observed pseudo-first-order rate constant (determined as the reciprocal of the half-life $\tau_{1/2}$) is correlated fairly well with the activity and basicity of the alkali (r = 0.955, 0.968), at any rate in the case of tetrahexylammonium chloride.

Table 3. The influence of the NaOH concentration on the half-life of quaternary onium salts in the chlorobenzene–aqueous alkali two-phase system at 60 °C.[16]

NaOH concentration, wt.%	$\tau_{1/2}$, h		
	$(C_6H_{13})_4N^+Cl^-$	$(C_6H_{13})_4N^+Br^-$	$Bu_3P^+C_{16}H_{33}Br^-$
10	78		
15	29	312	20
25	12		
30	6	30	4.5
40	0.75		
50	0.4	13	0.25

The available literature data on the stability of phosphonium salts in the presence of alkali are fairly contradictory. Compared with ammonium salts, these compounds are stable on heating, decomposing at temperatures above 300 °C.[20] On the other hand, the rate constant for the reaction of tetrabenzylphosphonium iodide with NaOH at 39 °C is 2.72 litre mol^{-1} min^{-1},[21] which is greater by approximately three orders of magnitude than the decomposition constant of benzyltrihexylammonium chloride under analogous conditions (the above value was estimated from the data of Landini et al.[16]). In another place in the same monograph,[19] it is stated that benzyl-substituted phosphonium salt are less stable than their ammonium analogues in the presence of NaOH. The contradiction between these data is due to the different reaction conditions.

It is noteworthy that the inhibition due to the decomposition of the catalyst differs kinetically from that considered in the previous section. Whereas in the inhibition induced by the poisoning of the catalyst by extraneous anions a sharp fall of the reaction rate is observed after the attainment of a specific threshold degree of conversion, in the given instance the rate of reaction falls gradually. Formally this phenomenon is described as first-order irreversible inhibition of the catalyst.[7] The kinetics of the decomposition of the catalysts were investigated in relation to the dehydrochlorination of the α-isomer of hexachlorocyclohexane catalysed by katamin AB.[22] The rate of this reaction was described adequately by the equation

$$\ln\{[C_6H_6Cl_6]/[C_6H_6Cl_6]_0\} = k_1[NaOH]c_{cat}[1-\exp(-k_2\tau)]/k_2,$$

where k_1 and k_2 are the effective rate constants for the dehydrochlorination and decomposition of the catalysts respectively and τ is the reaction time. The activation energies for these two reactions are 54 and 68 kJ mol^{-1} respectively. Istomin's data for the decomposition of the tetrabutylammonium hydroxide catalyst, which occurred independently of the main reaction, have been published.[10] The decomposition was found to be a zero-order process with a rate of reaction (r_{decomp}) independent of the current concentration of the catalyst:

$$r_{decom} = k^{eff}_{decomp},$$

where k^{eff}_{decomp} is the pseudo-zero-order rate constant for the decomposition of the catalyst.

However, the rate of reaction is a function of the initial catalyst concentration:

$$k^{eff}_{decomp} = k^0_{decomp} + k^1_{decomp}c^0_{cat},$$

where k^0_{decomp} and k^1_{decomp} are the rate constants for the decomposition of the catalyst at the interface and in the bulk of the film containing the catalyst.

This type of dependence can be achieved by the fact that, in the presence of highly concentrated alkali, the main bulk of the catalyst is concentrated in the film at the interface.[8] The catalyst in this film supplies the organic phase and the observed rate of its decomposition therefore remains constant as a function of time. The rate of decomposition of the catalyst depended very greatly on the basicity function (H_-):

$$\lg k^{eff}_{decomp} = (-17\pm1)+(0.77\pm0.09)H_-(r=0.982).$$

The activation energy for the decomposition of the catalytst is approximately 110 kJ mol^{-1}, while the activation energy for the dehydrochlorination reaction is lower by a factor of two. Thus the data in Refs. 22 and 10 agree. From this it follows that, when the dehydrochlorination takes place at a high temperature, then a constant supply of the fresh catalyst to the reaction mass is necessary to maintain its concentration at the required level.

III. Inhibition in a solid–liquid system and inhibition by onium salts

The inhibition effects are also manifested in solid–liquid systems. This is associated, firstly, with the adsorption–desorption of the substrate and catalyst on the solid surface and, secondly with the enormous role of water in phase transfer catalysis. As noted in a familiar monograph,[17] this role is "like the weather, discussed a lot but little understood". Hitherto the influence of water has been studied somewhat more effectively, but the discrepancy beween the data quoted has diminished little. Different workers reach diametrically opposite conclusions, which is apparently caused both by experimental errors and by the not always correct interpretation of the results. Nevertheless, the popularity of solid–liquid systems has been increasing, since the reaction proceeds at a higher rate in the absence of water as a consequence of the increased nucleophilicity of the anions. Furthermore, in certain cases the Gibbs free energy of reaction (2) in "dry" systems is greater and hence the equilibrium degree of conversion in substitution reactions of the type

$$RX + Y^- \rightleftarrows RY + X^- \qquad (2)$$

is higher.

The role of water in the reactions with participation of alkali is also considerable, since it is known that the basicity of the hydroxide ion in the absence of water of hydration is appreciably greater.[23]

The influence of water in substitution reactions in a solid–liquid system has been investigated.[24] It was established that, for X = Cl^- or Br^- and Y = F^-, Br^-, Cl^-, $HCOO^-$, or $MeCOO^-$ (in the forms of salts with K^+ or Na^+) and R = C_6H_{13}, C_8H_{17}, $C_{10}H_{21}$, or $PhCH_2$, reactions (2) catalysed by quaternary ammonium salts do not occur when the reactants in the solvent are thoroughly dried. This agrees with the data of Starks and Owens[1] but not with those of Zwan and Hartner.[25] Zwan and Hartner[25] investigated the reactions of benzyl chloride and hexyl bromide with solid KF, KCN, AcOK, and the potassium salt of adenine in acetonitrile catalysed by aliquat 336, 18-crown-6, and tetramethylenediamine. Aliquat 336 proved to be the most active catalyst in virtually all cases apart from the reaction with KCN. All the reactants and solvents were carefully dried and the reaction was carried out in a sealed tube in the presence of 4 Å molecular sieves. Unfortunately, the authors[25] do not quote the water content, which hinders the comparison of the results. It is of interest to note that the quaternary salt was established in the above study.

The influence of water on the kinetics of the consecutive-parallel 1,4-dichlorobutane formylation reaction has been analysed:[24]

$$Cl(C_2H_4)Cl \xrightarrow[k_1]{HCOONa} Cl(C_2H_4)OCOH \xrightarrow[k_2]{HCOONa} HCOO(CH_2)_4OCOH.$$

The constants k_1 and k_2 were calculated directly from the kinetic curves. Fig. 2 shows how the presence of water influences k_1. As can be seen, in the fully dried system there is no reaction, after the addition of traces of water the rate increases sharply, while on further addition of water it falls. A similar effect had been observed earlier.[1] According to the authors,[24] the results show that the quaternary salt is incapable of abstracting a non-hydrated ion from the crystal lattice.

An interesting effect has been observed in the study of the interaction of solid potassium formate, containing 0.015 mol% of water, with chlorodecane.[26] The reaction was carried out for a reactant ratio of 1.5:1 in *o*-dichlorobenzene at 75 °C. In the absence of the catalyst, the reaction did not occur and after 3 h the water content in the formate fell by only 10%. On the other hand, after the addition of even 5.5 mol% of aliquat 336 a rapid reaction begins with a first-order rate constant of 2×10^{-3} min^{-1} and approximately 90% of the water present in the initial formate is transferred to the organic phase. This happens also in the presence of a larger water content in the formate. The data are summarised in Table 4.

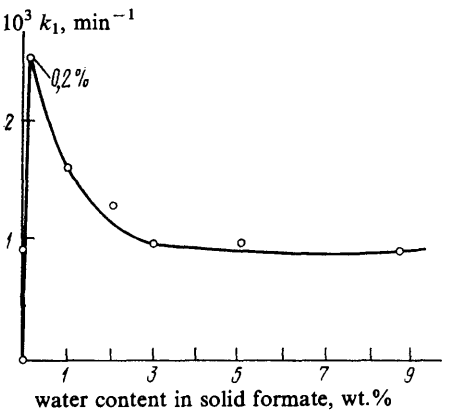


Figure 2. The influence of the water content in solid potassium formate on the observed rate constant for the formylation of dichlorobutane.[24]

Table 4. The influence of the quaternary salt on the dehydration of solid HCOOK in the alkylation of 1-chlorodecane in *o*-dichlorobenzene (T = 348 K, catalyst—aliquat 336).[26]

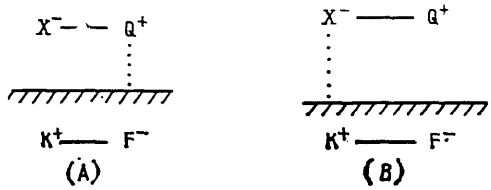
Water content in solid formate, mol%	Salt concentration*, mol%	Degree of transfer of water to organic phase, % of initial amount	k, min^{-1}
0.015	0.0	10	no reaction
0.015	5.56	88	$2 \cdot 10^{-3}$
1	5.56	51	
2	5.56	30	
0.015	19.44		$1 \cdot 10^{-3}$
0.015	39–56		$< 1 \cdot 10^{-3}$

* Relative to 1-chlorodecane.

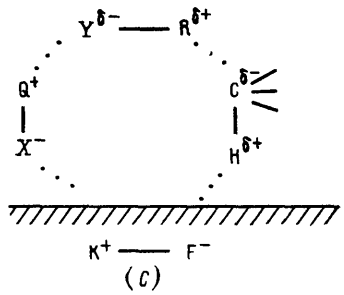
With increase in the concentration of the quaternary salt, the observed rate constant falls appreciably. This has been attributed[26] to the dehydration of the formate by the quaternary salt. The data obtained led to the conclusion that the observed effect is common to reactions in a solid–liquid system. However, it has been suggested[12] that a similar dependence, with an extremum in the dependence of the rate of reaction on the quaternary salt

concentration, is a result of effects associated with the adsorption of the catalyst on the solid surface. In the alkylation of MAAE by prenyl chloride in acetonitrile in the presence of solid KF, the dependence of the specific rate of reaction on the catalyst concentration also passed through an extremum. It was established that there is no ion exchange between QX and KF.

In earlier studies[27–29] of the reactions involving solid inorganic salts, it has been demonstrated that there are two types of adsorption of the catalyst on the surface of the solid reactant. The formation of two types of surface complexes of QX on KF was also postulated in the study described above:[12]



The MAAE adsorbed on the solid surface via the binding of the F^- ion to the CH group of MAAE is deprotonated. Complex (A) is thus of the "blind end" type since F^- is blocked. The adsorption of QX via Scheme (B) and the participation of the adsorbed complex in the alkylation process are confirmed, according to the author,[12] by data on the influence of the nature of Q^+ and X^- on the rate of alkylation (Table 5). These data agree to some extent with the nucleophilicity series quoted by Gordon.[30] Since prenyl iodide is not formed during the reaction, it was suggested that the alkylation proceeds on the surface of solid KF [Scheme (C)]:

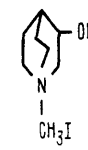


Alkylation via this scheme should lead to variable orders with respect to the component. The author[12] suggests that, if the QX concentration is higher than the MAAE concentration, the contribution of the "blind end" complex (A) increases, which explains the decrease in the rate of reaction with increase in the catalyst concentration. However, in our view, this does not agree fully with the kinetic scheme proposed by the author.

Table 5 also shows that the influence of the catalyst counterion is by no means always wholly determined by its lipophilic properties. This postulate has been confirmed by the results of Ali Abbas et al.[13]

Another interpretation of the dependence of the initial rates of reaction on the concentration of the solid reactant with an extremum has been proposed in studies[31,32] where the reaction of 1,2,4-trichlorobenzene with solid potassium phenoxide was investigated in the presence of copper and 18-crown-6. The authors explain this dependence in terms of the influence on the rate of reaction by the degree of surface coverage of the solid reactant by the catalyst (18-crown-6) and use the Langmuir equation in the description of the adsorption-desorption process involving the crown-ether–potassium phenoxide complex on the surface of the phenoxide, i.e. they used the mathematical procedures for heterogeneous catalysis in phase transfer catalysis. A synergistic effect was also noted in the above studies when two catalysts, such as metallic copper and 18-crown-6, were used.

Table 5. The influence of the nature of the phase transfer catalyst on the observed alkylation rate constant.[12]

Catalyst	$10^2 k_{obs}$, litre mol^{-1} min^{-1}	Catalyst	$10^2 k_{obs}$, litre mol^{-1} min^{-1}
Et_4NCl	0.16	Et_4NBr	0.38
Et_3NBzCl	0.14	Bu_4NBr	0.05
Bu_4NCl	0.18	Oct_4NBr	0.34
N-Benzylquininium chloride	0.06	Ph_3MePBr	0.37
Et_4NI	1.3		
Bu_4NI	0.64		0.42
Dibenzo-18-crown-6	0.065	Complex of 18-crown-6 with MeCN	0.37

Note. Reaction conditions: solvent—CH_3CN, T = 293–295 K, [PC] = [MAAE] = 0.2 M, KF/MAAE = 2, [QX] = 0.05 M.

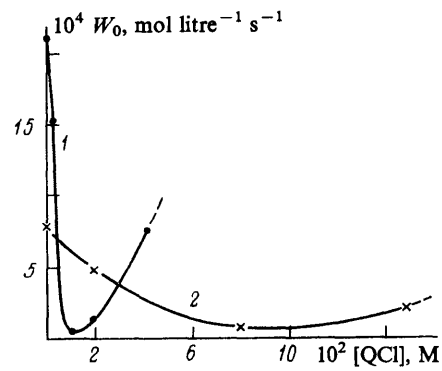
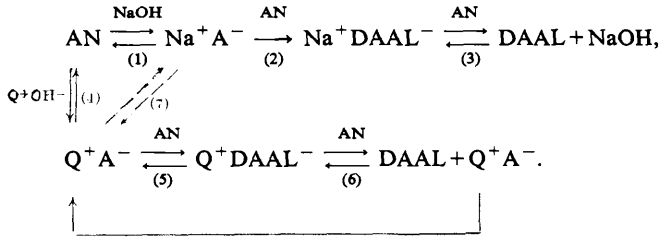


Figure 3. The influence of the new concentration of triethylbenzylammonium chloride on the initial rate of formation of diacetone alcohol at 40 °C in benzene solution in the presence of 50% aqueous NaOH at different initial molar acetone concentrations: *1*, 12; *2*, 8.[33]

Inhibition of the process by a quaternary ammonium salt has been observed not only in a solid–liquid system but also in a liquid–liquid system. Thus a study of the kinetics of the aldol condensation of acetone (AN) in the presence of 50% aqueous NaOH solution[33,34] established that, as a result of the addition of catalytic amounts of TEBA, the order of the reaction with respect to acetone changes and the initial rate of reaction falls appreciably (Fig. 3). This also entails the alteration of the composition of the

reaction products: considerable amounts of mesityl oxide (MO) and phorone (PHO) appear, while the amount of diacetone alcohol (DA) diminishes. The observed nature of the dependence of the initial rate of reaction on the Q^+Cl^- concentration persisted also on reducing the acetone concentration. The authors[33,34] explain the observed behaviour by a change in the reaction mechanism in the presence of the quaternary salt and propose the following process mechanism:



The reaction proceeds via the pathway (1)→(2)→(3) in the absence of Q^+Cl^- in the heterogeneous phase at the interface. Two molecules of acetone and water participate in it. After the introduction of the catalyst, the reaction can proceed via two pathways: (4)→(5)→(6) and (1)→(7)→(5)→(6). The heterogeneous pathway (1)→(2)→(3) is then blocked, as shown by the third order with respect to acetone of the reaction occurring in the presence of the catalyst.

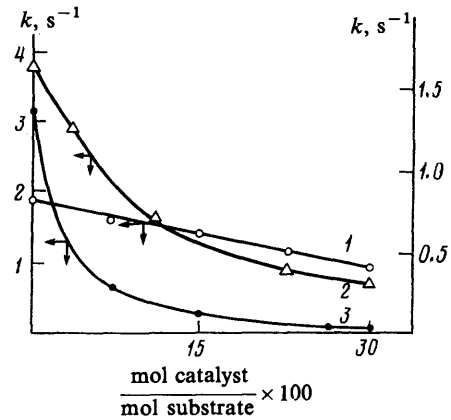


Figure 4. Dependence of the rate constant for the two-phase reaction on the catalyst concentration in the 1:1 benzene–water system at 25 °C:[35] *1*, 10^6k, t-BuCl + KNCS, $(n\text{-Bu})_4NBr$; *2*, 10^5k, hydrolysis of t-BuCl, $(n\text{-Bu})_4NBr$; *3*, 10^3k, hydrolysis of trityl chloride, $(n\text{-Bu})_4NCl$.

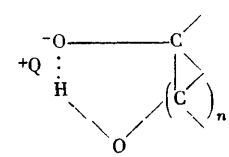
Inhibition of the reaction in a liquid–liquid system after the introduction of the phase transfer catalyst has also been observed in a study[35] of the substitution of tertiary alkyl chlorides by the thiocyanate ion (Fig. 4). Whereas in the reaction involving primary alkyl chlorides the introduction of the phase transfer catalyst accelerates the substitution, in the case of tertiary alkyl chlorides the introduction of a quaternary ammonium salt induces a marked inhibition. In the given instance, this is also a consequence of a change in the reaction mechanism, although it is not induced by the presence of the catalyst but is caused by a change in the structure of the substrate. On passing from a primary to a tertiary alkyl chloride, the S_N2 reaction mechanism changes to S_N1. This is confirmed by the fact that the hydrolysis of triphenylmethyl chloride (trityl chloride) is also inhibited sharply by tetrabutylammonium chloride.[35] Evidently, despite the fact that the quaternary salt transfers thiocyanate ions to the organic phase, the polarity of this layer is insufficient for the operation of the S_N1 mechanism. The reaction therefore takes place either in the aqueous layer or at the interface. The observed inhibition effect is induced by the removal of the thiocyanate ion from the reaction zone as a result of its extraction by the quaternary salt into the organic phase.

The inhibition of a number of other two-phase reactions by a phase transfer catalyst has been observed recently.[36] Thus the reaction of *p*-bromonitrobenzoylmethane with urotropine is inhibited by TEBA added in catalytic amounts. According to the author, this is induced by the transalkylation of TEBA with *p*-bromonitrobenzoylmethane. It was noted in the same study that, in the presence of TEBA, the acetylation of $p\text{-}O_2NC_6H_4C(O)CH_2NH_2$ by acetic anhydride in the presence of aqueous sodium carbonate proceeds with a lower yield as a consequence of the acceleration of the side reaction involving the cyclisation of the amino-derivative. However, the acetylation of 9,13-dimethyl-7-(1,1,5-trimethylcyclohex-5-enyl)nona-8,11,13-triene-10,15-diol by acetic anhydride in the presence of a phase transfer catalyst proceeds smoothly and with a satisfactory yield.[37]

All these features demonstrate that phase transfer catalysts are not a universal means of accelerating any heterophase process. In each specific case, the reaction mechanism plays the decisive role and not the presence in the system of two and more immiscible phases.

IV. Synergism and inhibition in multicomponent catalytic systems

This section is devoted to what is in our view the most interesting effect in phase transfer catalysis—the cocatalytic or, on the contrary, the inhibiting effect of compounds of substances added to the reaction system and capable of forming complexes with its components or a base of nucleophile stronger than the compounds present initially. Systems with alkalis have been most thoroughly investigated. At an early stage, in the study of the Williamson reaction under phase transfer conditions, it was observed that in the presence of alcohol an appreciably greater amount of the base passes to the organic phase than under the usual conditions.[18] The extracted alkoxide anion is a very powerful base. Thus the basicity of a 0.001 M solution of benzyltrimethylammonium t-butoxide in t-butyl alcohol is 1000 times higher than the basicity of a similar potassium t-butoxide solution.[38] It has been shown[39] that the most effective additive to quaternary ammonium salts, ensuring the maximum extraction of the base into the organic phase, is pinacol—2,3-dimethylbutane-2,3-diol. It was suggested that this is induced by the formation of a stable ion pair having the structure



It is essential to note that, in the absence of a quaternary salt, even the most effective diols increase the basicity of the organic phase extremely insignificantly, in contrast to polyglycols. This served as a basis for the application of a system comprising a quaternary ammonium salt and a diol in the synthesis of alkynes from 1,2-dihalo-derivatives,[40] because it had been shown earlier that 1,2-dibromoalkanes are readily dehydrobrominated by solid KOH in the presence of tetraoctylammonium bromide.[41] The following products are formed on elimination of 1,2-dihaloalkanes (Table 6):

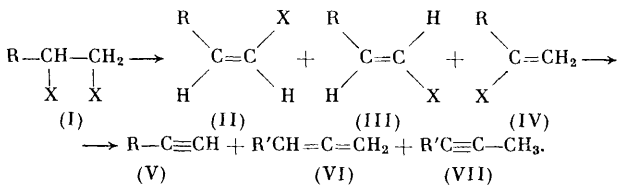


Table 6. Dehydrohalogenation of 1,2-dibromooctane by 50% KOH.[40]

Catalyst	Cocatalyst	Yield of products, %		(I)
		(V)	(II)–(IV)	
Oct_4NCl	Нет	0	70	30
	EtOH	0	88	12
	$C_5H_{11}OH$	10	90	0
	$C_7H_{15}OH$	8	92	0
	$HO(CH_2)_6OH$	48	52	0
	$HO(CH_2)_8OH$	50	50	0
	Hexane-2,5-diol	50	50	0
	2-Methylpentane-2,4-diol	44	56	0
	2,3-Dimethylbutane-2,3-diol	39	61	0
	2,5-Dimethylhexane-2,5-diol	39	61	0
	PEG 200	2	98	0
	PEG 1000	31	69	0

Note. Reaction conditions: amount of dihalo-derivative 5.36 mmol; amount of KOH 500 mmol, amount of catalyst 10^{-4} mol, amount of cocatalyst 2 × 10^{-4} mmol, amount of petroleum ether 5 ml, temperature 75 °C, time 2.5 h.

It has been established,[40] that apart from tertiary diols, primary diols in which the OH groups are separated by 6–8 carbon atoms are also extremely effective.

Fig. 5 shows how the yield of the elimination products varies in the presence of the cocatalyst (in the given instance pinacol) and in its absence.[40] The effect is most marked in the case of the least reactive chloro-derivative. It is extremely striking that the quaternary ammonium salt (QAS)–diol catalytic system does not ensure, in contrast to poly(ethylene glycols), the isomerisation of an alk-1-yne to an allene and an alk-2-yne. In all probability, this is induced by the completely different structure of the catalytic complexes involved in the reaction, because, as mentioned previously, we find, firstly, that, in contrast to polyglycols, diols do not increase the basicity of the organic phase in the absence of a QAS and, secondly, that the addition of a QAS to polyglycols also does not induce an increase in the basicity of the organic phase.[39] It is also noteworthy that, like other primary alcohols, ethanol is a fairly weak cocatalyst. Nevertheless, QAS–alcohol systems have been used widely by many investigators in elimination and alkylation reactions.[42] The study of the kinetics of the dehydrochlorination of 1,2-dichloroethane, catalysed by the TEBA–benzyl alcohol mixture,[43] showed that the dependence of the initial rate of reaction on the benzyl alcohol concentration passes through an extremum. The formal order of the reaction with respect to the concentration of alkali was ~2.5. In order to account for this, an extremely complex kinetic scheme was postulated. However, our calculations showed that the substitution of the activity of NaOH for its concentration leads to the first order of the reaction with respect to the above reactant, which renders the authors' entire reasoning[43] concerning the proposed mechanism extremely ill-founded. It is also essential to note that the intermediate complex, whose formation has been postulated,[43] cannot be produced for physical reasons.

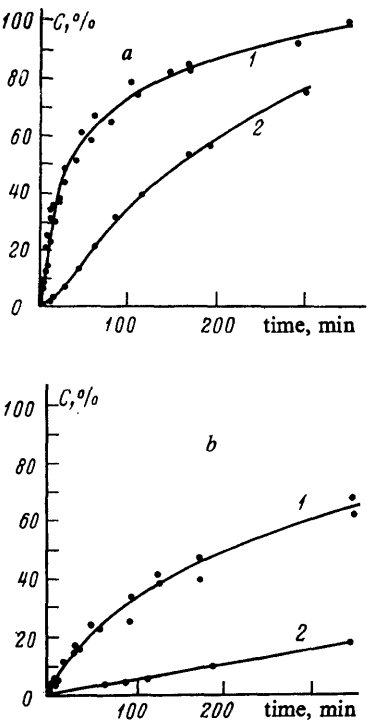


Figure 5. Elimination of 1,2-dibromooctane (*a*) and 1,2-dichlorooctane (*b*) by solid KOH in the presence of $(C_8H_{17})_4NBr$ with (curves *1*) and without (curves *2*) the addition of pinacol.[40]

The influence of a large number of different added proton-donating compounds on the katamin-catalysed dehydrochlorination of the α-isomer of hexachlorocyclohexane has been investigated.[22] Fig. 6 illustrates the dependence of the initial rate of reaction on the concentration of the additive. The dashed line represents the initial rate of reaction in the absence of the additive. Whereas the addition of a carboxylic acid inhibits the reaction, as might have been

expected, while that of benzyl alcohol accelerates it (the acceleration is directly proportional to the alcohol concentration), the addition of phenol and pentachlorophenol leads to complex relations. In our view, this is associated with the formation of complexes of the above compounds with the substrate, because according to Brandston's data,[11] phenols and other weak acids can be extracted in the presence of alkali by quaternary salts not only in the form of anions but also in the unionised form as a complex with the QAS. In particular, it has been shown that, after the addition of a base and a QAS to a phenol or carboxylic acid solution in methylene chloride or a similar solvent, the RO^-Q^+, $RO^-Q^+(ROH)$, $RO^-Q^+(ROH)_2$, etc. species are formed in the organic phase. Species of this kind can interact, in their turn, with the substrate. The formation of substrate–QAS–additive ternary complexes has been demonstrated by spectroscopic methods. The degree of association of the complex $CHCl_3/NEt_3$/TEBA calculated from IR spectroscopic data is 0.13.[44]

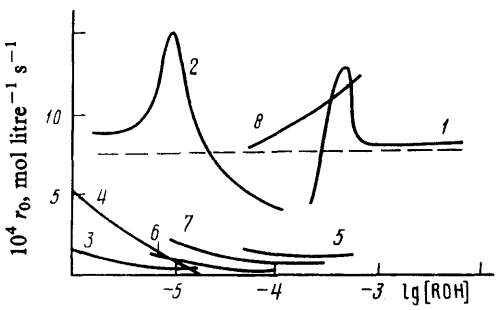


Figure 6. The influence of added proton-donating compounds on the rate of alkaline dehydrochlorination of the α-isomer of hexachlorocyclohexane in catalysis by katamin AB;[22] Additives: *1*, phenol; *2*, C_6Cl_5OH; *3*, $C_5H_{11}COOH$; *4*, picric acid; *5*, L-histidine; *6*, VIK-1 (mixture of α-methyl-substituted carboxylic acids, C_7-C_9 fraction); *7*, *o*-$HOC_6H_4SO_3H$; *8*, $C_6H_5CH_2OH$.

The available data[45] suggest that the following processes take place in the system:

$$ROH + NaOH \rightleftarrows NaOR + H_2O,$$
$$NaOR_w + QCl_w \rightleftarrows QOR_w + NaCl_w,$$
$$QOR \rightleftarrows QOR_{org},$$
$$QOR_w + nROH_w \rightleftarrows (QOR.nROH)_w,$$
$$(QOR.nROH)_w \rightleftarrows (QOR.nROH)_{org},$$
$$NaOH_w + QCl_w \rightleftarrows QOH_w + NaCl_w,$$
$$QOH_w + nROH_w \rightleftarrows (QOH.nROH)_w,$$
$$(QOH.nROH)_w \rightleftarrows (QOH.nROH)_{org}.$$

The role of the base can be assumed in the given instance by both $(QOH.nROH)_{org}$ and NaOH (through the interface). The QOR and $(QOR.nROH)_{org}$ species are most probably not reactive in the given process, which explains the extremum in the dependence of the initial rate of dehydrochlorination on the phenol concentration. The acceleration of the alkali elimination reaction after the addition of phenol to the QAS was observed also in the synthesis of phenylacetylene.[46] Unfortunately, detailed data are not available. The results of Sirovskii et al.[22] show that the effect of the additive depends on its acidity. Compounds with $pK_a < 5$ cause inhibition, those with $5 < pK_a < 10$ give rise to both synergism and inhibition, and those with $pK_a \geqslant 10$ give rise to synergism alone. On the other hand, according to another study,[47] the addition to the system of compounds more acid than water, particularly phenol, inhibits the substitution of hexyl chloride by sodium formate. The authors[47] believe that the presence in the system of compounds promoting extraction as a result of the formation of hydrogen bonds via the scheme

$$QX_{org} + HZ_w \rightleftarrows QX\ldots(HZ)_{n(org)}\ [\text{or } Q^+(HXZ)^-\ldots(HZ)_{n-1(org)}],$$

inhibits the process in all cases. In the light of the data presented below, this conclusion appears to be not entirely justified.

The synergistic effect of a mixture of two types of phase transfer catalysts has been observed in the alkylation of malonic ester by alkyl halides.[48] When a mixture of aliquat with crown-ethers was used, the initial rate of alkylation and sometimes the yield of the product were higher than would be expected from the simple summation of the catalytic effects. However, the mechanism of the cocatalytic action is not entirely clear in this instance.

It is of interest to note that the addition of an acid to the QAS increases the yield of the product in the bromination of cyclopentadiene by sodium hypobromite:[49]

$$C_5H_6 + NaOBr \xrightarrow{QX+RCOOH} C_5Br_6.$$

The corresponding data are presented in Table 7. The addition of the carboxylate anion probably promotes the extraction of the OBr^- into the organic phase.

Table 7. The influence of the catalyst on the yield of hexabromocyclopentadiene.

Concentration of $[(C_{7-9}H_{15-19})_3NMe]_2SO_4$, mM	Concentration of VIK-1*, mM	Yield of hexabromocyclopentadiene, %
0	0	56.3
7.75	0	28.0
0.775	3.05	65.4
1.55	6.1	78.1
3.10	12.2	50.0
7.75	30.5	48.4

Note. Reaction conditions: temperature from 0 to 5 °C, $V_{org}/V_w = 0.11$
*VIK-1 is a mixture of α-methyl-substituted aliphatic carboxylic acids (C_5-C_7 fraction).

In studies[44,50,51] devoted to the synthesis of cyclopropyl ethers by the addition of dichlorocarbene to olefins, the synergism, observed for the first time by the authors, occurring when mixtures of TEBA with a series of complex-forming agents are used, was investigated. Fig. 7 presents an example of the synergistic effect of TEBA and

triethylamine in the formation of 7,7-dichloronorcarane from cyclohexene and $CHCl_3$ on treatment with solid KOH. For a quantitative description of the effects of additives, the synergistic coefficient was used: $K_s = \eta_3/(\eta_1 + \eta_2)$, where η_1 and η_2 are the yields of the products when the phase transfer catalyst and the additive respectively are used separately and η_3 is the yield for the mixture comprising equimolar amounts of the catalyst and the additive. Depending on the mixture composition, an acceleration (synergism of the catalysts) or inhibition (antagonism of the catalysts) were observed (Table 8).

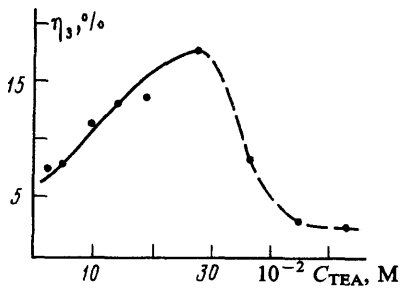


Figure 7. Dependence of the yield of 7,7-dichloronorcarane on the content of the triethylamine (TEA) in the reaction mixture (20 °C, 5 min, molar ratios cyclohexene: chloroform: solid NaOH: TEBA = 1:5:9.04:0.02; when TEBA at a concentration of 0.5 mM is used without added triethylamine, η_1 = 4.8%, while in the presence of triethylamine at a concentration of 0.5 mM without added TEBA, η_2 = 2.3%).[44]

The use of certain additives (for example, NEt_3, activated charcoal) in non-catalytic amounts leads to a complex variation of K_S (an initial increase followed by a sharp decrease). A similar picture has been observed also after the introduction into the catalytic mixture of a third component (for example, ethanol) capable of forming a complex both with the phase transfer catalyst or the additive and with $CHCl_3$. K_S depends also on the ratio of the components and the reaction temperature and is determined by the nature and content of alkali in the reaction mixture. A decrease in the amount of alkali introduced into the reaction lowers the observed synergistic effect as far as antagonism ($K_S < 1$).

In all probability the reaction is accelerated in the $CHCl_3$ deprotonation stage. Homoassociated species, in which the proton of one molecule is located between the two C–Cl bonds of a neighbouring molecule as a result of the formation of hydrogen bonds, are known to be formed in liquid $CHCl_3$.[52] Under the reaction conditions, the presence of such associated species can give rise to steric hindrance to the attack by the hydroxide ion on the C–H bond in $CHCl_3$, which leads to the formation of the anion CCl_3^-. Tertiary amines and quaternary ammonium salts exist in $CHCl_3$ as complexes with chloroform of types (VIII) and (IX):[52,53]

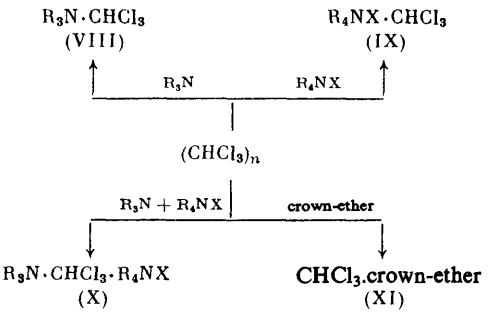


Table 8. The yields of 7,7-dichloronorcarane in the presence of various catalysts and their mixtures.[51]

Components of catalytic mixture [a]	Yields, %			K_S
	η_1	η_2	η_3	
TEBA/NEt_3	16.3	7.2	51.1	2.17
TEBA/PhOH	16.3	2.0	47.7	2.6
TEBA/EtOH	16.3	2.8	54.8	2.86
TEBA/Bu_3PO	16.3	2.2	55.8	3.02
NEt_3/ARA-5p* anion exchanger	7.2	1.1	3.0	0.36
NEt_3/PEG-4000	7.2	6.5	13.6	0.99
NEt_3/Sintanol DS-10**	7.2	5.5	30.7	2.42
NEt_3/15-crown-5	7.2	10.1	36.0	2.08
NEt_3/DB-18-crown-6	7.2	15.1	44.1	1.98
TEBA/activated charcoal	16.3	0.8	40.3	2.35
DB-18-crown-6/activated charcoal	15.1	0.8	17.9	1.12
TEBA/DB-18-crown-6	16.3	15.1	58.6	1.87
TEBA/15-crown-5	16.3	10.1	56.8	2.15

Note. Reaction conditions: T = 283 K, 2 mol% of catalyst, SKT charcoal.

*The ARA-5p anion-exchange resin contains the $[C_6H_5CH_2N^+.(CH_3)_3]Cl^-$ exchange groups.

**Sintanol is the monoalkyl ether of poly(ethylene glycol) $C_{10}H_{21}O.(C_2H_4O)_{10}H$.

In complexes of this kind, the C–H bond in $CHCl_3$ should be more polar than in the homoassociated species. After the simultaneous introduction into $CHCl_3$ of a phase transfer catalysis and an additive, one may expect the formation, together with complexes (VIII) and (IX), of mixed complexes (X) in which the polarisation of $CHCl_3$ is more pronounced than in two-component complexes, as shown by IR and ^1H NMR spectroscopic data.

Thus the $CHCl_3$ molecule removed from the homoassociated species as a result of binding into complexes (VIII)–(IX) is activated as a consequence of the polarising action of the catalyst, which facilitates the heterolysis of the C–H bond and the formation of CCl_3^-. In binary mixtures of catalysts, deprotonation should take place more readily, since the phase transfer catalyst and the additive exert a concerted polarising action on different centres in the $CHCl_3$

molecule [complex (X)]. Since all the catalysts and additives listed in Table 8 are capable of forming complexes of different nature with $CHCl_3$ [including complex (XI)], it becomes understandable why the independent use of compounds which are not traditional phase transfer catalysts but exhibit donor–acceptor properties leads to the formation of dichloronorcarane (η_3 = 0.8–2.8%) and why their use in a mixture with the phase transfer catalyst gives rise in most cases to a synergistic effect ($K_S > 1$). The postulate that the acceleration of the addition of dichlorocarbene takes place in the deprotonation stage is supported by the analogous influence of additives also in reactions of other CH acids when the reaction takes place under the conditions of phase transfer catalysis and involves the stage indicated: in the intramolecular cyclisation of γ-chloropropyl mesityl sulphone in the presence of dimethyl sulphoxide (DMSO) and in deuterium exchange involving DMSO.[44] Overall, the nature of the activity of the above phase transfer catalysts and catalytic mixtures in these reactions is the same as in the dichlorocarbene addition reactions.

Cases of the inhibition of the reaction (Table 8) can be best explained by steric hindrance to attack on the C–H bond of the chloroform by the hydroxide ion OH^- in the pre-reaction three-component complex. This explanation is confirmed by the finding that, when a series of $Alk_4NX/NAlk'_4$ pairs (Alk = C_1–C_4; Alk′ = C_1–C_{20}) are used, the synergistic coefficient changes from $K_S > 1$ to $K_S < 1$ with increase in the length of the Alk or Alk′ carbon chain. However, one cannot rule out additional causes of the non-additive changes in the reaction rate such as the formation of complexes between the catalyst and the additive,[54] the modification of the catalyst by the additive,[41] or the participation of the catalyst and the additive in different stages of the process.

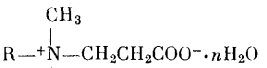
In some cases inhibition is induced by the solvent (benzene or toluene).[55] In reactions involving the alkylation of acetone by prenyl chloride, inhibition was observed after the replacement of part of the acetone by toluene despite the zero order of the reaction with respect to acetone.[55] The authors explained this effect by the "inhibiting" influence of toluene. The Lineweaver–Burk plots of the observed dependence of the rate constant on the catalyst concentration at different benzene concentrations consists of a set of straight lines intersecting in one point, which indicates inhibition of a mixed type. According to the authors,[55] in the given instance the solvent forms solvate complexes with QX and QA. Here A^- is acetone enolate, whose concentration is defined by the equation $[A^-] = K_e[AN]a_{OH^-}a_{H_2O}$, where K_e is the equilibrium constant for the deprotonation of the acid HA by OH^-, a_{OH^-} the activity of the hydroxide ion, a_{H_2O} the activity of water, and [AN] the concentration of acetone in aqueous alkali. The authors estimate the constant K_e as the ratio $K_{HA}/K_{H_2O} = 10^{-20}/10^{-16}$. According to their data,[55] 30% of acetone dissolved in 50% NaOH is enolised. Calculation of kinetic data showed that QX is bound by toluene approximately 6 times more effectively than QA. This is induced by the more pronounced lipophilicity of QA and by the fact that Cl^- is more effective solvated by toluene than A^-.[55]

Consideration of the above instances of synergism and inhibition permits the conclusion that complex formation processes in fact determine the mode of the action of the additive—synergistic or inhibiting. As a rule, synergistic action is manifested on formation of ternary complexes incorporating the phase transfer catalyst, the substrate, and the additive. The binding of the additive in a complex with only one of the components leads to inhibition.

V. Catalysis by betaines

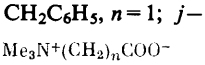
At first sight the topic of this section does not fit within the general framework of the review. However, we believe that the transition from the use of two-component catalytic systems to the construction of bifunctional catalysts is an entirely logical stage and that the use of betaines as such catalysts is one of the first steps in this direction.

It has been stated in a monograph[56] that, in the presence of the betaine $(C_{12}H_{25})_3N^+CH_2COO^-$, the interaction of alkyl halides with aqueous alkali is 10–50 times faster than in the presence of the usual onium salts. The application of betaines of the type $R_3N^+(CH_2)_nCOO^-$ and $C_{12}H_{25}N^+R_2(CH_2)_nSO_3^-$ as promoting agents for the alkaline dehydrochlorination reactions of chlorobutanes and chlorobutenes was described as early as 1973.[57] A wide scale study of betaines as phase transfer catalysts has been undertaken recently.[58,59] Gol'dberg et al.[68] synthesised a series of betaines having the following structure:

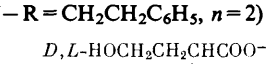


(XII, *a*–*j*)

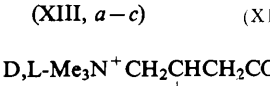
(*a*–R = CH_3, *n* = 2; *b*–R = C_2H_5, *n* = 1; *c*–R = n-C_3H_7, *n* = 0; *d*–R = iso-C_3H_7, *n* = 2; *e*–R = n-C_6H_{13}, *n* = 1; *f*–R = n-$C_{10}H_{21}$, *n* = 1; *g*–R = n-$C_{12}H_{25}$, *n* = 1; *h*–R = n-$C_{16}H_{33}$, *n* = 0; *i*–R = $CH_2C_6H_5$, *n* = 1; *j*–R = $CH_2CH_2C_6H_5$, *n* = 2)



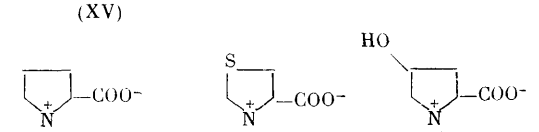
(XIII, *a*–*c*)



(XIV)



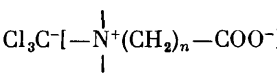
(XV)



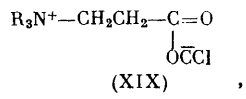
L-(XVI) L-(XVII) L-(XVIII)

The betaines (XIII)–(XVIII) were tested as catalysts of two-phase reactions involving dichlorocarbene: the conversion of styrene into dichlorocyclopropane, dehydration of benzamine, and *N*-formylation of pyrrolidine. The betaine based on *b*-alanine (XIII*b*), homoserine (XIV), proline (XVI), and carnitine (XV), in the presence of which the yields of products attained were close to those obtained with the aid of the usual phase transfer catalyst, proved to be the most effective.[58] The betaines (XII*a*–*j*) have also been used in the conversion of styrene into dichlorocyclopropane and in the dehydration of benzamine and their activity proved to be close to that of TEBA. The use of these betaines in the Williamson reaction was found to be less effective; the yield of benzyl propyl ether in the reaction of propanol with benzyl chloride was lower by a factor of approximately 3 than in the case where NBu_4HSO_4 was used.[59]

It has been suggested[58,59] that the mechanism of the catalysis by betaines differs from that proposed for the usual onium salts, because betaines are incapable of solubilising the CCl_3^- anion in the form of an ion pair. On formation of a bis-ion pair of the type



the catalytic activity should have increased with increase in the length of the chain connecting the carboxy-group to the onium centre. However, the opposite behaviour is observed: the catalytic activity falls in the sequence (XIII*a*)–(XIII*b*)–(XIII*c*). The authors[58,59] believe it to be more likely that the electrophilic dichlorocarbene interacts with the carboxylate anion to form the betaine (XIX)



(XIX) ,

which is capable of migrating into the bulk of the organic phase and acting similarly to the ylide formed when trialkylamines are used as catalysts. This mechanism is confirmed by the absence of a relation between the lipophilicity of the onium component of the catalyst and its catalytic activity (Table 9).[59]

Table 9. The reaction of styrene with dichlorocarbene in the presence of the betains (XII).[59]

Catalyst (XII)	Reaction time, h	Yield of product, % of theoretical	Catalyst (XII)	Reaction time, h	Yield of product, % of theoretical
Without catalyst	4.5	4	*f*	0.5	98
TEBA*	0.5	71	*g*	0.5	81
a	2.5	59	*h*	0.5	80
b	0.5	64	*h**	0.5	79
c	0.5	75	*i*	2.5	70
d	0.5	58	*j*	2.5	31
e	0.5	100			

Note. Reaction conditions: 1.7 mmol of styrene, 2.5 ml of $CHCl_3$, 1.5 ml of 50% aqueous NaOH, 1 mol% of catalyst, temperature 25 °C.
* 0.5 mol% of catalyst.

The high catalytic activity of betaines, comparable to the activity of the usual onium salts, leads to the possibility of "constructing" new catalytic salts, leads to the possibility of "constructing" new catalytic systems containing in one molecule both a catalyst and a promoting agent fragment. The carboxylate group need not necessarily be used as the promoting agent. There are data showing that the introduction of the OH^- or NH_2 group into the quaternary salt molecule in the β-position relative to the onium centre also increases the catalytic activity.[60] It is also known that the activity of chiral catalysts increases after the introduction of the OH group in the β-position relative to the nitrogen atom. All these features provide extensive opportunities for investigators who have a lively imagination and are skilled in the art of organic synthesis.

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Translated from *Uspekhi Khimii* 60 736–763 (1991) U.D.C. 541.621.2:547.64

Skeletal rearrangements of cage compounds with medium rings

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ABSTRACT. Data on skeletal rearrangements in the chemistry of cage compounds are reviewed. The main principles of thermodynamically controlled isomerisation of cage hydrocarbons and syntheses of mono- and polycage structures are considered. Data on skeletal reconstruction accompanying functionally substituted carbo- and thia-containing cage-type polycyclanes are systematised. The rules for skeletal interconversions of isomeric tricyclic structures are considered.

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I. Introduction

The chemistry of cage compounds, first arising with and receiving significant development from adamantane, now includes its structural isomers, homologues and heteroanalogues, polyadamantanes, and also carbo- and heterocage compounds of many other types. The method of synthesis by skeletal rearrangement occupies a conspicuous place in this region of chemistry, which is distinguished by structural diversity. The various skeletal reorganisations of non-cage polycyclanes into cage systems, skeletal transformations of cage compounds themselves into compounds with more stable isomeric structures and also the interconversions of cage structures, characteristic of individual groups, are widely represented.

Skeletal rearrangements form the basis of important routes for the synthesis of both cage hydrocarbons and of functional derivatives of cage polycyclanes. The synthesis of adamantane and its alkyl homologues from non-cage precursors (adamantisation) and the synthetic approaches to mono- and polycage hydrocarbons based on available precursors of other cage structures are based on isomerisation under the action of strong Lewis acids. The conversions of functionally substituted cage polycyclanes by addition, elimination and substitution reactions accompanied by skeletal rearrangements open a route to cage compounds of various classes. The skeletal transformations indicated are represented mainly by adamantisation in the monograph[1] and in the known reviews on the chemistry of adamantane and other cage compounds.[2–6] McKervey has also considered skeletal rearrangements of cage tricyclanes[7] and syntheses of polyadamantanes by isomerisation of penta- and hexacyclic hydrocarbons.[8] In recent years data have been obtained on the skeletal transformations of cage hydrocarbons, acting as intermediates in processes for the adamantisation of non-cage substrates, routes have been developed for the synthesis of a series of unique non-adamantane cage structures on the basis of skeletal conversions of actual cage compounds, and important general rules have become apparent for the skeletal reorganisations of cage compounds under the action of chemical reagents.

The present review is devoted to the correlation of data available at the present time on skeletal conversions of cage and thiacage compounds containing predominantly five- and six-membered rings. Systematisation of literature material has been carried out for a series of cage and polycyclic systems with the same number of rings and a single structural formula.

II. Skeletal transformations of cage tricyclanes

The discovery in 1975 of a single-stage method of synthesis of adamantane, and then of alkyladamantanes, by the isomerisation of available saturated tricycloalkanes with ten or more carbon atoms catalysed by strong Lewis acids, played an exceptionally important role in the development of the chemistry of adamantane itself and of cage compounds in general. Investigations on adamantisation of non-cage tricyclic precursors and especially of such hydrocarbons as *endo*-tetrahydrodicyclopentadiene (THDCP), perhydroacenaphthene and perhydrofluorene attracted much attention and culminated in the design of an industrial means of obtaining adamantane and preparative methods of synthesis of different alkyl homologues of it. Hydrocarbons of cage structure, represented mainly by isomers and homologues of adamantane, became the objects of further investigations on the thermodynamically controlled isomerisation of tricycloalkanes. Together with the isomerisation of the hydrocarbons indicated skeletal transformations of tricyclanes of cage structure also include skeletal rearrangements accompanying reactions of functional derivatives. Of the known types of similar rearrangements the present review includes mainly the transformations occurring without a change in the number of skeletal carbon atoms. Conversions of the 'adamantane–homoadamantane' and 'noradamantane–adamantane' types are not considered in the review.

1. Isomerisation of tricycloalkanes into adamantane hydrocarbons

The high thermodynamic stability of adamantane (1) in comparison with the stability of other structural isomers of $C_{10}H_{16}$-tricyclanes (Table 1) and the ability of certain Lewis acids to generate and support the concentration of cationic intermediates necessary to effect skeletal rearrangements form a basis for obtaining adamantane both from THDCP and from tricyclanes of cage structure. The isomerisation of the latter under the action of $AlBr_3$ proceeds under milder conditions and more rapidly than the isomerisation of THDCP which was shown for the example of twistane, tricyclo[4.4.0.0^{3,8}]decane, (2) [9] and protoadamantane, tricyclo[4.3.1.0^{3,8}]decane (3).[10] The latter together with 2,6-trimethylenenorbornane (5) are intermediates in the isomerisation of *exo*-1,2-trimethylenenorbornane (4).[11] The isomerisation of protoadamantane (3) into adamantane also occurs in the gas phase over Pd, Pt, and Rh at temperatures greater than 150 °C.[12]

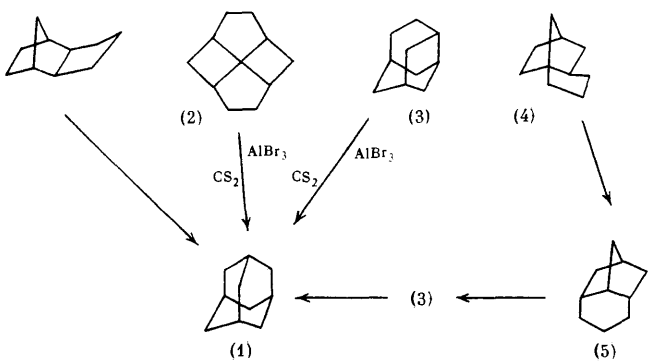
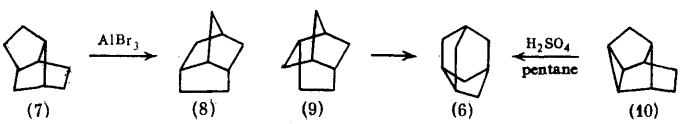


Table 1. Calculated data for the heats of formation of some $C_{10}H_{16}$-tricyclanes.[11]

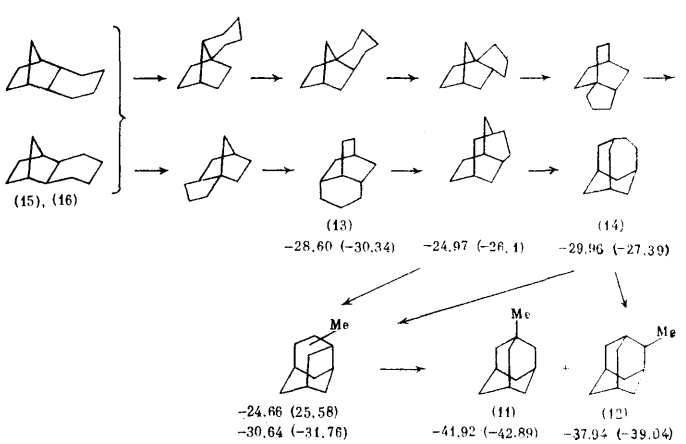
$C_{10}H_{16}$-isomers	H° (gas, 25 °C), kcal mol^{-1}
Adamantane (1)	−32.6
Protoadamantane (3)	−21.1
2,6-Trimethylenenorbornane (5)	−20.2
exo-1,2-Trimethylenenorbornane (4)	−16.7
Twistane (2)	−13.3
endo-Tetrahydrodicyclopentadiene	−16.8

The data presented are experimental confirmation of the theoretical mechanism proposed by Whitlock and Siefken for the conversion of THDCP into adamantane allowing for the heats of formation of the isomeric tricyclodecanes and based on a critical analysis of possible routes of conversion of intermediates (at least 2897 variants).[9] According to the indicated mechanism the process includes a series of sequential skeletal conversions of tricyclodecanes. The three final steps of this process are the conversions of (4) → (5) → (3) → (1).

An example of the isomersiation of C_9H_{14}-tricyclononanes to the lower homologue of adamantane is the conversion of brexane, tricyclo[4.3.0.0^{3,7}]nonane (7), under the action of $AlBr_3$ into noradamantane, tricyclo[3.3.1.0^{3,7}]nonane (6). The conversion indicated most probably proceeds through such intermediates as brendane, tricyclo[4.2.1.0^{3,7}]nonane (8), and twistbrendane, tricyclo[4.3.0.0^{3,8}]nonane (9).[13] The interaction of deltacyclane, tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (10) with sulphuric acid also leads to noradamantane and is the result of fission of the cyclopropane ring and subsequent isomerisation.[14]



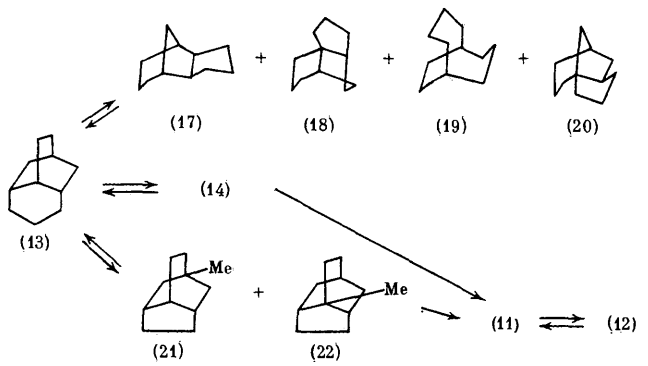
The isomerisation of C_{11}-tricyclic hydrocarbons into methyladamantanes (11) and (12) under the action of strong Lewis acids is similar to the isomerisation of $C_{10}H_{16}$-tricyclanes into adamantane and was described for the first time using non-cage precursors, viz. various tricycloundecanes and methyltricyclodecanes as examples. When studying these isomerisations 4-isohomotwistane, tricyclo[5.3.1.0^{3,8}]undecane (13), and homoadamantane, tricyclo-[4.3.1.1^{3,8}]undecane (14), were isolated and identified. Osawa and co-workers[15] have proposed the following mechanism for the isomerisation of tricycloundecanes (15) and (16) well-founded on calculated data for the thermodynamic stability of 69 isomeric C_{11}-tricyclanes. Values for the heats of formation of intermediates of carcase structure are given in the scheme.†



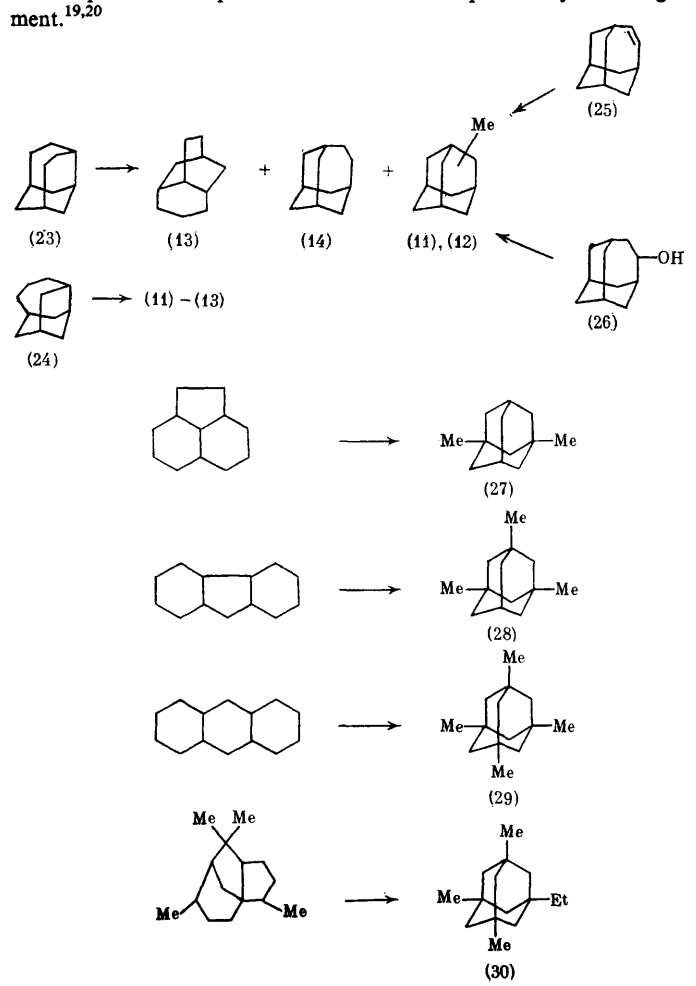
The isomerisation of 4-isohomotwistane (13) was the subject of a separate study carried out under kinetically controlled conditions using Brønsted acid (CF_3SO_3H, H_2SO_4). Under the action of these agents a complex mixture of isomeric tricyclanes was obtained from the compound indicated. The mixture contained tricycloundecanes (17)–(20), which are thermodynamically less stable than the initial compound, together with the more stable isomers,

† Here and subsequently data are given calculated according to Engler and in parentheses according to Allinger (in kcal mol^{-1}).

methylhomotwistanes (21) and (22) and homoadamantane (14), which is slowly converted into methyladamantanes (11) and (12).[16,17]

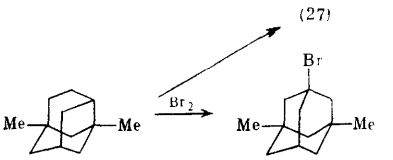


Definite differences were established between the conversions of the isomeric homoprotoadamantanes (23) and (24) under the action of CF_3SO_3H. Homoadamantane (14) predominates in the mixture of structural isomers obtained from hydrocarbon (23). The isomerisation of compound (24) under the same conditions leads predominantly to compound (13).[18] The latter also predominates in the mixture of isomers (11–14) formed on conversion of homoadamantene (25) and homoadamantanol (26) in conc. H_2SO_4 in the presence of pentane which is accompanied by rearrangement.[19,20]



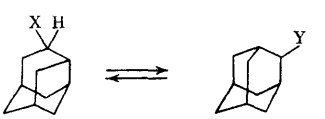
According to concepts[7] developed in recent years the isomeric polycycloalkanes with the same number of rings and same empirical formula are isomerised under the action of strong Lewis acids under thermodynamically controlled conditions to the most stable isomer of the given series, viz. the so-called stabilomer.

Thus adamantane is the stabilomer of the $C_{10}H_{16}$-tricyclanes, noradamantane is the stabilomer of the C_9H_{14}-tricyclane series and 1-methyladamantane of the $C_{11}H_{18}$-tricyclane series. The corresponding alkyl homologues of adamantane (27)–(30) play the role of stabilomers in the series of tricylanes from $C_{12}H_{20}$ to $C_{15}H_{26}$. Usually non-cage compounds serve as precursors of these compounds. Individual examples of the skeletal interconversions considered for compounds of cage structure are represented only in the $C_{12}H_{20}$ series.[7,21]



2. Skeletal interconversions of functionally substituted adamantanes and protoadamantanes

The thermodynamically controlled isomerisation of $C_{10}H_{16}$-tricyclanes comprises a cascade of rearrangements terminating in the rearrangement of protoadamantane into adamantane. The rearrangement indicated may be considered to be irreversible in the hydrocarbon series. In contrast to the hydrocarbons, the possibility of reciprocal skeletal conversions of the following type has been established for functionally substituted protoadamantanes and adamantanes.

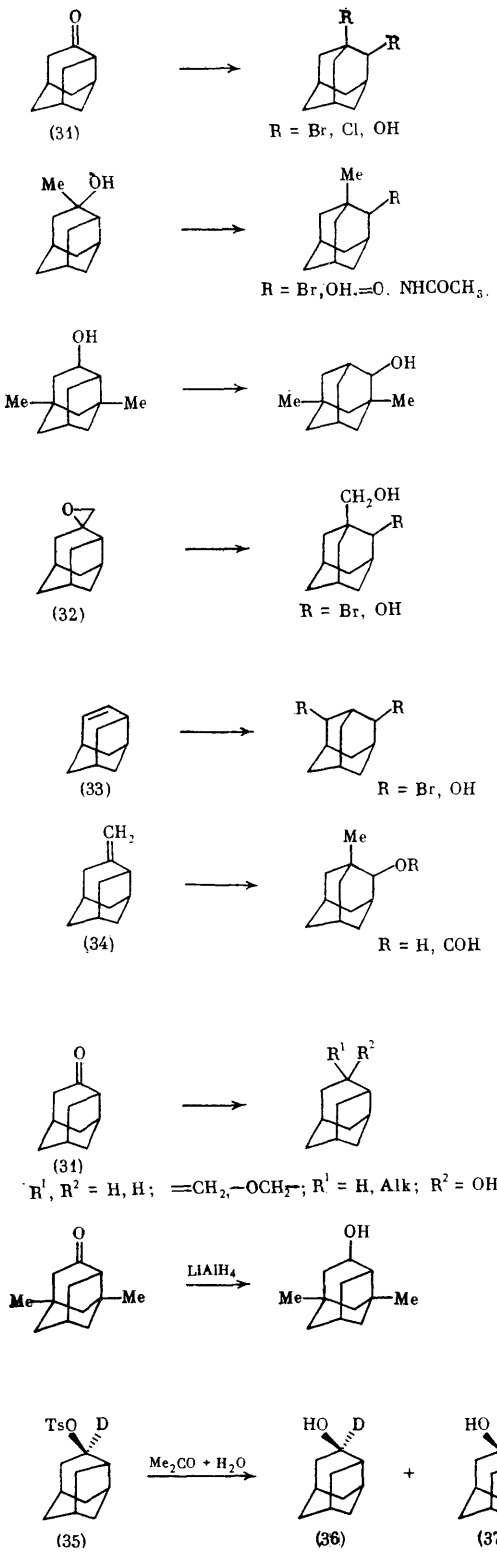


The 'protoadamantane → adamantane' rearrangement proceeds readily and completely in reactions of protoadamantan-4-one (31), its ethyleneketal,[10,22,23] alkyl substituted 4-hydroxyprotoadamantanes,[21,22,24–27,28] on interacting protoadamantane-4-spiro-oxirane (32) [28] with electrophilic reagents and also in reactions proceeding in the presence of acids. Some examples of reactions of the type indicated are shown below.

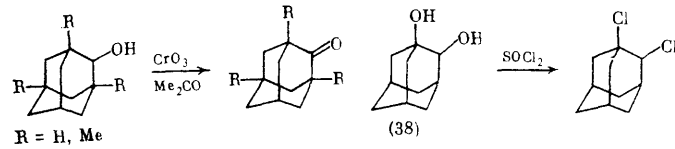
Rearrangement of the protoadamantane structure into adamantane also occurs in reactions of electrophilic addition to protoadamantene (33) [22,23,29] and to 4-methyleneprotoadamantane (34).[29]

The participation of compounds of the proto-structure in nucleophilic substitution reactions, in Grignard reactions and in the reduction of ketones with metal hydrides occurs with retention of the initial structure.[21–27,29–31]

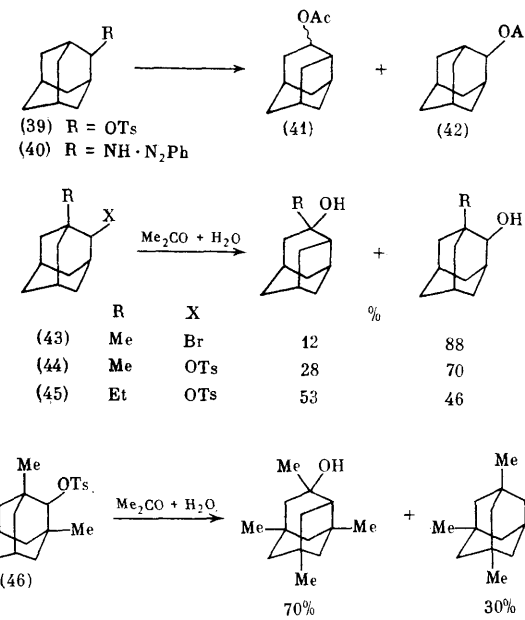
Hydrolysis of deuterated protoadamantyl tosylate (35) in 60% aqueous acetone leads to the isomeric alcohols (36) and (37). This result indicates the occurrence of a degenerate 'protoadamantane–protoadamantane' isomerisation.[10]



In the 2-substituted adamantane series the oxidation of alcohols[22,27] and the exchange of hydroxyl groups in diol (38) by Cl atoms under the action of $SOCl_2$ [22] proceed with retention of the adamantane structure.



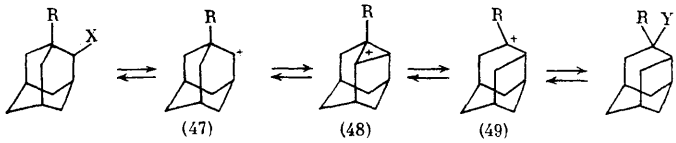
The first example of an 'adamantane → protoadamantane' rearrangement was discovered by Whiting and co-workers[30,31] on acetolysis of 2-tosyloxyadamantane (39). The reaction product contained 0.4% acetate (41) of rearranged structure in addition to acetate (42) of the initial structure. On deamination of 2-aminoadamantane by the phenyltriazene method the yield of rearranged acetate from compound (40) was 7.5%. With the introduction of a substituent into the neighbouring junction position the tendency towards this rearrangement grows and was established for the examples of the hydrolysis of bromide (43) [32] and tosylates (44)–(46).[10,24,33–35]



The mechanism proposed for the conversion of 2-substituted adamantanes into 4-substituted protoadamantanes in nucleophilic substitution reactions comprises the formation of 2-adamantyl cation (47) and its transformation through the bridging ion (48) into 1-protoadamantyl cation (49).

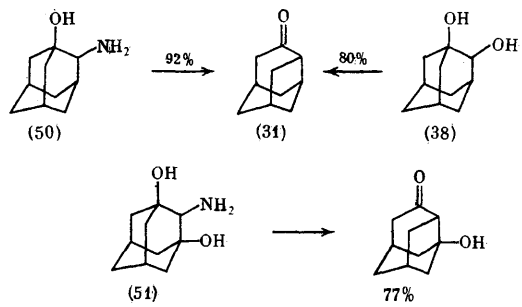
The presence of a substituent at the bridgehead position assists rearrangement since in this case the isomerised ion is tertiary which facilitates the course of a reaction by an S_N1 mechanism in difference to the initial secondary ion which reacts with difficulty in

a nucleophilic substitution reaction of S_N2 or S_N1 mechanism. Acids catalyse the reverse rearrangement.[33–37]



(47) (48) (49)

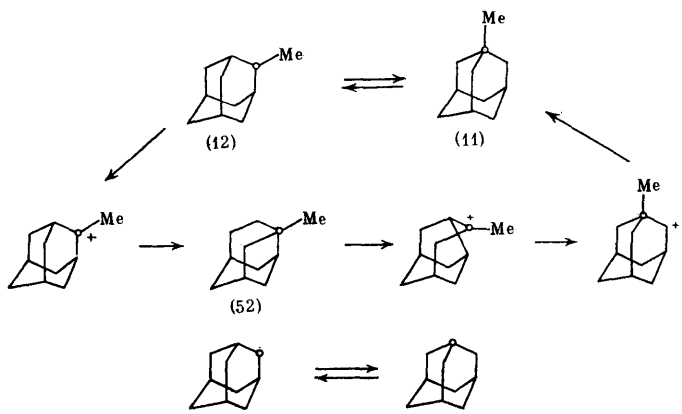
A high yield of rearrangement products is achieved on deaminating aminoalcohols (50) [10] and (51) [38] and on dehydration of alcohol (38) with dilute sulphuric acid.[22] In the case of compounds (38) and (50) the reaction indicated leads to the formation of protoadamantanone (31), a key compound in the protoadamantane series. However the conversion of the available 1-hydroxyadamantane under the action of $Pb(AcO)_2-I_2$ is chiefly used for obtaining preparatively the ketone indicated.[39,40]



(50) (31) (38)

(51) 77%

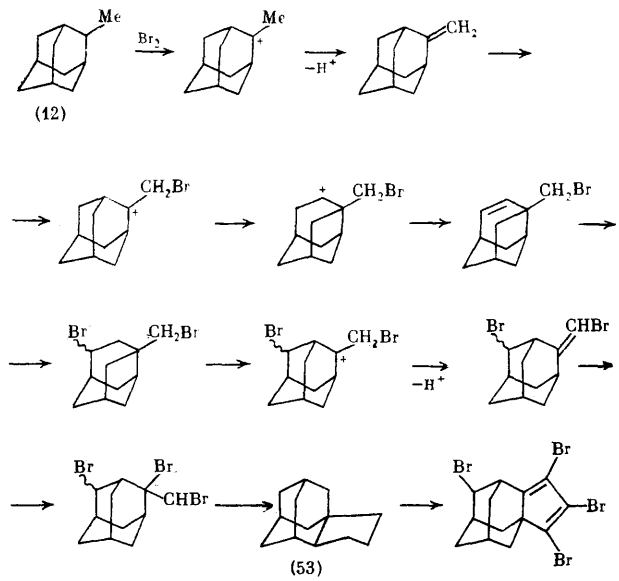
It is assumed that skeletal reorganisations of the type being considered proceed like certain conversions of 2-alkyladamantanes and of adamantane itself under the action of strong Lewis acids or with the participation of electrophiles. The isomerisation of 2-methyladamantane (12) into 1-methyladamantane (11) under the action of $AlBr_3$ comprises a conversion of the 'adamantane–protoadamantane–adamantane' type according to the mechanism proposed by Majerski and Schleyer.[41] The degenerate isomerisation of adamantane itself under the action of $AlBr_3$ most probably proceeds by an analogous mechanism.[42] These conclusions were drawn on the basis of results obtained using isotopic labels.



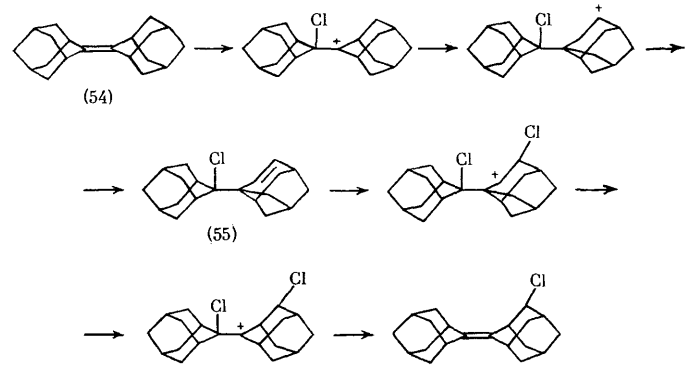
(12) (11)

(52)

The course of the process through protoadamantyl intermediates is used to explain the formation of the unexpected bromination products from such adamantane hydrocarbons as 2-methyladamantane (12) [43] and 1,2-trimethyleneadamantane (53).[44]

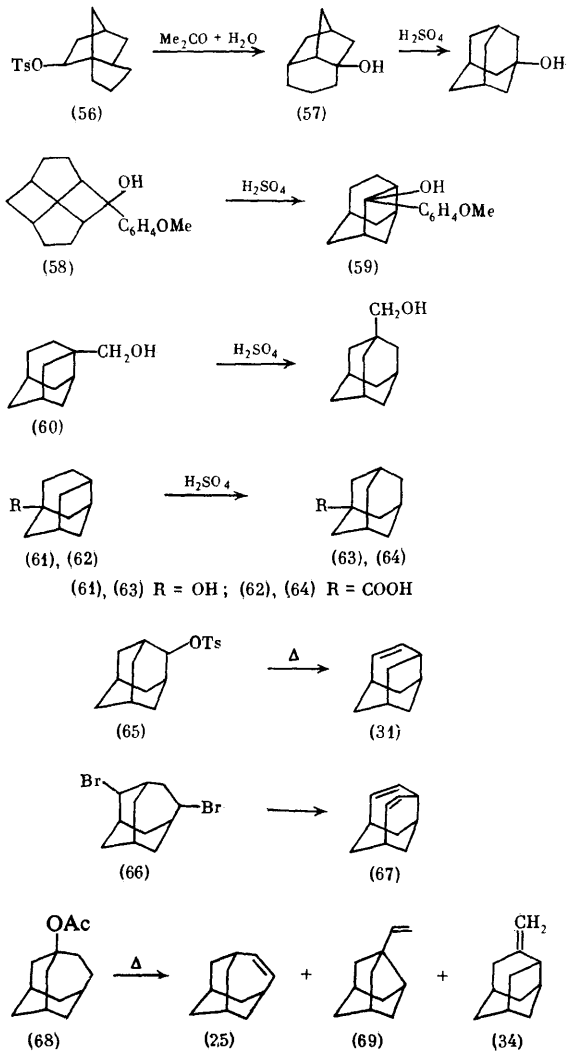


A mechanism has been proposed for the reaction of adamantylideneadamantane (54) with chlorine, the key stage of which is the formation of a protoadamantene-like intermediate (55).[45]



Individual examples of skeletal rearrangements of other types are known in addition to the interconversions of 2-substituted adamantanes and 4-substituted protoadamanatanes for functionally substituted protoadamantanes and cage tricyclanes of other structure considered in this section. Thus the hydrolysis of tosylate (56) with a 1,2-trimethylenenorbornane structure in aqueous acetone leads exclusively to alcohol (57) with a 2,6-trimethylenenorbornane structure as the rearranged product. The latter is isomerised into 1-adamantanol on storage in sulphuric acid.[46] Under the same conditions 2-*p*-anisyltwistan-2-ol (58) is isomerised into alcohol (59) with a protoadamantane structure,[9] but the bridge-substituted protoadamantanes (60)–(62) are isomerised into the corresponding bridge-substituted adamantanes.[21,47] A mechanism may be proposed

for the isomerisation of compound (61) which includes stages analogous to the conversion of (52) → (11).

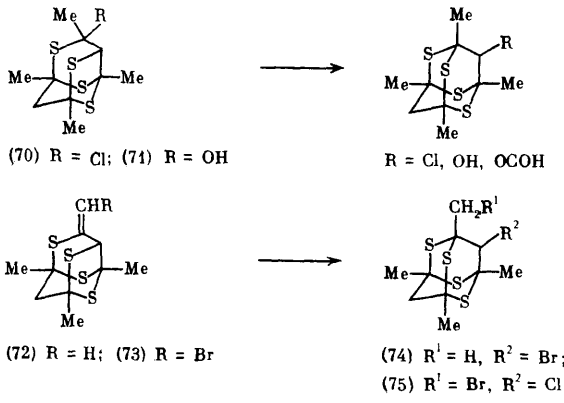


Rearrangements leading to olefins of related structure have been discovered in elimination reactions of derivatives of adamantane and homoadamantane. Thus pyrolysis of 2-adamantyl tosylate (65) leads to protoadamantene.[48] Dehydrobromination of dibromohomoadamantane (66) in hexamethylphosphoramide is accompanied by skeletal rearrangement and leads in 85% yield to diene (67) with the structure of a protohomoadamantane.[49] Olefins of rearranged structure, viz. 3-vinylnoradamantane (69) and 4-methyleneprotoadamantane (34), were also formed on pyrolysis of 1-acetoxyhomoadamantane (68) together with homoadamantene (25).[29]

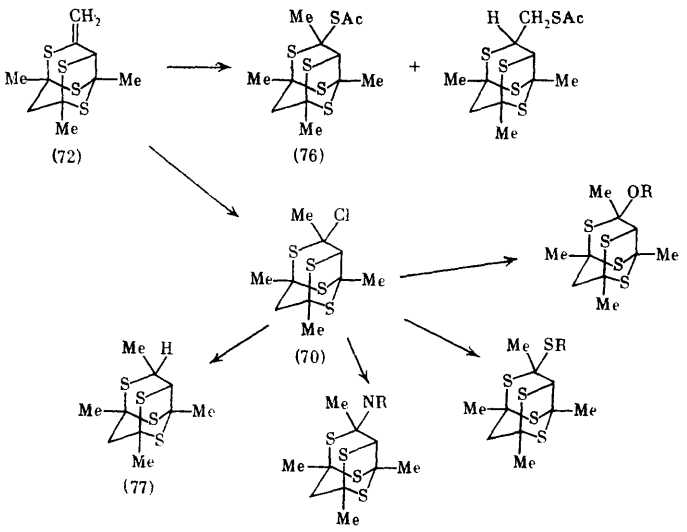
3. Skeletal conversions in the 1,3,5,7-tetramethyl-2,4,6,8-tetrathia(proto)adamantane series

Interconversions of isomeric cage structures occur in reactions of 2,4,6,8-tetrathia-analogues of adamantane and protoadamantane methylated at the bridge position.

Compounds of rearranged structure are formed from chloride (70) and alcohol (71) with a tetrathiaprotoadamantane structure under conditions of acid solvolysis.[50] Isomerisation of the chloride indicated occurs spontaneously on storage in the solid form for 10 days and also by the action of an excess of dry HCl in ether and in AcOH.[51] A similar rearrangement accompanies the hydrohalogenation of olefins (72) and (73) in AcOH,[52] which leads to bromide (74) and bromochloro-compound (75) respectively with a tetrathiaadamantane structure.

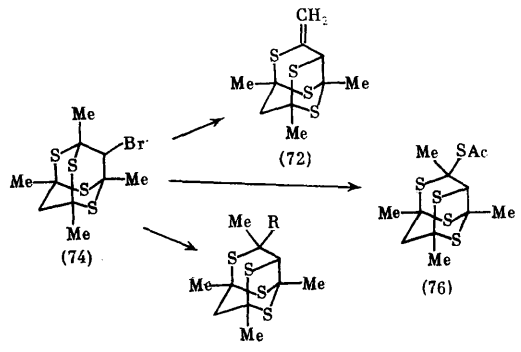


The reaction of olefin (72) with thioacetic acid[53] and its hydrochlorination under mild conditions[51] occur with retention of the proto-structure. Chloride (70) reacts readily with nucleophiles with the formation of compounds of the same structure.[54] Reductive dechlorination of the same chloride with $LiAlH_4$ leads to an *endo*-1-methyl-3,5,7-trimethyl derivative (77) with the proto structure.[55]



A 'tetrathiaadamantane → tetrathiaprotoadamantane' rearrangement accompanies the reaction of bromide (74) with nucleophiles. Thus with AcONa/NaOH or pyridine a dehydrobromination occurs leading to olefin (72) as the sole reaction product, on interaction

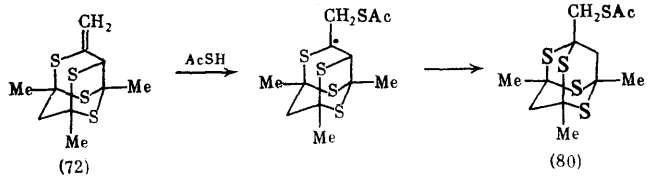
with AcSH in the presence of NaOH a rearranged thiolacetate (76) is formed.[54] Hydrolysis of compound (74) in 80% aqueous dioxan gives a mixture of alcohol (78) and olefin (72) in the ratio 2.8 : 1, and in 85% aqueous methanol a mixture of compounds (72), (78) and methoxy derivative (79) in the ratio 0.8 : 1 : 1.9.[51]



(78) R = OH; (79) R = OMe

The occurrence under ionic reaction conditions of a rearrangement of tetrathia(proto)adamantanes is analogous to the rearrangement of the 'adamantane ⇄ protoadamantane' type considered in the previous section. Since the synthetic availability of key compounds proved to be different in the carbo- and thia-containing tricyclane series different cycles of conversions were carried out, however on comparing a single reaction type in the series indicated their identical structural direction was well marked. It is important to record that in comparison with compounds of the adamantane series the 9-substituted tetrathiaadamantanes displayed a greater tendency towards rearrangement.

The occurrence of a rearrangement under radical reaction conditions was established in the interaction of olefin (72) with 1 equiv. thioacetic acid in ether, leading to thiolacetate (80). The rearrangement indicated had no analogy in the adamantane series.[53]



III. Isomeric conversions of tetracyclic hydrocarbons

Investigations on the thermodynamically controlled isomerisation of tetracyclanes have been carried out in the $C_{11}H_{16}-C_{16}H_{26}$ series. Hydrocarbons of cage structure were used in the first three series of tetracyclanes indicated in difference to tricyclanes as starting materials.

An *a priori* prediction of the stabilomer among $C_{11}H_{16}$ tetracyclanes was impossible. In accordance with the calculated heats of formation of 16 not too strained isomers selected from 2486 theoretically possible tetracyclanes of the composition indicated it was concluded[56] that 2,4-ethanonoradamantane (tetracyclo-(5.3.1.$0^{2,6}$.$0^{3,9}$]-undecane) (81) and 2,8-ethanonoradamantane-(tetracyclo-[6.2.1.$0^{2,6}$.$0^{3,10}$]undecane) (82) had approximately equal and the highest thermodynamic stability in the given series (Table 2). Experimental data on the isomerisation of synthetically available isomers, viz. tetracyclo[6.3.0.$0^{2,6}$.$0^{2,9}$]undecane (83), noriceane(tetracyclo[5.3.1.$0^{1,6}$.$0^{4,9}$]undecane) (84) and methanotwistane (tetracyclo-[6.2.1.$0^{1,7}$.$0^{4,9}$] undecane) (85), enabled it to be established that 2,4-ethanonoradamantane (81) was the stabilomer in the series indicated. Thus isomerisation of tetracyclanes (83)–(85) under the action of $AlBr_3$ leads to a mixture of hydrocarbons (81) and (82) in the ratio 97 : 3 in addition to the disproportionation product (11).

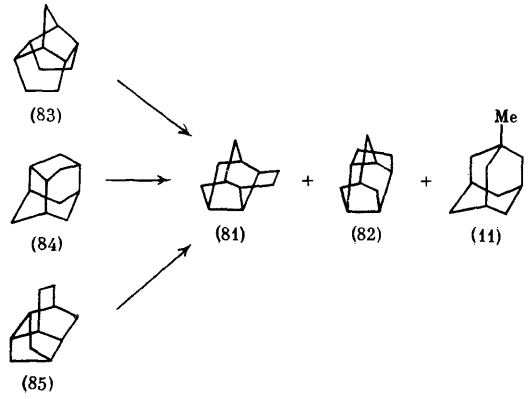
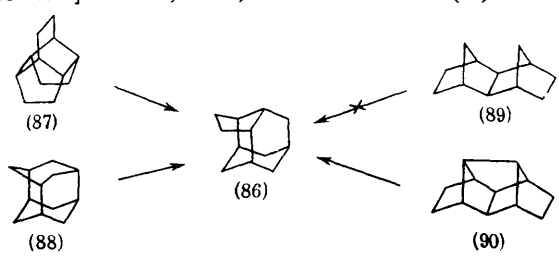


Table 2. Calculated data for the heats of formation of some $C_{11}H_{16}$-tetracyclanes.[56]

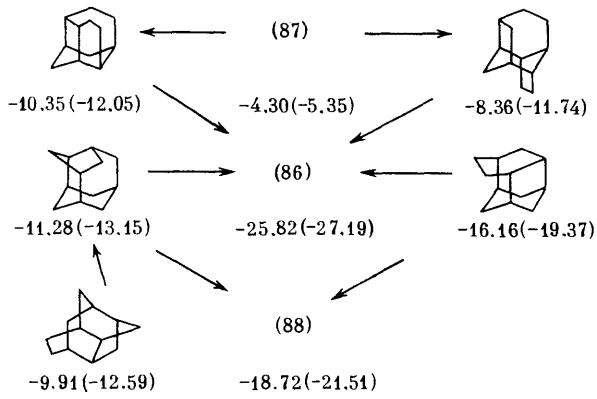
$C_{11}H_{16}$-isomers	$H°$ (gas, 25 °C), kcal mol^{-1}
2,4-Ethanonoradamantane (81)	−13.21 (−13.16)
2,8-Ethanonoradamantane (82)	−13.19 (−13.17)
Noriceane (84)	−7.21 (−10.42)
Tetracyclo[6.3.0.$0^{2,6}$.$0^{2,9}$]undecane (83)	−4.00 (−2.22)
Methanotwistane (85)	0.17 (−4.86)

The isomerisation of tetracyclanes (83) and (84) led directly to compound (81) while methanotwistane (85) was initially isomerised to hydrocarbon (82) which then isomerised slowly to (81). The formation of noriceane (84) was also recorded in the initial step of this process.

2,4-Ethanoadamantane, tetracyclo[6.3.1.$0^{2,6}$.$0^{5,9}$]dodecane (86), was detected for the first time by Landa and co-workers[57] in oil from Hodonin. Since compounds of the adamantane structure most probably arise in oil by isomerisation, Kent and Schleyer[58,59] put forward the hypothesis that 2,4-ethanoadamantane itself is the stabilomer in the $C_{12}H_{18}$-tetracyclane series. This was confirmed experimentally by carrying out the isomerisation of tetracyclo[6.4.0.$0^{4,12}$.$0^{5,9}$]dodecane (87) and iceane, tetracyclo-[5.3.1.$1^{2,6}$.$0^{4,9}$]dodecane,[88] to 2,4-ethanoadamantane (86) with $AlBr_3$.



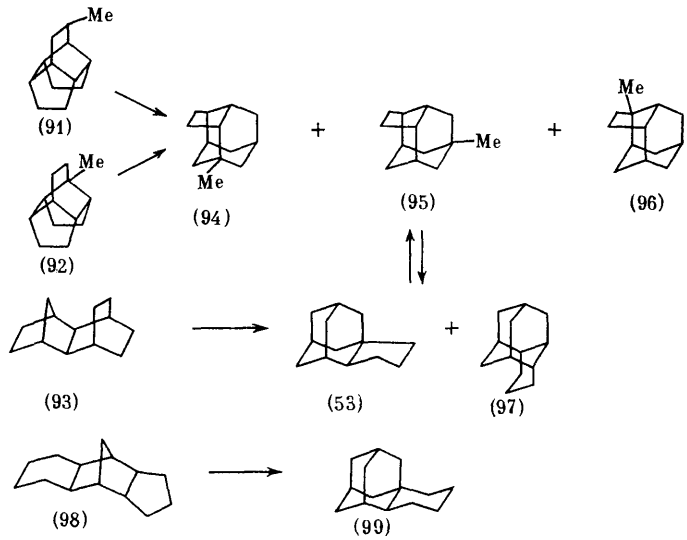
Possible routes for the rearrangement of $C_{12}H_{18}$ tetracyclanes are shown in the following scheme in which are given calculated values for the heats of formation of the hydrocarbons, i.e. for the initial, for possible intermediates and for the final isomerisation product.

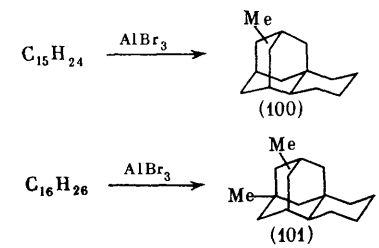


As is seen, 2,4-ethanoadamantane is 21–22 kcal mol^{-1} more stable than tetracyclane (87) and 6.7 kcal mol^{-1} more stable than tetracyclane (88). The ease of the (87) → (86) rearrangement is undoubtedly due to the fact that both possible routes of conversion include only two 1,2-alkyl shifts. In the case of iceane the rearrangement most probably occurs by transformation of the carbocation resulting from the action of the Lewis acid.

In difference to tetracyclanes (87) and (88) which have the same composition, tetracyclane (89) does not undergo isomerisation under the action of $AlBr_3$ but disproportionates leading to a $C_{12}H_{20}$-alkyladamantane.[58] It is interesting to note that 2,4-ethanoadamantane is formed together with other tetra- and pentacyclanes as the disproportionation product of the $C_{12}H_{16}$ pentacyclane (90),[59] and of a structural isomer of the latter (see section V).

The isomerisation of $C_{13}H_{20}$-tetracyclanes leads to various products depending on the structure of the substrate and the reaction conditions. A mixture of three isomeric methylethanoadamantanes (94)–(96) in the ratio 5:3:2 was formed under mild conditions from methyltetracyclododecanes (91) and (92). Similarly tetracyclotridecane (93) gave a 97:3 mixture of 1,2- and 2,4-trimethyleneadamantanes (53) and (97). Under forcing isomerisation conditions the reciprocal conversion of the indicated two groups of products was observed and a mixture was formed of compounds (53) and (94)–(97) in the ratio 42:27:19:8:3 together with products of side reactions. The calculated heats of formation of the compounds indicated did not correspond with the experimental results which does not permit a conclusion to be drawn as to the stabilomer in the series under consideration. On the other hand in the $C_{14}H_{22}$-tetracyclane series the experimental data on the isomerisation of hydrocarbon (98) and the calculated data indicated unequivocally that 1,2-tetramethyleneadamantane (99) is the stabilomer in this series.[60] The latter is also formed as a disproportionation product on rearranging certain $C_{14}H_{20}$-pentacyclanes (see section V).



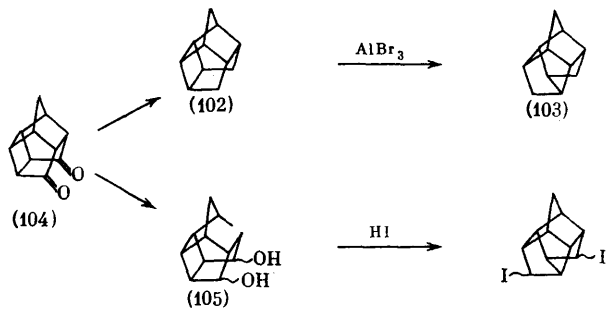


The isomerisation of tetracyclanes of composition $C_{15}H_{24}$ and $C_{16}H_{26}$ of non-cage structure with $AlBr_3$ leads to methyl- and dimethyl-substituted 1,2-tetramethyleneadamantanes (100) and (101) respectively.[61]

IV. Skeletal rearrangements of $C_{11}H_{14}$-pentacyclanes

Skeletal conversions in this series are mainly represented by the isomerisation of pentacyclo[6.2.1.0^{2,7}.0^{4,10}.0^{5,9}]undecane (102) into trishomocubane, pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (103), and by analogous skeletal rearrangements in reactions of numerous functionally substituted derivatives of pentacyclane (102). The latter are convenient subjects for investigation since they may readily be synthesised from the available diketone (104), itself the product of the photocyclisation of the Diels-Alder adduct of *p*-benzoquinone and cyclopentadiene. Proceeding from the diketone indicated, first Underwood and Ramamorthy,[62] and then Eaton and co-workers[63] by another route, effected the synthesis of trishomocubane. The formation of the trishomocubane structure in these syntheses occurred by intramolecular cyclisation in the corresponding tetracyclic intermediate. In several recent studies approaches have been developed to trishomocubane, and its mono- and disubstituted derivatives, based on the skeletal rearrangement of C_{11}-pentacyclic substrates. Thus trishomocubane has been obtained by the

isomerisation of pentacyclane (102) with $AlBr_3$.[64] The same authors have described a rearrangement leading to the trishomocubane structure in the reaction of diol (105) with HI.[65]



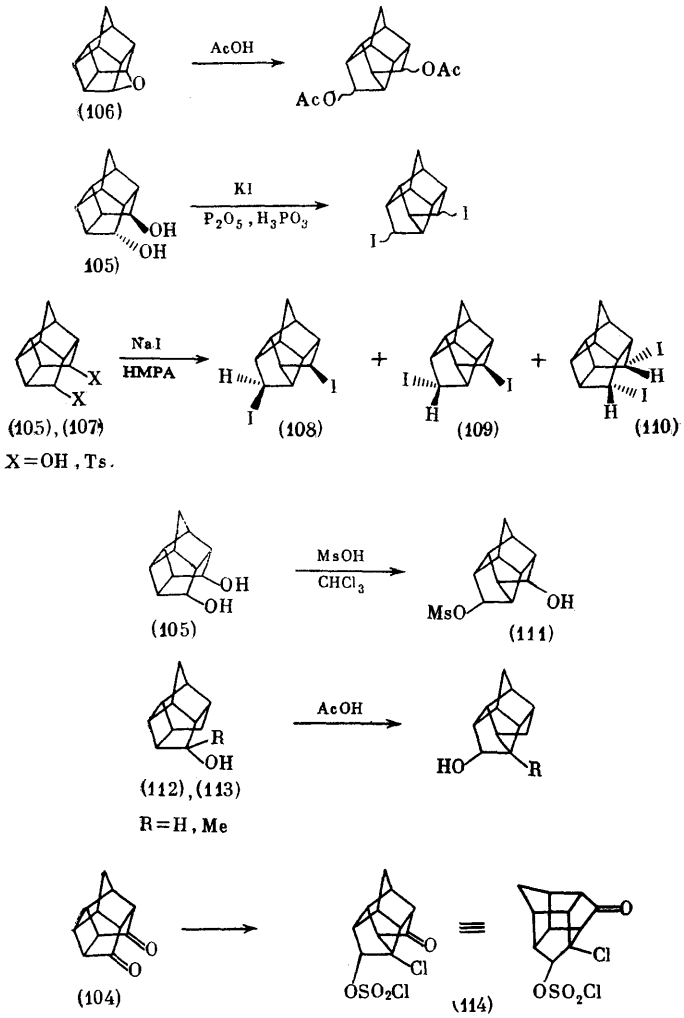
The interaction of diol (105) with a mixture of H_3PO_4, P_2O_5 and KI and fission of the oxygen bridge of the oxa-'bird-cage' (106) in AcOH is accompanied by rearrangement and leads exclusively to a trishomocubane derivative.[66] By reacting diol (105) and tosylate (107) with NaI in hexamethylphosphoramide, diiodides of rearranged structure (108) and (109) are formed together with diiodide (110) of initial structure.[67,68]

Table 3. Calculated data for the heats of formation of some $C_{11}H_{14}$-pentacyclanes.[65]

$C_{11}H_{14}$-isomers	H° (gas, 25 °C), kcal mol^{-1}
Trishomocubane (103)	9.38 (11.32)
Pentacyclo[6.2.1.0^{2,7}.0^{4,10}.0^{5,9}]undecane (102)	19.62 (21.93)
Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (120)	23.88 (26.58)
Homobasketane (115)	40.99 (43.82)

A rearranged hydroxymesylate (111) is formed on reacting diol (105) with methanesulphonic acid.[69] Alcohols (112) and (113) are isomerised into the corresponding compounds of the trishomocubane structure by reaction with acetic acid.[70]

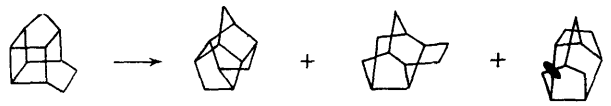
Compounds, which in their turn were obtained from diketone (104), are transformed in the above examples into the trishomocubane structure. The single example of a similar conversion of diketone (104) is its reaction with chlorosulphonic acid leading to a trisubstituted trishomocubane (114).[71–73]



Kent and co-workers[65] carried out an analysis of the stability of the isomeric cage $C_{11}H_{14}$-pentacyclanes which were selected from the 15358 possible cage isomers after excluding very strained structures. The results showed that trishomocubane itself is the thermodynamically most stable isomer in this series (Table 3). An insignificant difference in energy (10 kcal mol^{-1}) and the possibility of a (102) → (103) transition by a simple 1,2 shift in the secondary cation explains the ease of the considered rearrangement. It would be noted that examples of the reverse rearrangement, probable in reactions of functional derivatives of trishomocubane, have not as yet been described.

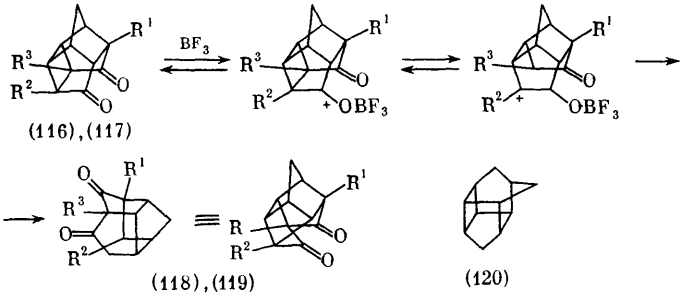


Results of studies[74] in which trishomocubane was obtained by isomerisation of homobasketane (115) with $AlBr_3$ are in agreement with the given theoretical analysis. The $C_{11}H_{16}$-isomers (81) and (82) were formed as well as compound (103) in the reaction indicated.



(115) (103), 82,0% (81), 6,4% (82), 11,1%

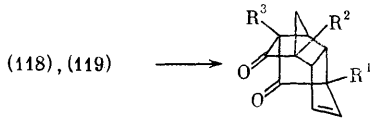
Introduction of alkyl groups at the α-position to the carbonyl group in diketone (104) may assist skeletal reorganisation which diketone (104) itself does not undergo. Thus dimethylketones (116) and (117) are isomerised by BF_3 etherate into compounds (118) and (119) respectively with the structure of a pentacyclo-[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane.[75] The indicated isomerisation is even more interesting since the unsubstituted pentacycloundecane (120) is thermodynamically less stable than pentacycloundecane (102) (Table 3).



(116), (117) (118), (119) (120)

(116), (118) R^1=H ; R^2, R^3=Me ; (117), (119) R^1, R^2=Me, R^3=H.

The corresponding tetracyclic enediones (121) and (122) are obtained on pyrolysis of pentacyclic compounds (118) and (119).[75]

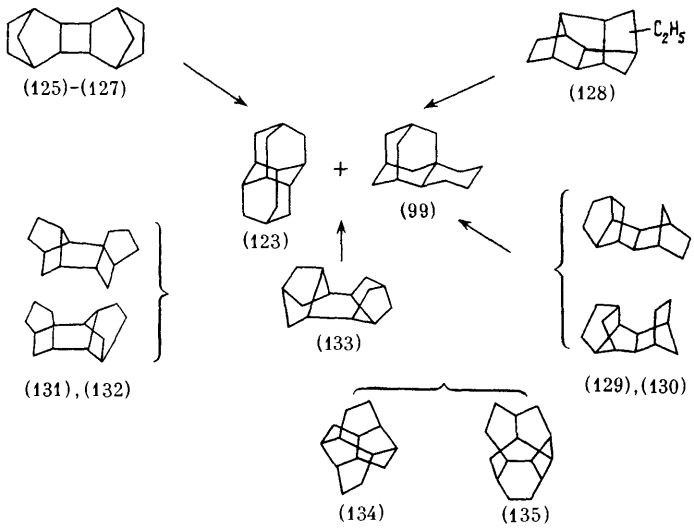


(118), (119) (121), (122)

V. Syntheses of polycage compounds of the condensed type based on skeletal transformations of monocage polycyclanes

The main principles of the thermodynamically controlled isomerisation of polycycloalkanes apparent in investigations on the synthesis of monocage structures have been further developed in approaches to polycage compounds of a condensed type of structure such as diamantane (123) and triamantane (124). In the same way that adamantane is the stabilomer of the $C_{10}H_{16}$-tricyclanes, diamantane is the stabilomer of the $C_{14}H_{20}$-pentacyclanes and triamantane the stabilomer of the $C_{18}H_{24}$-heptacyclanes. The problem of the selection of a suitable precursor proved to be a key issue in investigations on the synthesis of the polymantanes indicated.

Diamantane was isolated for the first time from Hodonin oil[57] and was synthesied at almost the same time by a [2 + 2] rearrangement of norbornene photodimers (125)–(127).[76] In this synthesis the yield of diamantane was 1 to 10% depending on which stereoisomer was used. 1,2-Tetramethyleneadamantane (99) formed by disproportionation of the starting materials predominated in the reaction product.[77,78]



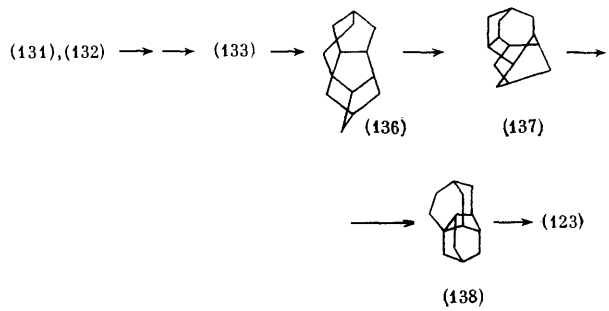
(125)-(127) (128) (123) (99) (133) (131), (132) (129), (130) (134) (135)

The search for other precursors then led to cage pentacyclane (128) isomerisation of which gave diamantane in 30% yield.[77,78] Diamantane was obtained in 25% yield on using hydrogenated Katz dimers (129) and (130).[78] The most suitable precursor for diamantane proved to be tetrahydro-Binor-S (131) and (132). On isomerisation of the latter with $AlBr_3$ in CS_2 the yield of diamantane was 65% and with $AlBr_3$ in CH_2Cl_2 82%.[77–80] One of the intermediates, viz. *trans*-pentacyclo[8.2.1.$1^{2,5}$.$0^{3,7}$.$0^{8,12}$]tetradecane (133), was isolated and identified during the conversion.[78] Recently the synthesis of diamantane in high yield by isomerisation of hydrogenated dimers of cycloheptatriene (134) and (135) has been described.[81]

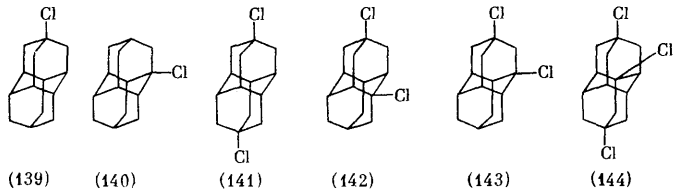
Table 4. Calculated data for the heats of formation of some $C_{14}H_{20}$-pentacyclanes.[82]

$C_{14}H_{20}$-isomers	$H°$ (gas, 25 °C), kcal mol^{-1}
Diamantane (123)	10.7
Protodiamantane (138)	31.1
Intermediate (137)	28.0
Intermediate (136)	40.8
Intermediate (133)	34.9
Tetrahydro-Binor-S (131)	62.16
(132)	54.15
(2+4)-dimers of norbornene (129)	49.77
(130)	57.15
(2+2)-dimers of norbornene *exo, trans, exo*-(125)	57.62
exo, trans, endo-(126)	62.57
endo, trans, endo-(127)	68.03

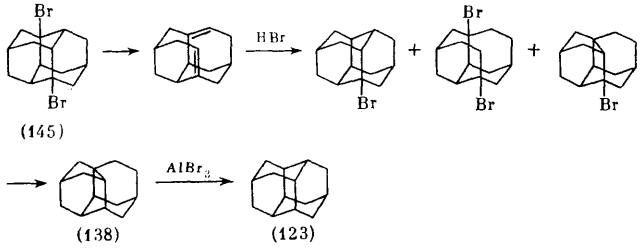
A theoretical analysis of the rearrangement of pentacyclotetradecanes into diamantane has been carried out.[82] According to the calculated data obtained for various precursors, for a vast number of possible intermediates and for diamantane itself, the latter was the thermodynamically most stable isomer among the $C_{14}H_{20}$-pentacyclanes (Table 4). A possible mechanism for the isomerisation of hydrocarbons (131) and (132) comprises the following sequence of skeletal conversions which is completed by the rearrangement of protodiamantane, pentacyclo[7.3.1.1^{4,2}.1^{1,7}.0^{6,11}]-tetradecane (138), into diamantane.



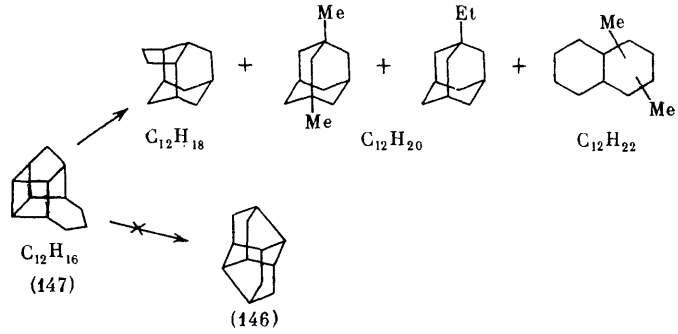
The possibility was shown in several examples of combining two steps, viz. the isomerisation of tetrahydro-Binor-S into diamantane and functionalisation of the latter. Thus chloroadamantanes (139) and (140) were obtained from tetrahydro-Binor-S with $AlCl_3$ and acetyl chloride, and dichloroadamantanes (141)–(143) were obtained on using $AlCl_3$ and paraformaldehyde.[80,83] Chlorosulphonic acid converts tetrahydro-Binor-S into 4,9-dichlorodiamantane (141) or into 1,4,9-trichlorodiamantane (144) depending on the duration of reaction.[84]



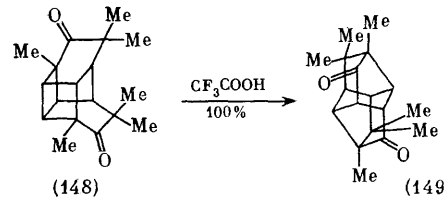
Gund and Schleyer[85] carried out the synthesis of protodiamantane (138) using dibromodiamantane (145) as starting material. Isomerisation of (138) into diamantane (123) proceeded readily with $AlBr_3$ or H_2SO_4 in methylcyclohexane.



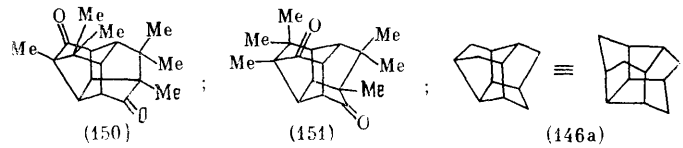
Attempts to obtain the lower homologue of diamantane, viz. bisnordiamantane (146) by the isomerisation of pentacyclo[5.5.0.0^{2,5}.0^{3,12}.0^{4,8}]dodecane (147) have been unsuccessful. The $C_{12}H_{16}$ hydrocarbon mentioned did not isomerise with $AlBr_3$ under mild conditions and under forcing conditions its conversion led only to a disproportionation product.[74]



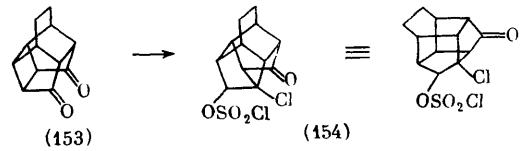
In contrast to hydrocarbon (147) the hexamethyldiketone (148) with the dihomobasketane structure, pentacyclo[6.4.0.0^{2,7}.0^{3,12}.0^{4,9}]-dodecane, readily isomerised in boiling trifluoroacetic acid or in benzene in the presence of toluene-*p*-sulphonic acid into compound (149) with the bisnordiamantane structure.[86] Theoretical analysis of the isomerisation showed that compound (149) is 3–6 kcal mol^{-1} less stable than isomers (150) and (151). In the C_{12} pentacyclane hydrocarbon series the stabilomer is pentacyclo[6.4.0.0^{2,6}.0^{3,11}.0^{4,9}]-dodecane (152), which is 8 kcal mol^{-1} more stable than bisnordiamantane (146).



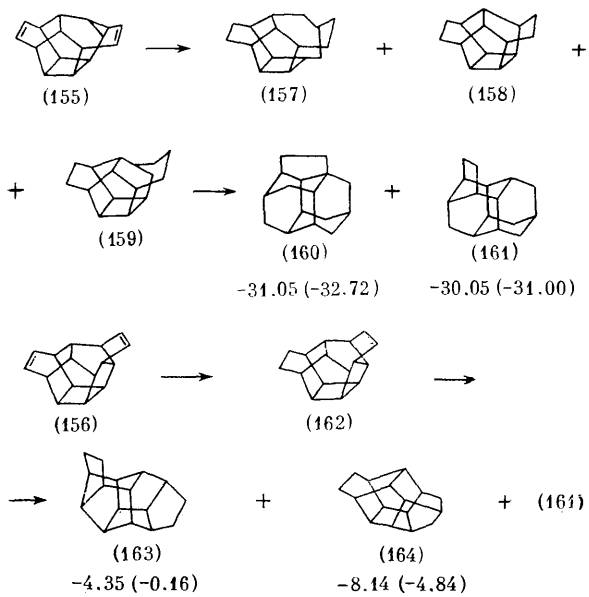
The fact that the isomerisation of compound (148) does not lead to the formation of the stabilomer is most probably explained by the absence of a suitable route for further skeletal isomerisation in this case.[87]



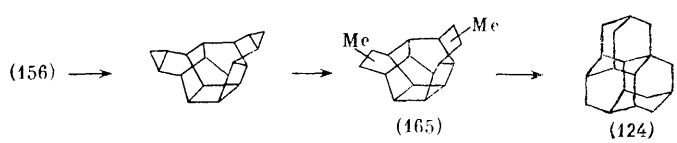
The reaction of diketone (153) with chlorosulphonic acid is accompanied by a skeletal rearrangement and leads to the chloroketo-sulphonyl chloride (154) with a pentacyclo[7.3.0.0^{2,7}.0^{3,11}.0^{6,10}]-dodecane structure. The formation of the stabilomer structure was not observed in this case either.[72]



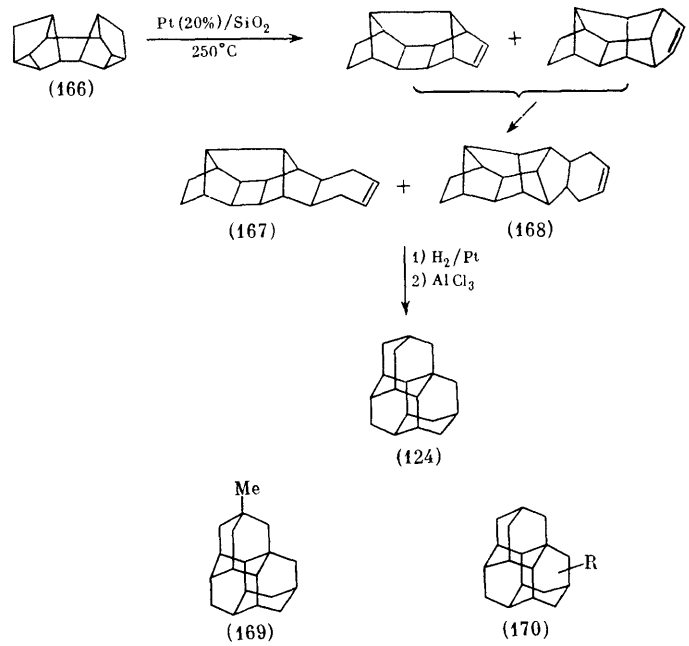
The synthesis of polymantanes of composition $C_{16}H_{20}$, isomers of ethanodiamantanes and diethanobisnordiamantane, was effected on the basis of the cage dimers of cyclooctatetraene (155) and (156). Hydrogenation of the first of these led to a mixture of hexacyclohexadecanes (157)–(159), the isomerisation of which with $AlBr_3$ gave a mixture of (C_1)-ethanodiamantane (160) (85%) and (C_s)-ethanodiamantane (161) (15%).[88] The first isomer is more stable than the second according to molecular mechanical calculations. From the product of hydrogenation of the second dimer, compound (162), a mixture was obtained of (C_2)-bisethano-bisnordiamantane (163) (73%) and compound (164) (13%) with a structure related to 'bird-cage'. Compound (161) (~20%) was also formed on using a complex containing $AlBr_3$ and t-butyl bromide and is the disproportionation product in the given reaction.



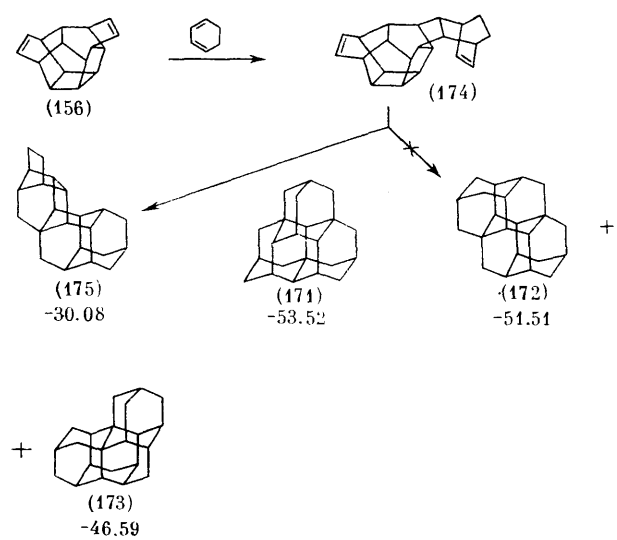
In the first synthesis of triamantane (124) by the isomerisation of $C_{18}H_{24}$ heptacyclanes Schleyer and co-workers[89] started from cyclooctatetraene dimer (156) which had served for the synthesis of polycyclane (165). Isomerisation of the latter with $AlBr_3$ led to triamantane in 1% yield.



Polycyclanes (167) and (168) obtained from Binor-S (166) proved to be the most suitable precursors of triamantane. Isomerisation of the dihydro derivatives of the latter led to triamantane (124) in 60% yield.[90] Methyltriamantane (169) and pentanotriamantane (170) were prepared by a modified diene synthesis using isoprene or cyclopentadiene as diene component.[8]



Attempts to obtain tetramantanes (171)–(173) by isomerisation of polcyclane (174), synthesised from cyclooctatetraene dimer (156), led only to a structural isomer of tetramantane, viz. bastardane (nonacyclo[11.7.1.1^{2,18}.0^{3,16}.0^{4,13}.0^{5,10}.0^{6,14}.0^{7,11}.0^{15,20}]-docosane) (175).[88] According to the calculated data shown in the scheme bastardane is less stable than tetramantanes (171)–(173). Thus the isomerisation process in the present example is not completed by the formation of the stabilomer but finishes at the stage of obtaining the kinetically stable structural isomer.



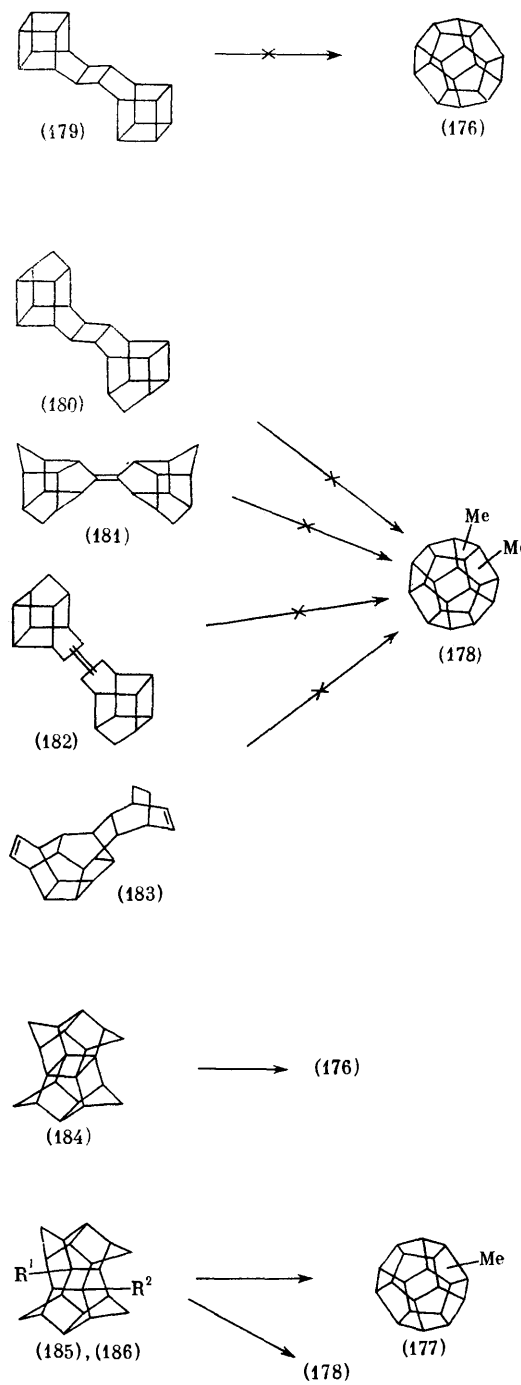
VI. Skeletal rearrangements of $C_{20}H_{20}-C_{22}H_{24}$ polycyclanes in approaches to the synthesis of dodecahedrane

The problem of the synthesis of dodecahedrane (176), a spherical system of composition $C_{20}H_{20}$, containing twelve repeatedly linked cyclopentane rings has attracted significant attention in the last decade.[91,92] Paquette and co-workers[93,94] reported the first preparation of dodecahedrane in 1982 by a 23 stage synthesis. Among the various approaches developed to achieve this goal were repeated attempts to obtain dodecahedrane and its alkyl homologues by the thermodynamically controlled isomerisation of polycage precursors. This synthetic route was exceptionally tempting since it might have enabled dodecahedrane to be obtained in one stage. Such an approach was based on the *a priori* hypothesis that dodecahedrane is the stabilomer of the $C_{20}H_{20}$ dodecacyclane series. The obtaining of the appropriate calculated data required to select the stabilomer in this series did not indeed seem possible in view of the astronomical number of isomeric cage structures.

Bicage compounds of various types were used as precursors in experimental attempts to isomerise dodecacyclanes into dodecahedrane or its alkyl homologues (177) and (178). The photodimer of basketane (179) [95] and the photodimer of homobasketane (180) [74] were subjected to isomerisation with Lewis acids. Attempts have also been described to isomerise bicage olefins (181) and (182) and also cage diene (183), obtained in the diene synthesis reaction of cyclooctatetraene dimer and cyclohexadiene.[74] They were all unsuccessful.

The bicage $C_{20}H_{20}$ dodecacyclane, 1,1,1,1-pagodane (184), recently attracted attention as a precursor of dodecahedrane. The former failed to isomerise to dodecahedrane with strong acids, however, the isomerisation was effected in the gas phase over a catalyst ($Pt/Re/Al_2O_3$, Pd/C, Rh/C, Pd/Al_2O_3).[96,97] The alkyl homologues of dodecahedrane (177) and (178) were obtained similarly. The corresponding compounds (185) and (186), with structures related to pagodane, were used as precursors.[97] This approach to the synthesis of dodecahedrane derivatives has been further developed.[98,99]

The data presented in the review demonstrate the wide synthetic possibilities of applying to cage compounds methods based on skeletal rearrangements and, most of all, on the thermodynamically controlled isomerisation of hydrocarbons. Investigations carried out up to the present time on the isomerisation indicated enable ideas to be formulated on stabilomer structure and applied in practice to the creation of new synthetic principles, previously unknown in organic chemistry. Doubtless further investigations in this area will serve as a basis for finding effective approaches to the many unique cage structures, including the hypothetical. It is also possible to suggest that further development of methods of synthesis of functional derivatives, including interconversions of isomeric structures may be found in the chemistry of cage and heterocage compounds.



(185) R^1=Me, R^2=H; (186) R^1, R^2=Me

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Translated from *Uspekhi Khimii* **60** 764–798 (1991) U.D.C. 678.743:542.944.6

Chemical dehydrohalogenation of halogen-containing polymers

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ABSTRACT. This review is concerned with the dehydrohalogenation of halogen-containing polymers as a method of obtaining polymers with a system of conjugated multiple bonds. Different dehydrohalogenating agents are described and the mechanism, kinetics and structure of the reaction products are examined.

The bibliography includes 159 references.

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I. Introduction

Dehydrohalogenation of halogen-containing compounds has been studied in detail[1] in the field of organic chemistry and is widely used for the synthesis of unsaturated compounds.[2]

In the chemistry of macromolecular compounds the majority of studies on the dehydrohalogenation of halogen-containing polymers were carried out previously in order to find effective stabilisers for these polymers, in particular for poly(vinyl chloride) (PVC), because of their low resistance towards heat and light. A number of reviews have been devoted to the thermal degradation of PVC.[3–18]

Several methods for the dehydrohalogenation of halogen-containing polymers are known.[3] However, thermal and photodehydrohalogenation as well as dehydrohalogenation by means of X-radiation and γ-radiation result in the formation of cross-linked products with short sequences of conjugated multiple bonds. Dehydrohalogenation by chemical agents can give considerably longer segments of conjugation, particularly under mild conditions (at reduced temperatures).

At the beginning of the 1960's studies in which the directed dehydrohalogenation of halogen-containing polymers was investigated as a method of obtaining polymers that contain a system of conjugated multiple bonds in the main chain started to be published in the scientific literature. A considerable amount of experimental experience in this field of polymer-like reactions has been built up so far, but reviews devoted to the chemical dehydrohalogenation of polymers are absent from the literature. Therefore, the aim of the present reivew is to correlate the literature data on the dehydrohalogenation of halogen-containing polymers by different chemical agents and to examine the structure of the reaction products as well as the kinetics and mechanisms of the reactions that occur.

II. Dehydrohalogenation by alkalis

Alkali metal hydroxides, in particular those of Na and K, are widely used as dehydrohalogenating agents. However, aqueous solutions of NaOH and KOH only react effectively with halogen-containing polymers at high temperatures. Thus, for example, in order to dehydrochlorinate PVC completely with aqueous solutions of NaOH and KOH the reaction must be carried out at 250–270 °C.[19] At these temperatures the contribution from side reactions involving cross-linking and oxidation of the resulting sequences of conjugated double bonds increases considerably. At lower temperatures the reaction takes place extremely slowly. Thus, in the dehydrofluorination of poly(vinylidene fluoride) (PVDF) powder with an aqueous solution of NaOH at 90 °C for 5 h, there is only 7.8% elimination of HF.[20] Reactions with PVC [21] and vinylidene chloride–vinyl chloride copolymer[22] occurred in a similar manner.

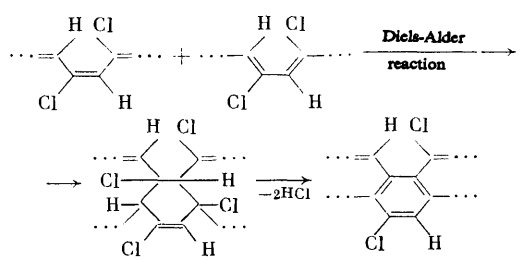
1. Dehydrohalogenation in the presence of phase-transfer catalysts

By using quaternary ammonium and phosphonium halides[20–27] and hydroxide[28] and also crown ethers[20,29] as phase-transfer catalysts it was possible to increase significantly the rate of alkaline dehydrohalogenation of halogen-containing polymers.

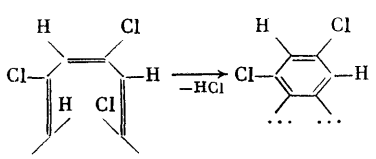
In a number of studies the dehydrohalogenation of PVC,[21,26,27] poly(vinylidene chloride) (PVDC),[29] PVDF,[20,23,25,28] and vinylidene chloride–vinyl chloride copolymer containing 5–20% of the latter (Saran)[22,24] was investigated. A high degree of conversion was achieved on average after 15–20 h at 60–100 °C, although data exists on the surface modification of PVDF films[23,25] and the dehydrochlorination of PVC [21] and Saran[22] that were carried out at room temperature. The reactions were conducted using powders,[20,21,24,27,28] films,[20,21,23–26] and solutions[22] of the polymers.

In the dehydrochlorination of PVC in the presence of quaternary ammonium or phosphonium halides,[21,26] black compounds are formed that undergo aerial oxidation and which have a conjugated polyene structure of the *trans*-polyacetylene type. As the reaction takes place, characteristic absorption bands appear in the IR spectra of the products due to isolated (1670 cm^{-1}) and conjugated (1560 cm^{-1}) C=C double bonds as well as an absorption band at 580 cm^{-1} attributed to bending vibrations of C–H bonds in *trans*-olefinic bonding.[21]

In the dehydrohalogenation of PVDC, Saran, and PVDF in the presence of onium salts, the reaction products are black powders or films that have the halogen-substituted polyene structure $-(-CX=CH-)_n-$, (X = Cl, F) and are stable towards aerial oxidation,[20,24] in contrast to dehydrochlorinated PVC.[21] In the IR spectra of the products from the dehydrohalogenation of poly(vinylidene halides) intense absorption bands occur in the region of 1600 cm^{-1} which correspond to stretching vibrations of conjugated C=C double bonds, and much less intense bands appear in the region of 2170 cm^{-1} that are attributed to the stretching vibrations of C≡C triple bonds which can be formed by the elimination of two molecules of hydrogen halide from a single vinylidene unit of the polymer.[20,22,24,29] In addition to that, in the IR spectra of the dehydrohalogenation products of these polymers, absorption bands have been recorded in the region of 865 and 3400 cm^{-1} that are attributed to aromatic structures and OH groups respectively. According to the authors of two studies,[24,29] aromatisation of the polyene sequences can occur via a Diels–Alder reaction followed by dehydrohalogenation of the resulting cyclohexene structures:



or as the result of intramolecular cyclisation via 1,6-elimination:



The authors attribute the low content of C≡C triple bonds in the dehydrohalogenation products at high degrees of conversion to aromatisation of the polyene sequences. Hydroxyl groups occur in the polymer as a result of nucleophilic substitution of the halogen atoms in the polymer by the hydroxyl ion.[24]

In the IR spectra of the dehydrohalogenation products with a high degree of conversion the absorption bands characteristic of the initial polymers have become very weak.

In several studies[20–22,24] a wide range of quaternary ammonium and phosphonium halides were used as phase-transfer catalysts; these differed according to the number of carbon atoms in the hydrocarbon substituents on the nitrogen or phosphorus atom—from tetramethylammonium bromide to an Adogen catalyst [trialkylmethylammonium (C_8-C_{10}) chlorides]. The activity of the onium salts in dehydrohalogenation reactions depends mainly on the number of carbon atoms in the catalyst molecule and is limiting in nature. For the dehydrohalogenation of PVC and PVDF the reaction occurred more rapidly and the conversion reached a maximum when tetrabutylammonium bromide (TBAB) was used as the catalyst. In the dehydrochlorination of Saran the best catalyst proved to be tetrapropylammonium bromide (TPAB). Similar results were obtained when the analogous phosphonium salts were used.

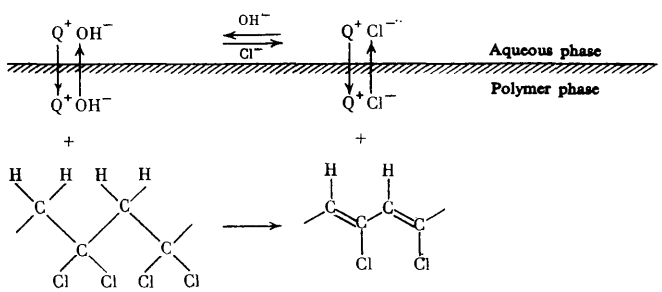
The limiting dependence of the activity of the catalyst on the number of carbon atoms in the substituents is accounted for using the concept of the hydrophile-lipophile balance (HLB). An increase in the lipophilic nature of the catalyst assists the reaction up to a given maximum. With a further increase in the number of carbon atoms the alkyl substituents of the catalyst inhibit its diffusion into the polymer. In two-phase aqueous organic reactions the negatively charged bases form ion pairs with the positive onium ions and are then extracted into the organic phase, where reaction takes place. Since exchange of anions at the phase boundary or in the aqueous phase occurs much more rapidly than the reaction between an ion pair and substrate (polymer), the rate of reaction mainly depends on the concentration of catalyst in the organic phase.[21] In the dehydrohalogenation of polymers a layer of reaction products that are insoluble is formed on their surface, significantly inhibiting diffusion of the dehydrohalogenating agent into the polymer, i.e., the reaction is self-inhibited.[25]

For a quantitative determination of the HLB the use of function D was proposed:

$$D = (\delta - \delta_w)^2/(\delta - \delta_o)^2,$$

where δ, δ_w, and δ_o are the solubility parameters of the onium salts, water (δ_w = 23.4) and the organic phase (polymer) respectively.[30] The catalytic activity of the onium salts increases with a decrease in the value of D,[24] in other words, it depends on the affinity of the ion pair for the organic phase (polymer), where dehydrohalogenation occurs. In the dehydrochlorination of Saran, TPAB had the greatest activity (higher and lower analogues were less active),[24] while in the dehydrohalogenation of PVC and PVDF, TBAB proved to be the most active.[20,21] This difference can be attributed to the more hydrophilic nature of PVDC compared to PVC and PVDF, which have similar solubility parameters.[20]

The mechanism of the dehydrohalogenation of PVDC under heterogeneous conditions in the presence of a phase-transfer catalyst (Q^+Cl^-) has been schematically represented.[24]



The ammonium hydroxide formed in the aqueous phase reacts with the polymer on the surface of the polymer particles according to an E_2 mechanism.[1] Molecules of Q^+OH^- penetrate the polymer phase and react with counterions of PVDC.

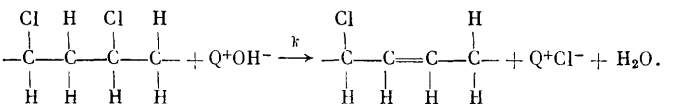
However, the empirically derived expression for the rate of dehydrochlorination of PVC [27] cannot be accounted for using this simple mechanism

$$v = k.[TBAB]^{0.43}.[NaOH]^{1.1},$$

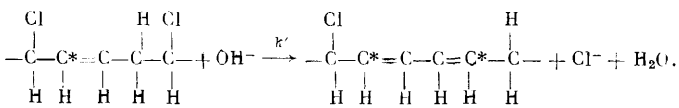
where [TABA] and [NaOH] are the concentrations of tetrabutylammonium bromide and alkali respectively. Therefore, Howang et al.[27] proposed the following mechanism of dehydrohalogenation that includes several stages in the case of PVC.

The initiation stage involves the elimination of HCl catalysed by a quaternary onium base (Q^+OH^-) with the formation of isolated

double bonds in the PVC chains

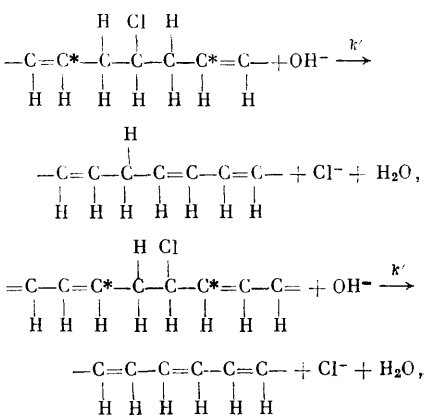


In the stage involving growth of the chain of conjugation, a vinyl chloride unit adjacent to a double bond in the presence of the OH^- anion readily loses HCl to form conjugated double bonds

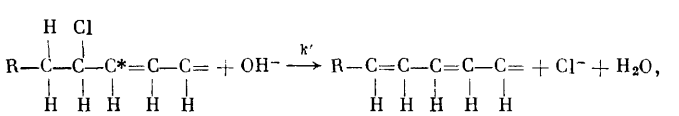


The carbon atoms of the extending conjugation front are marked with an asterisk.

In the termination stage elimination stops when two conjugation fronts in the same polymer chain meet



or when the end of the chain is reached by the front



where R are terminal groups of PVC.[27]

Dehydrohalogenation of halogen-containing polymers is assumed[21,24,26,27] to occur by a chain mechanism (zip process), according to which the isolated and conjugated double bonds in the polymer macromolecule activate the hydrogen and chlorine atoms in the α-position by increasing their activity and capacity to undergo elimination (allylic activation).

An expression for the rate of dehydrochlorination of PVC has been derived theoretically[27]

$$v = d[Cl^-]/dt = A^{1/2}[TBAB]^{1/2}[CH_2{-}CHCl]^{1/2}[OH^-],$$

where

$$A = k' \cdot k \cdot k_e \cdot K/(1+K) \cdot (k_e[OH^-] + k \cdot [CH_2{-}CHCl]);$$

$$K = [Q^+]_T/[Q^+]_p —$$

is the HLB coefficient; k' and k are the rate constants of the fundamental stages of dehydrochlorination; k_e is the rate constant of anionic exchange at the polymer–solution phase boundary; $[Q^+]_s$ and $[Q^+]_l$ are the concentrations of catalyst in the solid phase and in solution respectively. This expression correlates well with the experimentally determined value, which provides support for this mechanism.

It should be noted that when the dehydrohalogenation of polymers is carried out in solution with agitation, a precipitate of partially dehydrohalogenated polymer rapidly forms and the reaction continues in a similar manner to the reaction with powder. In the absence of agitation, when the organic phase is a solution of polymer, the activity of the catalyst depends on the organic solvent. Thus, in the dehydrochlorination of Saran in tetrahydrofuran (THF) solution the most effective catalyst proved to be TBAB,[22] whereas for solid Saran (powders and films) TPAB was more effective.[24] This difference in catalytic activity in the dehydrochlorination of solid Saran and its solution in THF can be attributed to the different solubility parameters of the solid copolymer (δ = 13.4) and THF (δ = 9.32).[22] For PVC, δ = 9.4–10.8.[24] When *o*-dichlorobenzene was used as the solvent, the dehydrochlorination of Saran was almost completely suppressed, while when 1,4-dioxan was used the reaction was faster than in THF.[22]

The degree of conversion in the aqueous alkaline dehydrohalogenation of polymers also depends on the concentration of catalyst and alkali and on the reaction temperature. When the concentration of catalyst is increased, conversion increases to a given level, after which it remains unchanged. This type of dependence is related to the fact that at high concentrations of catalyst a portion of it separates out from the aqueous phase to form an oily layer—it becomes a three-phase system. Therefore, the effective concentration of catalyst in the aqueous phase remains unchanged. At high concentrations of alkali a third phase of catalyst is also formed, and the dependence of conversion on the concentration of alkali with a constant concentration of catalyst is in the form of a curve with a maximum. At first, as the concentration of alkali in the aqueous phase increases, the conversion increases and reaches a maximum value, after which it starts to decrease. The drop in conversion is due to a decrease in the effective concentration of catalyst in the aqueous phase on increasing the concentration of alkali.[20–22,24]

In the dehydrochlorination of Saran in THF solution, KOH proved to be a more effective dehydrochlorinating agent than NaOH under the same reaction conditions. An increase in the concentration of Saran in THF solution led to a decrease in conversion, since the increase in viscosity of solution inhibited diffusion of ammonium hydroxide into the organic phase.[22]

The dependence of conversion on reaction temperature in the dehydrochlorination of PVC is limiting in nature with a maximum at about 70 °C. On increasing the temprature from 70 to 90 °C, the degree of conversion falls sharply. Initially this phenomenon was attributed to decomposition of the onium salts in alkaline solution at temperatures above 70 °C,[21] but more recent studies[20,24] have demonstrated that in the dehydrohalogenation of Saran and PVDF the degree of conversion increases with an increase in temperature even up to 110 °C. Therefore, the limiting dependence of conversion on temperature in the dehydrochlorination of PVC is attributed[24] to a change in the physical properties of the polymers at temperatures above the glass-transition temperature of PVC (about 80 °C), which can lead to a reduction in porosity of the PVC particles and a decrease in the rate of diffusion of the ammonium hydroxide into the polymer, in other words, there is a decrease in the overall rate of reaction.

In one study[28] in order to create milder conditions in carrying out the dehydrofluorination of PVDF, tetrabutylammonium hydroxide in a solution of t-butyl alcohol was used directly as the

dehydrohalogenating agent, as a result of which it was possible to avoid scissions of the polymer chain and obtain a fluorine-substituted polyacetylene structure on the surface of PVDF.

Crown ethers constitute another class of phase-transfer catalysts that are used in the dehydrohalogenation of halogen-containing polymers. The use of 18-crown-6 and dibenzo-18-crown-6 in the dehydrochlorination of PVC with aqueous solutions of NaOH or KOH proved ineffective.[21] In the aqueous alkaline dehydrofluorination of PVDF the catalytic activity of 18-crown-6 proved to be much lower than that of TBAB; while an attempt to use the more lipophilic dibenzo- and dicyclohexyl-18-crown-6 was unsuccessful because of the low solubility of the latter in the aqueous phase.[20]

However, when the dehydrochlorination of PVDC was conducted in the presence of 18-crown-6 in benzene, the reaction took place rapidly up to high degrees of conversion.[29] Dehydrochlorination was carried out in the three-phase systems: PVDC (film) + benzene + 18-crown-6 + KOH (pellets) and PVDC (film) + benzene + 18- crown-6 + KF/CaO. The degrees of conversion for systems with KF/CaO and KOH were similar, but the concentration of the crown complex with KF/CaO was 6 times lower than the concentration of the crown complex with KOH because of its low solubility in benzene. Hence it may be concluded that the system KF/CaO – 18-crown-6 is more effective in the dehydrochlorination of PVDC films in benzene.

At 80 °C after 1 h, elimination of 0.97 chlorine atoms on average per monomer unit with the formation a chlorine-substituted polyene structure has occurred. When dehydrochlorination is carried out for a more prolonged period further elimination of HCl occurs, and after 14 h 1.6–1.7 chlorine atoms are eliminated on average per monomer unit.

In the IR spectra of the dehydrochlorination products absorption bands are detected at 2170 cm^{-1} and at 866 and 755 cm^{-1}, which are attributed to stretching vibrations of C≡C triple bonds and bending vibrations of C–H bonds in aromatic structures respectively. When KOH is used in the dehydrochlorinating system, mainly C≡C triple bonds are formed at high degrees of conversion, while when KF/CaO is used aromatic structures are mainly formed by the above-mentioned Diels–Alder and intramolecular 1,6-elimination types of reaction, which can be illustrated by the ratio of intensities of the absorption band at 2170 cm^{-1} to those at 866 and 755 cm^{-1}. Thus, for the system with KOH, $I_{2170}/(I_{866} + I_{755}) = 1.2$, while for the system with KF/CaO, $I_{2170}/(I_{866} + I_{755}) = 0.3$.[29]

The rate of dehydrochlorination depended to a considerable degree on the reaction temperature. While 0.97 chlorine atoms were eliminated on average per monomer unit at 80 °C, when the reaction was carried out at 20 °C only 0.15 atoms were eliminated.[29]

2. Dehydrohalogenation by alcoholic solutions of alkalis

Treatment of halogen-containing compounds with alcoholic solutions of alkali metal hydroxides is a traditional method of dehydrohalogenation that has been used in both organic chemistry and polymer chemistry.

A number of studies have been devoted to the dehydrohalogenation of PVC,[31–33,35,43,44,55,57] PVDC,[36–38,41,42,45,56] PVDF,[40–42] poly(vinylidene bromide) (PVDB),[41,42] and also a polymer that had the structure of poly(1,2-dibromoethylene), obtained by the dehydrochlorination and subsequent bromination of PVC.[53]

When the dehydrohalogenation of halogen-containing polymers is carried out in solution, with other conditions being equal the rate of reaction depends on the polarity of the solvent. Thus, when the dehydrochlorination of PVC is carried out in dimethylformamide (DMF) solution, the rate of reaction, the conversion, and also the length of the resulting polyenes were considerably greater than when the reaction was carried out in THF solution.[31,32]

In the IR spectra[31,33] of the dehydrochlorination products of PVC there are absorption bands at 1005 cm^{-1} and 3010 cm^{-1} which are characteristic of bending and stretching vibrations respectively of C–H bonds in long *trans*-polyenes.[34] In the Raman spectra intense lines occur in the region of 1100 and 1500 cm^{-1} that are typical for stretching vibrations of carbon–carbon single and conjugated double bonds respectively.[35]

At degrees of conversion of 50–60%, the length of the polyene sequences formed in PVC macromolecules under the experimental conditions reaches a maximum value (about 40 conjugated C=C bonds), and then as dehydrochlorination progresses it decreases.[31,32] Bowley et al.[31,32] account for this phenomenon as follows. At degrees of conversion up to 50–60%, the long conjugated polyenes formed in the PVC macromolecules are separated by sections of unreacted polymer. These sections of the initial polymer sterically shield the polyene sequences from interchain cross-linking.[31] As dehydrochlorination progresses the unreacted sections disappear and at the same time there is an increased probability of cross-linking on the double bonds with scission of the chain of conjugation and a decrease in the length of the polyenes.[32] In fact, in the IR spectra of completely dehydrochlorinated PVC absorption bands occur at 2845 and 2920 cm^{-1} that are characteristic of stretching vibrations of C–H bonds in saturated structures.[32]

It should be noted that the degree and rate of dehydrochlorination and also the structure of the reaction products does not depend on the tacticity of the initial polymer.[31,32]

The dehydrochlorination of PVDC powder has been investigated in three studies.[36–38] The highest visually recorded rate of reaction was reached when a solution of KOH in isopropyl alcohol was used as the dehydrochlorinating agent. Solutions of LiOH and NaOH in methanol and ethanol proved less effective. The reaction was carried out at room temperature. Since no absorption bands characteristic of conjugated dienes and trienes were detected in the IR spectra of the intermediates, the authors conclude that elimination of HCl does not occur randomly at the same time in several sites of many macromolecules but has the form of a chain reaction.[36] After the first 4 h more than half of the initial chlorine content has been eliminated from the polymer. For complete elimination of chlorine 40–50 h is required.[37,38] In the IR spectra of the reaction products there is a rapid increase in a broad absorption peak at 1630 cm^{-1}, attributed to C=C double bond vibrations, which is shifted to 1590 cm^{-1} when the reaction is continued in excess of 12 h. The authors attribute this shift to a change in the environment of the carbon atoms from aliphatic (1630 cm^{-1}) to aromatic (1590 cm^{-1}). In the IR spectra of the reaction products there are also absorption bands at 1720 and 3440 cm^{-1}, attributed to vibrations of O=C< and OH groups respectively.[36,38] The authors account for the absence of absorption bands characteristic of C≡C triple bond vibrations in the IR spectra of the dehydrochlorination products of PVDC by the fact that at the first stage of the reaction the resulting chlorine-substituted polyene structures $-(-CH=CCl-)_n-$ react with each other by a Diels–Alder-type reaction (see above). Subsequent dehydrochlorination of the reaction products results in the formation of aromatic structures.[36,38] According to the dehydrochlorination mechanism put forward by Barton et al.[38] elimination of HCl from the polymer chain occurs via the formation of an ether in a

Williamson reaction[39] followed by the elimination of a molecule of isopropyl alcohol and the formation of a C=C double bond.

In the dehydrofluorination of PVDF both at room temperature[40] and at 50–100 °C [20] by a solution of KOH in isopropyl alcohol, in addition to absorption bands in the IR spectra of the reaction products at 3400, 1580, and 1100 cm^{-1} that are characteristic of OH groups, conjugated double bonds (C=C), and C–O–C ether bonds respectively, there is an absorption band in the region of 2050–2200 cm^{-1}, attributed to stretching vibrations of C≡C triple bonds.

The dehydrohalogenation of poly(vinylidene halides) (PVDF, PVDC, and PVDB) by a mixture of a saturated solution (25 wt.%) of KOH in ethanol and THF has been studied.[41,42] By using THF in the mixture it is possible to carry out dehydrohalogenation under mild conditions—at room temperature and below—because of its specific solvating nature and complexing ability, which reduces to a minimum the contribution of side reactions involving cross-linking, degradation, and nucleophilic substitution of halogen atoms by hydroxyl and ethoxy groups. It should be noted that addition of certain polar solvents [dimethyl sulphoxide (DMSO),[43,44] pyridine[45]] to an alcoholic solution of alkali resulted in an appreciable acceleration of dehydrohalogenation of PVC and PVDC. Solvation of the alkali metal cation with THF molecules increases the reactivity of the hydroxyl ion, which assists the dehydrohalogenation reaction.[41,42] The role of THF involves not only its catalytic effect on the elimination of hydrogen halide but also changing the conditions of interaction in the system polymer–reactive medium. This manifests itself in the swelling of polymers in THF, which assists the diffusion of dehydrohalogenating agent into the polymer. The optimum ratio of the components of the dehydrohalogenating mixture, in which the maximum rate of reaction and degree of dehydrohalogenation are achieved, is: 40 wt.% alcoholic solution of KOH + 60 wt.% THF.[41,42]

The theoretical reaction scheme of the dehydrohalogenation of poly(vinylidene halides) can be shown as follows:[41]

$$-(-CH_2-CX_2-)_n- \xrightarrow[-nHX]{} -(-CH=CX-)_n- \xrightarrow[-nHX]{} \longrightarrow -(-C\equiv C-)_l- \ldots =(=C=C=)_m=,$$

where $l + m = n$ and X is a halogen.

A feature of the dehydrohalogenation of polymers under heterogeneous conditions is that the rate of reaction depends not only on the strength of the carbon–halogen bond but also on the rate of diffusion of the dehydrohalogenating agent into the polymer substrate.[41] Therefore, the reaction occurs much more rapidly with powders than with films because of the degree of dispersion and highly extended surface of powders. Thus, the dehydrohalogenation of PVDF powder at room temperature was complete after 10 h, that of PVDC was complete after 1 h, and that of PVDB after 30 min.[41,42] The dehydrohalogenation of PVDF and PVDC films takes place much more slowly. An increase in reaction temperature results in a marked acceleration of dehydrohalogenation. In addition to the accelerating effect of heat on the chemical reaction this is also due to swelling of the polymers in THF, which assists diffusion of the reactants. In all, poly(vinylidene halides) can be arranged in the following order with respect to their rate of dehydrohalogenation: PVDB > PVDC > PVDF.[41]

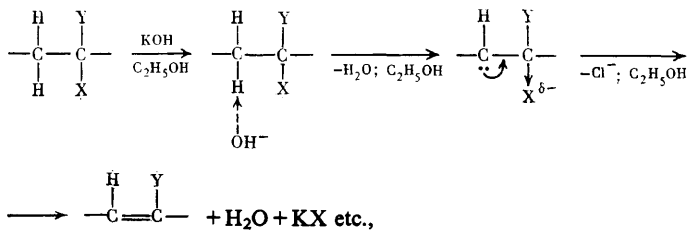
As the dehydrohalogenation of poly(vinylidene halides) takes place, in the IR spectra of the reaction products the absorption bands that are characteristic of vibrations due to the carbon–halogen bond over the frequency range 400–800 cm^{-1} disappear and new absorption bands appear in the region of 1600 cm^{-1} (very strong) and 2170 cm^{-1}, which are attributed to stretching vibrations of carbon–carbon double and triple bonds respectively.[41,42] A change of reaction temperature from –10 °C to 68 °C did not produce any appreciable change in the relative intensities of these bands. However, according to electronic Auger spectroscopy data, when the reaction is carried out at room temperature the dehydrochlorination products of PVDC contain about 15% cross-linked graphite-like structures, whereas at a lower temperature (–10 °C) products with a linear (one-dimensional) structure are formed. Evsyukov et al.[41,42] resolve the inconsistency between the IR and Auger spectroscopic data by assuming that in the chemical dehydrohalogenation of poly(vinylidene halides) a cumulene modification of carbyne (β-carbyne) is formed, and absorption of the cumulene structure appears in the region of 1600 cm^{-1}. This accounts for there being no differences in the IR spectra of poly(vinylidene halides) dehydrohalogenated at different temperatures since absorption of conjugated and isolated C=C double bonds also appears at about 1600 cm^{-1}.[46] It should be noted that previously the absorption band in the region of 2100–2200 cm^{-1} in the IR spectra of carbyne was attributed to vibrations due to polyyne structures while the band in the region of 1600 cm^{-1} was attributed to C=C double bond vibrations formed as a result of interchain cross-linking.[45,47] In order to confirm the validity of assigning the absorption bands in the region of 1600 cm^{-1} in the IR spectra to vibrations of cumulated double bonds of β-carbyne, a numerical calculation of the inherent vibrational frequencies of a cumulene chain was carried out,[48] taking into account ideas about the zigzag nature of a carbyne chain,[49,50] which at the present time have been experimentally confirmed.[51,52] The results of the calculation are in good agreement with the experimental IR spectra of the dehydrohalogenation products of poly(vinylidene halides).

By studying the electronic structure of the dehydrohalogenation products of poly(vinylidene halides) using Auger spectroscopy and also electron characteristic energy loss spectroscopy, it was possible to obtain complete confirmation of their one-dimensional cumulene structure.[41,42] On the curve of density of the valence states of dehydrochlorinated PVDC there are three well-defined maxima at energies of 16, 19, and 25 eV, which relate respectively to the base of the π-sub-band and the ceiling and base of the σ-sub-band. This position of the maxima on the energy scale is typical for linear structures and is in good agreement with the results of a calculation of the density distribution of states in the valence band of carbyne.[53] The position of the base of the π-sub-band at 16 eV is a clear indication of the cumulene nature of the bonds in the dehydrohalogenation products. The threshold of the loss function in the electron characteristic energy loss spectrum, which corresponds to the width of the optical forbidden band, is equal to 1 eV, which is also consistent with the results of calculation of the electronic spectrum of cumulene chains.[41,42]

In the Raman spectra of the dehydrohalogenation products of poly(vinylidene halides), two lines occur at about 1550 and 2150 cm^{-1}, corresponding to stretching vibrations of cumulated C=C double bonds in the polymer chain.[54] On increasing the wavelength of exciting light from 457.9 to 647.1 nm, the positions of the lines are shifted to lower frequency, which suggests that there are chain distributions according to the effective lengths of conjugation in the carbyne obtained.

An ionic mechanism has been proposed[41,42,55] for the dehydrohalogenation of halogen-containing polymers by an alcoholic

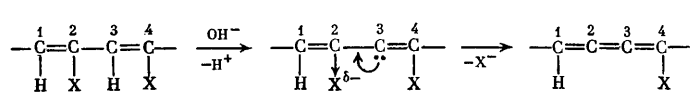
solution of alkali that is similar to the well-known mechanism in organic chemistry for the dehydrohalogenation of alkyl halides by bases.[1] According to this mechanism a hydroxide ion removes a proton from the chain of the initial polymer, leaving a free electron pair in its place. The halogen atoms on the neighbouring carbon atom acquire a partial negative charge as a result of the inductive effect and are readily detached by (alcohol) solvent molecules. The eliminated halogen ion is bound in solution to an alkali metal cation



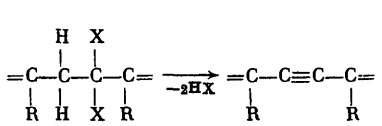
where X = Y is a halogen[41,42] or Y = H.[55]

Subsequent elimination of hydrogen halide from the units that are adjacent to the resulting double bond occurs with greater ease than for the initial polymer because of the allylic activation effect.[55]

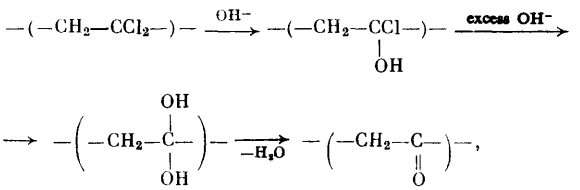
Using this mechanism, Evsyukov et al.[41,42] account for the formation of β-carbyne in the dehydrohalogenation of poly(vinylidene halides) in the following manner. At the first stage of the reaction a halogen-substituted polyene structure $-(CH=CX)_n-$ is formed. After removal of a proton from the resulting structure, a free electron pair is left in its place, according to the above mechanism. This pair causes a shift in electron density from the C(3) atom to the C(2) atom because the double bond between the C(3) and C(4) atoms prevents a shift in electron density to the C(4) atom. As a result of the redistribution of electron density the halogen atom on the C(2) carbon atom acquires a greater negative charge than the halogen atom on the C(4) carbon atom. As a result, elimination of a halogen ion actually takes place from the C(2) atom to form a cumulene structure.



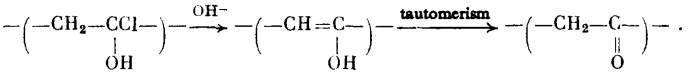
The C≡C triple bonds whose existence is indicated by the absorption band in the region of 2100–2200 cm^{-1} in the IR spectra of β-carbyne obtained by dehydrohalogenation of poly(vinylidene halides) occur as defect units in relation to the final cumulene structure. They can be formed by the elimination of two hydrogen halide molecules from the monomer units that occur in the polymer macromolecules between defect units[41,42]



These defects can comprise branching and "head-to-head" structures in the initial polymer as well as defects formed by side reactions involving cross-linking, oxidation, degradation, and nucleophilic substitution of halogen atoms by hydroxyl and alkoxy groups. The occurrence of hydroxyl groups in the polymer chain can lead to further side reactions[56]

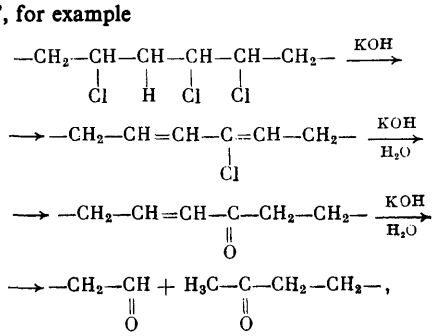


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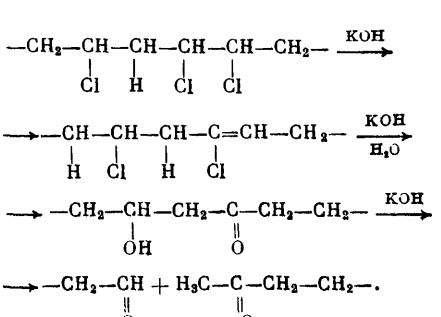


In a study[57] of the reaction between PVC and alkali, particular attention was given to the degradation of PVC with scission of the polymer chain. The reaction of PVC with an alcoholic solution of KOH was carried out in THF solution under specially selected conditions in order to prevent the rapid loss in solubility and precipitation of the polymer from solution. It was shown by Schwenk[57] that the Fikentscher coefficient determined by viscometry, which decreases during the reaction over a period of 90 min to 2/3 of its original value in the initial polymer, is not a reliable criterion of molecular weight in the case of branched polymer structures that are formed through side reactions involving cross-linking. For a more detailed study the author used gel permeation chromatography (GPC). However, in this case also a determination of the true molecular-weight distribution is made difficult by the presence of a colloidal fraction with intermolecular cross-linking in the solution of reaction products, which passes through a conventional filter but settles in a chromatographic column. Nevertheless, the GPC data clearly indicate the presence of a low-molecular weight fraction in the reaction products of PVC and KOH that is absent in the initial polymer.

From the analysis of model reactions Schwenk[57] has proposed different variants of the mechanism of the degradation of PVC with scission of the polymer chain by an alkali. In the opinion of Schwenk, it is most likely that degradation occurs at those sites of the polymer chain in which the monomer units are joined "head-to-head", for example



or



A reduction in the temperature of dehydrohalogenation leads to a decrease in the proportion of side reactions. Thus, for example, on treatment of a solution of PVC in THF with a solution of KOH in methanol at 60 °C, the reaction products contained 10 oxygen atoms for every 100 vinyl chloride units, whereas when the reaction was carried out at room temperature this was reduced to 2 oxygen atoms.[57]

A kinetic equation for the concentration of the polyenes formed by dehydrochlorination of PVC was derived by Shindo and Hirai[55]

$$[P_n] = K_n \cdot t^n,$$

where $[P_n]$ is the concentration of polyenes from n conjugated double bonds; t is the reaction time;

$$K_n = (1/n!)k_1k_2 \ldots k_n[KOH]^n.[PVC],$$

where $k_1, \ldots, k_n$ are the rate constants of the fundamental elimination reactions; [KOH] and [PVC] are the concentrations of KOH and PVC respectively.

A kinetic equation for the total concentration [E] of double bonds in the dehydrochlorination products of PVC was derived by Östensson and Flodin[44]

$$dE/dt = k_1([PVC]_0 - [E])([KOH]_0 - [E]),$$

which after integration gives

$$(1/\ln 10)([PVC]_0 - [KOH]_0).k_1t + \lg([PVC]_0/[KOH]_0) =$$

$$= \lg\{([PVC]_0 - [E])/([KOH]_0 - [E])\}.$$

In this case $[PVC]_0$ and $[KOH]_0$ are the initial concentrations of PVC and KOH respectively.

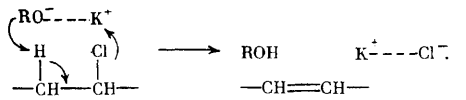
III. Dehydrohalogenation by alkali metal alkoxides

Alkali metal alkoxides (principally potassium t-butoxide) are used as widely as alkalis in the dehydrohalogenation of halogen-containing polymers. In a number of studies the dehydrohalogenation of PVC,[31,32,58–66] chlorinated PVC (CPVC),[65] PVDC,[56,66] and PVDF [40] by potassium t-butoxide[31,32,40,56,58–64] and sodium amoxide[65,66] was investigated.

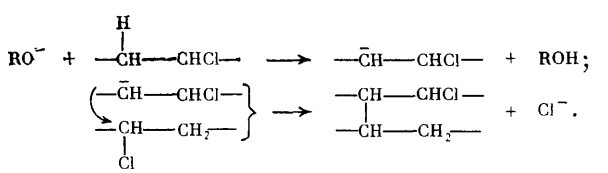
When potassium t-butoxide (t-C_4H_9OK) the KOH were used as the dehydrochlorinating agent under the same conditions, the rates and degrees of dehydrochlorination of PVC were similar. However, when t-C_4H_9OK is used, much longer polyene sequences (more than 65 conjugated C=C bonds) are formed than when KOH is used under the same conditions (about 40 units).[31,32] The rate and degree of dehydrohalogenation increase with an increase in polarity of the solvent.[31,32,56]

A study[61] of the dehydrochlorination of PVC by t-C_4H_9OK using GPC and UV spectroscopy showed that at the early stages of the process, macromolecules appear in the reaction products with a molecular weight similar to that of the initial polymer but containing short polyene residues (P_2 products). The concentration of such macromolecules (P_2) increases up to a degree of conversion of 10% and remains unchanged up to a degree of dehydrochlorination of 20%. Then, as the reaction progresses the concentration of P_2 decreases and is reduced to zero when the degree of conversion is 100%. Starting from a degree of dehydrochlorination of 4%, P_1 macromolecules appear in the reaction products with a molecular weight higher than the initial PVC and containing long polyene sequences. The concentration of P_1 increases as the reaction continues right up to complete dehydrochlorination. At advanced stages of dehydrochlorination, a small number of P_3 polyene macromolecules appear in the reaction products with a low molecular weight (200–800), which are formed as a result of side reactions involving chain scission.[61] Thus, products P_2, which are formed at the early stages of dehydrochlorination by elimination of several HCl molecules from the macromolecules of the initial PVC, as the reaction progresses undergo a further conversion to form products P_1 with a higher molecular weight than that of the initial polymer and containing long polyene sequences. Products P_1, in turn, partly undergo alkaline degradation to form products P_3 with a low molecular weight but containing long polyene sequences.

Elimination of HCl by the action of t-C_4H_9OK in pure THF is an ion pair reaction with the simultaneous removal of a proton and Cl^- anion:



This accounts for the solubility (lack of cross-linking) of the reaction products at high degrees of conversion. Some increase in the molecular weight of the reaction products relative to the initial PVC is attributed by Dussoubs et al.[61] to association of polyconjugated macromolecules without the formation of chemical cross-linked structures. In the opinion of the authors, when alcoholic solutions of bases (alkoxides or alkalis) are used, elimination of HCl occurs by an ionic mechanism through solvation of Cl^- anions with alcohol molecules, which makes side reactions involving cross-linking possible:



When the reaction is carried out in the presence of oxygen, the products of the complete dehydrochlorination of PVC are soluble in polar solvents.[62] However, the presence of oxygen leads to a reduction in the rate of dehydrochlorination and in the length of the resulting polyene sequences, which is due to the formation of a stable ternary complex of THF–oxygen–PVC, that has an affect on the subsequent course of the reaction.[63] When the dehydrochlorination of PVC is carried out in an atmosphere of argon, products with a polyacetylenic structure that are close in composition to the formula $(CH)_x$ are formed,[62] whereas for the dehydrochlorination product in an atmosphere of argon/oxygen (50% O_2) the formula $(CHO_y)_x$, where $y = 0.0032$, was established.[63]

The vibrational spectra of the dehydrohalogenation products of PVC, PVDC, and PVDF by treatment with t-C_4H_9OK are similar to the spectra of the dehydrohalogenation products of the corresponding polymers from treatment with alkalis,[31,32,40,56,62] as described above in Section II. However, when CPVC and PVDC are dehydrochlorinated with sodium amoxide, chlorine-substituted polyene (chlorovinylene) structures are formed,[65,66] further dehydrochlorination does not occur, and in the IR spectra of the reaction products where is no absorption band in the region of 2100–2200 cm^{-1} characteristic of stretching vibrations of C≡C triple bonds. Moreover, during the dehydrochlorination of CPVC by sodium amoxide, a side reaction involving alkoxylation occurs,[65]

whereas in the dehydrochlorination of PVC by t-C_4H_9OK side reactions involving substitution were not observed.[60]

It was shown by Bowley et al.[31,32] that the rate and degree of dehydrochlorination of PVC as well as the structure of the reaction products do not depend on the tacticity of the initial polymer. However, it was concluded by Martinez et al.[64] from UV spectroscopic data that at the early stages of dehydrochlorination of PVC, elimination of HCl occurs selectively in isotactic and heterotactic triads. In the case of a *gauche* conformation in these triads, elimination occurs by a *syn* mechanism to give *cis* double bonds.

It should be noted that t-C_4H_9OK prepared directly during dehydrohalogenation exhibits considerably greater activity in the elimination of hydrogen halide than that prepared earlier. Thus, when tertiary butyl alcohol and metallic potassium are added to a solution of PVC in THF, on carrying out the reaction for 2 h at 60–65 °C the degree of dehydrochlorination reaches 95%, whereas when previously prepared t-C_4H_9OK is used under the same conditions only 30% dehydrochlorination is achieved.[67]

IV. Dehydrohalogenation by amines

The reactions of different halogen-containing polymers with amines have been widely studied and reported in the literature. A number of studies describe the dehydrohalogenation of PVC,[68–74] PVDC,[75,76] and their copolymers,[77] poly(vinyl bromide),[78] poly(α-chloroacrylonitrile),[79,80] as well as a number of fluorine-containing polymers[81,82] by aliphatic primary,[68,77,81] secondary,[68,75,81] and tertiary[68,74,78–81] amines, a wide range of aromatic amines such as aniline and its derivatives,[69,70,77,81] and also pyridine.[71–73,76,78,81]

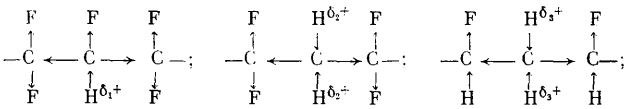
On reacting halogen-containing polymers with amines two competing processes occur—dehydrohalogenation and amination.[68–70,77,81,82] As the basicity of the amines used increases, the proportion of dehydrohalogenation reactions increases.[68,69,71,81] Amination can occur through the replacement of a halogen atom in the polymer chain[68,69,77] or addition to the double bonds formed by dehydrohalogenation.[81,82] Depending on the reaction conditions, the amination products can undergo intramolecular cyclisation[69,70] and intermolecular cross-linking.[68,69,77,82] Degradation of the macromolecules through the formation of carbocations[69] and aminolysis[81] is also possible. It should be noted that as the concentration of amine increases the proportion of amination reactions increases.[69]

Reactions between halogen-containing polymers and amines have been carried out over a wide temperature range—from room temperature to 200 °C. Aliphatic amines react with halogen-containing polymers even at room temperature[68,77] whereas a considerable increase in temperature is required for aromatic amines.[69,77]

The reactivity of halogen-containing polymers in dehydrohalogenation reactions increases with an increase in the number of halogen atoms in the fundamental unit. Thus, on treatment with n-butylamine at 78 °C, films made of poly(vinyl fluoride) $-(CH_2-CHF)_n-$ were inert towards the amine for 24 h. Films made of PVDF $-(-CH_2-CF_2-)-$ become black and brittle over a period of 4 h while for films made of polytrifluoroethylene $-(CHF-CF_2-)_n-$ this occurred over a period of 10 min.[81] Thus, these polymers can be arranged in the following order of reactivity:

$$-(-CHF-CF_2-)_n- > -(-CH_2-CF_2-)_n- > -(-CH_2-CHF-)_n-.$$

This effect is due to the fluorine (halogen) atoms having strong electron-withdrawing properties. As a result of the shift in electron density from the carbon atoms to the fluorine atoms, which in turn is compensated by a shift in electron density from the hydrogen atoms to the carbon atoms, the electrophilicity of the hydrogen atoms increases, thus assisting the removal of a proton by a base.[81] Thus, the reduction in reactivity in this series of fluoropolymers is caused by the reduction in electrophilicity of the hydrogen atoms:

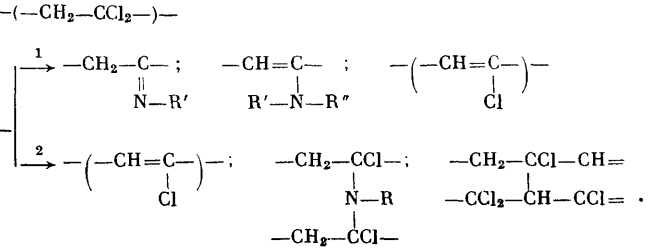


$\delta_1^+ > \delta_2^+ > \delta_3^+$.

In the IR spectra of the reaction products there are absorption bands which are characteristic of stretching vibrations of conjugated C=C double bonds (in the region of 1600 cm^{-1})[68,69,77,79] as well as N–H bonds (at about 3400 cm^{-1}).[68,69]

An analysis of the UV and visible absorption spectra of the products of the reaction between vinylidene chloride–vinyl chloride copolymer and various amines in comparsion with the spectra of β-carotene has been carried out.[77] In the spectrum of β-carotene characteristic absorption bands occur at wavelengths of 435, 460, and 486 mμ, whereas in the spectra of the products of the reaction between the copolymer and amines, no specific absorption bands were detected. On the basis of this observation, Nakagawa[77] concluded that the chromophoric groups of the reaction products differ considerably from the corresponding group in β-carotene with quite a long chain (11 units) of conjugated C=C bonds, i.e., the sections of conjugation in the dehydrochlorination products of the vinylidene chloride–vinyl chloride copolymer are shorter in length. Nakagawa attributes this to the fact that this copolymer has the structure of a block copolymer and therefore propagation of the chain of conjugation during dehydrochlorination, which is initiated on the more reactive vinylidene chloride units, is terminated on the vinyl chloride units.[77] It should be noted that amination and cross-linking reactions can also be the cause of breaks in the chain of conjugation. With an increase in basicity of the amines used, the rate of reaction increases and the proportion of dehydrohalogenation reactions increases. Thus, in dehydrochlorination of the above-mentioned copolymer, the amines used were arranged in the following order of reactivity: n-butylamines > cyclohexylamine ≫ N-methylaniline > aniline > *N,N*-dimethylaniline.

Depending on the basicity of the amine, reactions that occur with halogen-containing polymers can be divided into two types in accordance with the following scheme (in the case of PVDC);[77]

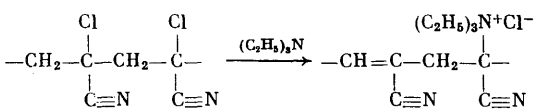


When an amine with low basicity (pK_a = 4–5) is used, the reaction takes place by scheme (*1*). In this case amination reactions occur to a considerable extent by a nucleophilic substitution mechanism (R′ = phenyl, R″ = methyl). When an amine with high

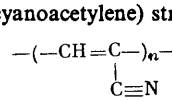
basicity is used (pK_a = 9–10) the reaction occurs by scheme (*2*). In this case dehydrochlorination is predominant at the initial stages of the reaction, while amination can occur by a mechanism involving the addition of amines (R = n-butyl, cyclohexyl) to the double bonds that are formed.[77]

Dehydrochlorination of poly(α-chloroacrylonitrile) (PCAN) in acetone solution by triethylamine results in the formation of a black polymer which is soluble in polar solvents and even in water.[79,80] In the IR spectra of the reaction products the absorption bands characteristic of C–Cl bond vibrations (640 cm^{-1}) in the initial polymer have disappeared and strong absorption bands at 1640 and 1730 cm^{-1}, characteristic of vibrations due to conjugated C=C bonds and O=C< carbonyl groups respectively, have appeared. In the region of 2100–2200 cm^{-1} appear two strong absorption bands that are characteristic of vibrations due to nitrile groups N≡C– that are conjugated (2215 cm^{-1}) and isolated (2250 cm^{-1}) relative to the main chain.[80]

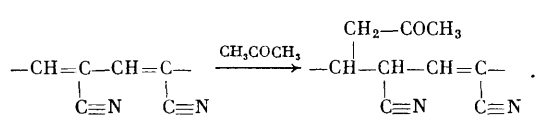
The solubility of the dehydrochlorination product of PCAN is caused by side reactions involving replacement of the chlorine atoms by a tertiary amine to form quaternary ammonium substituents



In fact, when the dehydrochlorination is heated for 4–5 h under vacuum at 180–190 °C triethylamine hydrochloride sublimes. At the same time there is a loss of solubility in water. In the IR spectrum of the thermally treated dehydrochlorination product the absorption band at 2250 cm^{-1} (isolated N≡C– groups) disappears and the strong band at 2200 cm^{-1} (conjugated N≡C– groups) remains. A very broad absorption band occurs over the range 1000 to 1700 cm^{-1} with a peak at 1630 cm^{-1}, which is characteristic of stretching vibrations due to conjugated C=C bonds of the polymer chain. Its complete solubility in DMF excludes the formation of cross-linked structures, so the final product of dehydrochlorination and thermal treatment of PCAN is assigned the polycyanopolyene (polycyanoacetylene) structure[80]

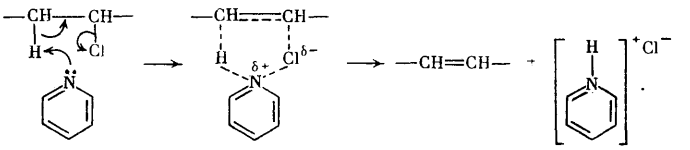


The presence of carbonyl groups in the dehydrochlorination products of PCAN is due to the occurrence of side reactions involving the addition of acetone to C=C double bonds, which is assisted by the strong electron-withdrawing effect of N≡C– groups:

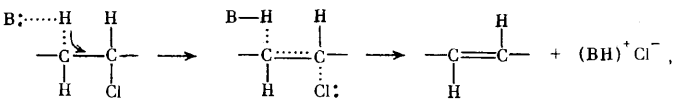


Reversible alkoxylation on the C=C double bonds takes place in a similar manner when dehydrochlorination is carried out with alkali metal alkoxides.[80]

In the reaction between halogen-containing polymers and pyridine at elevated temperatures dehydrohalogenation mainly occurs.[71–73,76] Poly(vinyl chloride) and pyridine have different solubility parameters (9.4 and 10.7 respectively), but PVC readily dissolves in pyridine. This is possible only if there is a specific interaction between pyridine and PVC. Therefore, by analogy with the mechanism for dehydrochlorination of PVC in dimethylformamide,[84,85] a mechanism for dehydrochlorination was proposed which included the formation of an intermediate complex between pyridine and polymer, assisting the elimination of HCl in the form of pyridine hydrochloride:[71,72]



Subsequently, on the basis that the double bonds formed by dehydrohalogenation mainly have a *trans* configuration, the reaction mechanism scheme was refined in the following way:[73]



B = pyridine.

With an increase in reaction temperature and time the degree of dehydrochlorination increases steadily.[71] The length of the polyene sequences and the total number of double bonds in the reaction products also increase steadily with an increase in time of dehydrochlorination.[72]

At the advanced stages of dehydrochlorination the polymer is precipitated from the reaction solution, which Mukherjee and Gupta[71,72] assume to be due to intensive cross-linking. It should be noted, however, that with an increase in the length of conjugation in the chain, the solubility of the reaction products decreases, which can also be the cause of precipitation of the polymer from solution.

At high temperatures and a prolonged reaction time the dehydrochlorination and cross-linking processes compete. The authors proposed a scheme involving intermolecular dehydrochlorination for the cross-linking reaction.[72] However, taking into account the mechanism for dehydrohalogenation as described above, involving β-elimination in the polymer chain, it may be concluded that the probability of an interchain dehydrohalogenation occurring is much less than an intrachain one. It is more probable that cross-linking processes occur by the mechanisms proposed for polymers with a system of conjugated multiple bonds, for example, that of polyacetylene.[86]

It should be noted that in the IR spectra of the products of dehydrochlorination of PVDC by amines, absorption bands corresponding to the vibrations of triple (–C≡C–) or cumulated (=C=C=) carbon–carbon double bonds were absent.[75–77]

V. Dehydrohalogenation by dimethylformamide

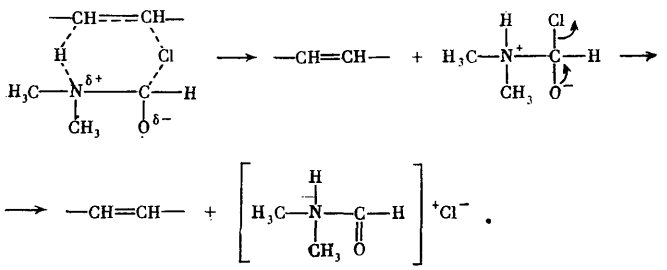
Certain *N*-substituted amides, such as *N*-methylpyrrolidone, *N,N*-dimethylacetamide (DMAA), and *N,N*-dimethylformamide (DMF), are polar aprotic solvents that have basic properties. Even with a slight increase in temperature they can eliminate HCl from PVC to form polyene structures.[83] The dehydrochlorination of PVC in DMF solution has been studied in the greatest detail in this field.[83–85,87–92]

In a study of the degradation of PVC in solution at a high temperature (198 °C) it was found that the rate of dehydrochlorination in DMF was higher than the rate of reaction in other high-boiling solvents such as ethyl benzoate, tritoluyl phosphate, dibutyl phthalate, dioctyl phthalate, benzophenone, benzyl alcohol, and dichloronaphthalene by a factor of more than 10^2.[84,87]

Moreover, according to the UV spectroscopic data, the length of the polyenes formed when the reaction was carried out in DMF considerably exceeded the length of the chain of conjugation when the above-mentioned high-boiling solvents were used.[85,87]

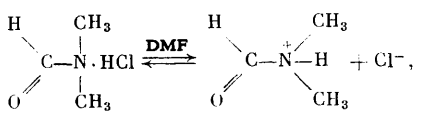
This effect is due to an interaction between PVC and DMF. This conclusion is supported by the fact that PVC is readily soluble in DMF despite the considerable difference in solubility parameters (9.6 and 12.1 respectively).[85] The role of the amide in dehydrochlorination was supported experimentally when the degradation of PVC was carried out in ethyl benzoate in the presence of acrylamide.[84]

As a result of the formation of an intermediate complex between DMF molecules and the fundamental units of the polymer, the dissociation energy of the C–H and C–Cl bonds is reduced, assisting the elimination of HCl.[84,85,87] The HCl separated by dehydrochlorination binds to the solvent:



The dehydrochlorination of PVC in DMF is autocatalytic in nature. This is due not only to the action of DMF [88] but also to the effect of amine-type impurities[89,90] present in it as well as the reaction products (HCl and Cl^-) accumulating in solution.[90] Dimethylformamide, even when freshly prepared, always contains small quantities of dimethylamine, formic acid, and dimethylammonium formate,[93] the content of which varies from 10^{-3} to 10^{-2} mol litre^{-1}.[90] Moreover, at high temperatures DMF decomposes to dimethylamine and formic acid. The destruction of DMF can be accelerated by the HCl eliminated during dehydrochlorination.[94] Dimethylformamide hydrochloride,[95] formed during dehydochlorination, decomposes at temperatures above 90 °C to carbon monoxide and dimethylamine hydrochloride, which can also catalyse dehydrochlorination.[85] The rate of dehydrochlorination of PVC in dilute DMF solutions is directly proportional to the concentration of free dimethylamine. By extrapolation of the rate of reaction to zero concentration of dimethylamine, it is possible to estimate the dehydrochlorination of PVC in "absolutely pure" DMF. The rate of reaction in pure DMF is 10^2 times higher than the rate of degradation of PVC powder in the absence of a solvent with other conditions being equal.[90]

The dimethylformamide and dimethylamine hydrochlorides formed during dehydrochlorination in DMF solution are present in a dissociated state[96]



or

$$(CH_3)_2NH \cdot HCl \overset{DMF}{\rightleftharpoons} [(CH_3)_2NH_2]^+ + Cl^-.$$

Halide ions in dipolar aprotic solvents (such as DMF, DMAA, etc.) are both strong bases and strong nucleophiles[97] and can accelerate dehydrochlorination.[90]

Thus, the autocatalytic nature of the dehydrochlorination of PVC in DMF is due to the effect of amine-type impurities and the reaction products (HCl and Cl^-).

A kinetic equation for the autocatalytic dehydrochlorination of PVC in DMF solution which is in good agreement with the experimental data was derived empirically[88]

$$dX/dt = kX \cdot (1 - X),$$

where X is the number of moles of eliminated HCl per fundamental unit of HCl, k is the rate constant of the reaction. However, it was shown subsequently[91] that this equation is approximate and can only be used to represent the kinetics of dehydrochlorination of PVC in DMF at a high concentration of polymer and high reaction temperatures. At the initial stage, dehydrochlorination is initiated in a basic medium (pH 10–12) and results from the interaction between PVC and DMF and amine-type impurities. As HCl is eliminated the pH of solution is reduced to 4–2 and Cl^- and HCl become the main catalytic agents. Therefore, to represent the kinetics of the process Fikhman et al.[91] used an equation with two rate constants, proposed for the autocatalytic thermal degradation of PVC powder

$$q = \frac{K_1}{K_2}\left\{\exp\left[K_2\left(1+\frac{K_1}{K_2}\right)t\right]-1\right\}\Big/\left\{1+\frac{K_1}{K_2}\exp\left[K_2\left(1+\frac{K_1}{K_2}\right)t\right]\right\},$$

where q is the quantity of HCl eliminated from PVC after time t per fundamental unit of polymer; K_1 is the rate constant of dehydrochlorination of PVC due to the basicity of DMF; K_2 is the overall rate constant, including the catalytic effect of chlorine-containing products formed in solution.[92] This equation effectively represents the experimental results obtained in the dehydrochlorination of PVC in DMF over a wide range of temperatures, concentrations of polymer, and different added components used to inhibit or accelerate dehydrochlorination.[91]

In general the dehydrochlorination of PVC in DMF solution should be given by an S-shaped curve, which can arbitrarily be divided into three sections: 1) acceleration of dehydrochlorination catalysed by DMF and basic impurities; 2) the autocatalytic action of HCl and the Cl^- ion is superimposed on it in an acid medium; 3) dehydrochlorination is inhibited by cross-linking of dissolved PVC and the formation of long conjugated polyenes.[91] The first two sections are effectively represented by the kinetic equation with two constants. The energies of activation of dehydrochlorination calculated from the Arrhenius equation in two different studies[91,88] are similar (23.5 ± 0.5 and 22.2 kcal mol^{-1} respectively).

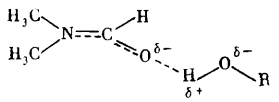
When dehydrochlorination was carried out under vacuum or in an atmosphere of nitrogen the length of the resulting conjugated polyenes amounted to 13–16 –CH=CH– units, whereas in the presence of oxygen it did not exceed 4–5 units, which is due to oxidation of the double bonds, leading to breaks in the chain of conjugation.[85]

On increasing the concentration of polymer in solution, the length of the resulting polyenes increases. As the reaction progresses dehydrochlorination slows down, which is due to partial cross-linking of the polymer as a result of side reactions and a reduction in activity of the macromolecular segments as well as the formation of polyenes with a long chain of conjugation.[91]

The degree of dehydrochlorination increases with an increase in reaction time. When THF is added to the reaction solution, the rate of reaction and degree of dehydrochlorination decrease in direct proportion to the concentration of DMF. On increasing the

concentration of polymer in solution the rate of reaction and degree of dehydrochlorination increase.[98]

Addition of water or methanol to the reaction solution results in considerable inhibition of dehydrochlorination, which is due to the formation of hydrogen bonds and hence a reduction in basicity of DMF:[98]



R = H or CH_3.

A study of the reaction of PVC in different solvents at temperatures of 100–170 °C showed that in solvents that have considerable nucleophilicity and basicity (pyridine, morpholine) dehydrochlorination and substitution reactions occur in parallel. In solvents that have considerable basicity but weak nucleophilicity (DMF, DMAA), elimination of hydrogen halide mainly occurs. In solvents that have weak nucleophilicity and basicity (THF, cyclohexanone, nitrobenzene), PVC remained unchanged. When solvents that have weak basicity but strong nucleophilicity are used (dioctyl phthalate, benzyl alcohol), substitution reactions occur to a considerable degree.[98]

VI. Dehydrohalogenation by complexes of *N*-substituted amides with metal salts

In a number of studies the dehydrohalogenation of PVC,[99–104,106,107,109–111] poly(vinyl bromide),[99] and also PVDC, CPVC, and vinylidene chloride–vinyl chloride copolymer[111] by complexes of *N*-substituted amides with metal salts has been investigated.

The structure of the dehydrohalogenation products depends on the reaction conditions, the structure of the initial polymer, and also on the nature of the solvent (amide) and salt used.

On increasing the content of the metal salts in solution, the concentration of polymer, and the reaction temperature (from 80 to 110 °C), the degree of dehydrohalogenation and the rate of reaction increase.[99–101] The degree of dehydrohalogenation also increases with an increase in reaction time[99,100] and the degree of polymerisation of the initial polymer.[102]

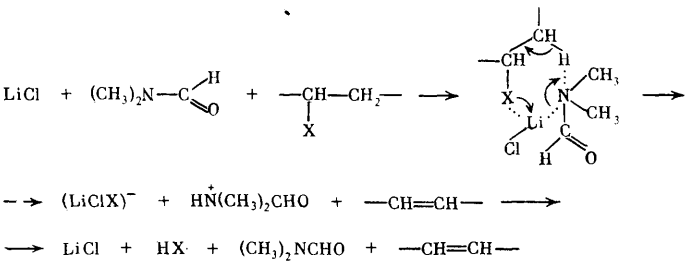
The presence of oxygen in the reaction mixture leads to a reduction in the rate of dehydrohalogenation and to the occurrence of side reactions involving degradation of the polymer.[102] Dilution of the reaction solution with tetrahydrofuran leads to a reduction in the degree of dehydrohalogenation and the rate of reaction.[99]

It should be noted that on reaching a degree of conversion of 30–40% the dehydrohalogenation products become insoluble and precipitate from solution.[99]

As dehydrochlorination of PVC takes place, in the IR spectra of the reaction products there is a decrease in intensity of the absorption band in the region of 690 cm^{-1} which is a characteristic of stretching vibrations due to C–Cl bonds in the initial polymer and new intense absorption bands appear in the region of 1000 and 1600 cm^{-1} that are characteristic of C–H bond bending vibrations in *trans*-polyenes and stretching vibrations due to conjugated C=C double bonds respectively.[101,103,104] A very weak band appears in the region of 730 cm^{-1} which could be attributed to bending vibrations of the C–H bonds on a C=C double bond in a *cis* configuration.[104] When dehydrochlorination is carried out in the presence of oxygen, an intense absorption band occurs in the IR spectra of the products at 1760 cm^{-1} which is characteristic of vibrations due to the O=C< group.[103]

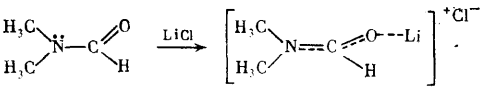
Dehydrochlorination of PVC in the system DMF–LiCl ($LiBr_2$, $MgCl_2$) resulted in the formation of long polyene structures with the number of conjugated double bonds $n > 14$. A broad maximum occurred at 550 mμ in the absorption spectrum in the UV and visible regions. In the spectra of the dehydrochlorination products of PVC in the system DMF–lithium acetate or magnesium chloride hydrate ($MgCl_2 \cdot 6H_2O$) a series of maxima that are characteristic of absorptions due to relatively short polyenes with the number of units $n = 4-14$ is observed. Zinc, copper, cobalt, nickel, and cadmium chlorides as well as lithium carbonate proved inactive in dehydrohalogenation.[99]

The system LiCl–DMF was first used in the dehydrobromination of bromoketosteroids,[105] and a mechanism for this was proposed that involved elimination of hydrogen halide as a result of the simultaneous attack by a lithium cation and DMF on alkyl halide and the concerted electron rearrangement in a six-membered ring including the halogen-containing compound, a DMF molecule, and a LiCl molecule:



X = halogen.

However, this mechanism, in attaching most importance to the coordinating power of the cation, does not explain the activity of some salts and the inactivity of others in dehydrohalogenation.



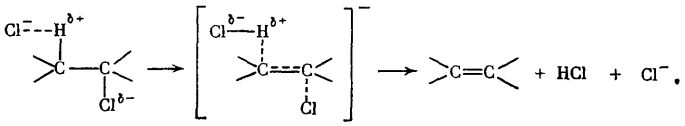
Lithium chloride forms a stable complex with DMF,[101] which occurs in dissociated form in DMF solution. As was mentioned above in Section V, halide ions in dipolar aprotic solvents are strong bases and nucleophiles.[97] Therefore the main dehdyrohalogenating agents in the sytstem DMF–metal salts are anions (in particular Cl^-)[99] and their ion pairs.[106,107] Nucleophilic substitution of halogen atoms in polymers by Cl^- and Br^- atoms does not inhibit further dehydrohalogenation. But if irreversible substitution reactions with nonhalide ions occur, the length of the polyene sequences formed during reaction is limited by the presence of these substituents. Thus, when lithium acetate or magnesium chloride hydrate is used for dehydrohalogenation, substitution reactions by the acetate and hydroxyl groups lead to a decrease in length of the resulting polyenes.[99]

Despite their solubility in DMF, heavy metal salts do not dissociate,[108] which accounts for the inactivity of these salts in dehydrohalogenation. Moreover, some salts form stable complexes with DMF (such as $ZnCl_2$) and inhibit dehydrohalogenation.[90,102]

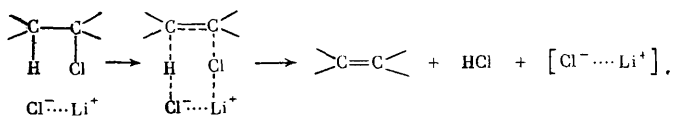
The rate of dehydrochlorination of PVC in the presence of LiCl and the structure of the reaction products depend to a considerable extent on the stereostructure (tacticity) of the initial polymer and the

polarity of the solvent.[102,106,109] When hexamethyltriamidophosphate (HMTP) is used as the solvent, the rate of reaction and length of the resulting polyenes are considerably greater than that when DMF is used.[106,109] Dehydrochlorination of syndiotactic PVC in both DMF and HMTP results in the formation of considerably longer polyene structures than with an atactic polymer. On increasing the syndiotactic content in the initial PVC, the rate of dehydrochlorination in DMF decreases (the energy of activation increases sharply), whereas in HMTP the rate of reaction increases and the energy of activation decreases.[106,109] This phenomenon is attributed to the existence of two parallel dehydrohalogenation mechanisms that are in an equilibrium which is shifted in favour of one of them depending on the stereostructure of the initial polymer and the polarity of the solvent.[106]

(A). Mechanism involving β-elimination $(E_2)^1$ by a halide ion (Cl^-):



(B). Mechanism involving dehydrohalogenation by a $[Cl^- \ldots Li^+]$ ion pair:



If the role of the solvent is ignored, it may be observed that a syndiotactic structure of the polymer is conducive to mechanism (A)' whereas an isotactic structure assists mechanism (B).

The concentration of unsolvated Cl^- anion and solvated Li^+ ion is considerably higher in HMTP than in DMF. Therefore the basic nature of Cl^- is more clearly defined in HMTP and hence, ionic mechanism (A) predominates in the dehydrochlorination of PVC, whereas in DMF mechanism (B), involving the action of an ion pair, is predominant.[106]

The energy of activation of dehydrochlorination in each specific case is the sum of the energies of activation of the respective mechanisms and depends on the tacticity of the initial polymer and the polarity of the solvent. The length of the polyene chains thus depends not only on the contribution from side reactions involving cross-linking, substitution, and oxidation but also on the equilibrium between the dehydrohalogenation mechanisms. Ionic elimination (A) leads to the formation of longer polyenes than with the ion-pair mechanism (B).[106]

On the whole, dehydrochlorination of PVC in the system DMF–LiCl involves two stages. At the first (rapid) stage dehydrochlorination of iso- and hetero-tactic structures in the macromolecules takes place with the formation of short polyene residues. At the second (slow) stage dehydrochlorination of the syndiotactic structures occurs with the formation of long sequences of conjugated C=C double bonds.[110] The variation in length of the polyenes formed during dehydrochlorination depending on the tacticity of the initial PVC is due to the stereospecific nature of the fundamental stages of elimination of HCl.[104,110]

The activity of the alkali metal salts depends on the electronegativity of the cation and the dipole moment of the salt. The rate of dehydrochlorination of PVC increases in the series LiI < NaI < KI < RbI. The solvating capacity of DMF relative to the cation of the ion pair $M^+(DMF)_nI^-$ (M = metal) increases as the electronegativity of the cation decreases (from 1.0 for Li to 0.8 for Rb). Therefore, as the electronegativity of the M^+ cation decreases, the contribution from the solvent increases and the anion of the ion pair approximates in nature to a free ion, in other words, its basicity increases.[107]

In a series of lithium halides the rate of dehydrochlorination increases in the following order: LiI < LiBr < LiCl.[107] Solvation of anions decreases as their diameter decreases,[97] hence the basicity of the anions in solution increases.

The use of lithium salts formed by anions having significant nucleophilicity (cyanide, thiocyanate, nitrite, as well as organic salts such as acetate, benzoate, phenate, and thiophenate) led to a reduction in the rate of dehydrochlorination compared to the system LiCl–DMF and the formation of short polyenes as a result of side reactions involving substitution.[101]

The rate of dehydrochlorination of PVC by the system LiCl–DMF is given by the equation[101]

$$dHCl/dt = k_1.[PVC].[LiCl] + k_2.[PVC]_1.[LiCl] + \ldots + k_n.[PVC]_{n-1}.[LiCl],$$

or

$$dHCl/dt = k_1.[PVC]_0.[LiCl].e^{-k.[LiCl].t},$$

where k_n is the rate constant of a simple elimination to form 1, 2, ... n conjugated double bonds; $[PVC]_0$ is the initial concentration of PVC; $[PVC]_n$ is the concentration of macromolecules containing 1, 2, ... n conjugated double bonds; [LiCl] is the concentration of LiCl; and t is the reaction time.

For the initial rate of reaction (when $t \to 0$) the kinetic equation has the form

$$dHCl/dt = k_1.n.[PVC]_0.[LiCl].$$

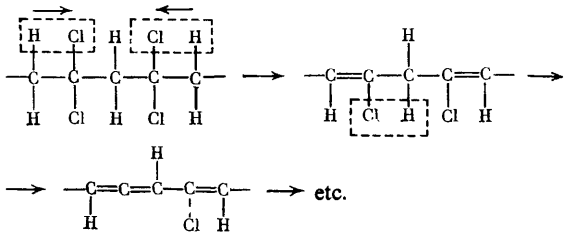
Dehydrochlorination of polymers containing more than one chlorine atom per monomer unit (PVDC, CPVC, and vinylidene chloride–vinyl chloride copolymer) occurs much more rapidly compared to pure PVC and reaches higher degrees of conversion (in the dehydrochlorination of PVDC about 1.4 chlorine atoms are eliminated on average per monomer unit).[111] This effect is consistent with the results obtained in a study of the dehydrofluorination of fluorine-containing polymers by amines[81] and is due to the increase in activity of the hydrogen atoms and a reduction in the dissociation energy of the carbon–halogen bond as the content of halogen in the polymer increases.

The structure of the reaction products during dehydrochlorination by the system LiCl–DMF also depends on the content of chlorine in the initial polymers. In the dehydrochlorination of polymers containing up to 64% chlorine, long polyene sequences are formed with the number of conjugated double bonds $n > 14$. However, dehydrochlorination of polymers containing more than 64% chlorine leads to the formation of relatively short polyenes ($n = 6-13$).[111] Laurent et al.[111] attribute this phenomenon to the "mutual restriction" of the growing polyene residues through their isolation by a methylene carbon atom:

$$-CH=CH-CH=CH-CH_2-CH=CH-CH=CH-.$$

With an increase in chlorine content in the polymer the rate of initiation of dehydrochlorination increases and therefore several growing polyene sequences can be formed at the same time in the polymer chain, which increases the probability of their "mutual restriction". However, this explanation of the interrruption of conjugation is acceptable only for PVC and poly(vinyl bromide).

Taking into account the degree of dehydrochlorination reached, where in the case of PVDC 1.4 Cl atoms are eliminated on average per monomer unit, it may be concluded that for polymers with a high chlorine content, the methylene and chloromethylene groups remaining in the polymer as a result of the "mutual restriction" of the growing polymers should undergo further dehydrochlorination:



The decrease in length of the resulting polyenes with an increase in chlorine content in the initial polymers is likely to be due to side reactions involving cross-linking at a relatively high temperature of dehydrochlorination (80–100 °C). Moreover, according to elemental analysis and IR spectroscopic data, the reaction products contain nitrogen- and oxygen-containing groups, which the authors assign respectively to free DMF retained by the precipitated polymer or to oxidised structures. However, it is possible that with an increase in the chlorine content of the polymer, the probability of substitution reactions taking place between the halogen-containing polymer and DMF or its degradation products is increased.

VII. Dehydrohalogenation by alkali metal amides

In a number of studies dehydrochlorination of PVC,[112–115] CPVC,[113,114] and PVDC [113,114,116–118] by alkali metal amides in liquid ammonia was investigated. The reaction has been carried out over a wide temperature range (from −60 to 50 °C) with polymer solutions and also powders and films. When dehydrohalogenation is carried out at temperatures above −33 °C (the boiling point of ammonia) an increase in pressure in the reactor is required.

By using alkali metal amides it is possible to achieve complete dehydrohalogenation even at low temperatures, which reduces the contribution from side reactions involving cross-linking to a minimum and assists the formation of structures with long sequences of conjugated multiple bonds. Thus, for example, completely dehydrochlorinated PVC, which contains no chlorine, melts at a temperature of 395–410 °C,[112,115] which is an indication of the linear structure of the dehydrochlorination product (absence of spatial cross-linking).

Dehydrohalogenation of halogen-containing polymers in solution[114] occurs more rapidly than with powders or films.[45] The degree of dehydrohalogenation increases with an increase in temperature and reaction time as well as with an increase in concentration of the alkali metal amide.[113,114,117]

As dehydrochlorination takes place the absorption bands characteristic of the initial polymers in the IR spectra of the products disappear and absorption bands appear at 990, 1600, and 3030 cm^{-1}, characteristic of bending vibrations of C–H bonds on a *trans*-C=C double bond, stretching vibrations of conjugated C=C double bonds, and stretching vibrations of the C–H bonds on a C=C double bond respectively.[45,113–117] In the IR spectra of the dehydrochlorination products of PVDC and CPVC an absorption band also occurs at 2200 cm^{-1}, which is attributed to stretching vibrations of C≡C triple bonds.[45,113,114,116,117]

A study of the dehydrochlorination products of PVC using X-ray diffractometry showed that these products have a structure that is similar to that of noncrystalline *trans*-polyacetylene.[114,115]

In the EPR spectra of the products of the complete dehydrochlorination of PVC a narrow solitary signal appears with a line width of 7–12 E.[112,114,115] As the degree of dehydrochlorination increases the line width decreases.[115] The value of the *g*-factor is 2.000 ± 0.005.[112] For the dehydrochlorination products of PVDC a narrower line in the EPR spectrum (5–9 E) is characteristic. As the degree of dehydrochlorination increases the spin-lattice relaxation time decreases and reaches a value of 10^{-6} s.[116]

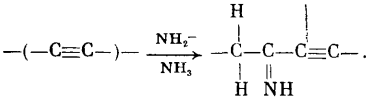
From an examination of the EPR spectra it may be concluded that delocalisation of the unpaired electrons, which are stabilised by the long chain of conjugated multiple bonds, occurs in the dehydrochlorination products.[114] As the degree of conversion increases, the concentration of unpaired electrons increases and reaches a value of 1.4×10^{21} spin g^{-1} for the dehydrochlorination product of PVDC.[116]

It should be noted that dehydrochlorination of PVDC by alkali metal amides in liquid ammonia has been proposed as a counter-synthesis of carbyne[116] occurring by a two-stage mechanism[117]

$$-(-CH_2-CCl_2-)_n- \xrightarrow[-n\mathrm{HCl}]{} -(-CH=CCl-)_n- \xrightarrow[-n\mathrm{HCl}]{} \longrightarrow -(-C\equiv C-)_n-$$

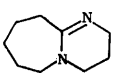
In four studies[112–115] elemental analysis data are given according to which the sum of the content of carbon and hydrogen in products of the exhaustive dehydrochlorination of PVC, containing no chlorine, differs from 100%. The authors attribute this difference to the presence of oxygen that is formed in the dehydrochlorination products as a result of oxidation reactions. Moreover, completely dehydrochlorinated PVC and PVDC did not contain nitrogen.[112–115] However, in a study[117] of the dehydrochlorination of PVDC with sodium and potassium amides in liquid ammonia at −55 and 0 °C it was shown that the main process of HCl elimination is accompanied by amination as a side reaction. Thus, for example, when dehydrochlorination was carried out at 0 °C for 30 h, the reaction products contained 8.3% nitrogen. It was shown that the content of nitrogen in the reaction products rises with an increase in the time of dehydrochlorination, the concentration of alkali metal amide in solution, and the degree of dehydrochlorination.[117]

In fact, alkali metal amides have considerable nucleophilicity in addition to high basicity. Therefore, when the dehydrohalogenation of halogen-containing polymers by alkali metal amides in liquid ammonia is carried out, side reactions involving nucleophilic substitution of the halogen atoms are to be expected. In addition to this, addition reactions of ammonia to multiple bonds are also possible[117]



VIII. Dehydrohalogenation by 1,8-diazabicyclo-[5.4.0]undec-7-ene

In recent years studies in which the strong organic base 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)



is used as a dehydrohalogenating agent for halogen-containing polymers have made their appearance in the scientific literature.[58,119–122]

Soga et al.[58,119] studied the dehydrochlorination of samples of PVC with a varying degree of polymerisation by DBU in polar solvents. The solvents used were dimethyl sulphoxide, THF, HMTP, and DMF. The reaction was carried out at 65 °C for 20 h. It was shown that the degree of dehydrochlorination did not depend on the molecular weight of the initial PVC.

As a result of dehydrochlorination long sequences of conjugated C=C double bonds are formed. A determination of the length of the polyene sequences from the data of elemental analysis gave a value of 8–15 –CH=CH– units. Samples of dehydrochlorinated PVC contained 2.8–4.9% residual chlorine and also 5.0–7.5% nitrogen, which in the opinion of the authors, was due to the partial doping of the resulting polyene with DBU molecules.[58]

In the IR spectra of the dehydrochlorination products a very strong absorption band occurs at 1015 cm^{-1} which is characteristic of a *trans*-polyacetylene.[58,119] In the UV spectra a broad absorption band occurs in the region of 670 nm, which is attributed to $\pi \rightarrow \pi^*$ electronic excitations.[58] After partial hydrogenation of the dehydrochlorination product of PVC alloyed with potassium, absorption bands occurred at 240, 280, 310, 340, 380, 400, and 420 nm in the UV spectra, which were attributed by the authors to $\pi \rightarrow \pi^*$ transitions in $-(-CH=CH-)_n-$ structures, where n = 2, 3, 4, 5, 6, 7, and 8 respectively.[119]

In the X-ray diffraction spectrum of the polyenes obtained there is a weak halo at 2θ = 20–25 °C, which is an indication of the very low degree of crystallinity.[58] With an increase in molecular weight of the initial PVC the intensity of this halo decreases, which suggests a decrease in the degree of crystallinity.

The dehydrochlorination of PVC films was studied by Danno et al.[120,121] Dehydrochlorination was carried out in two stages. At the first stage the reaction was carried out in a mixture of DMF and methanol at a volume ratio of 2:3 at 50 °C for 36 h in a current of nitrogen, in order to prevent the PVC films dissolving in the reaction mixture. As dehydrochlorination took place, in the IR spectra of the reaction products the intensity of the absorption bands due to C–Cl bonds in the region of 600–700 cm^{-1} that were characteristic of the initial PVC decreased and new bands appeared at 1010 and 3015 cm^{-1}, characteristic respectively of bending and stretching vibrations of C–H bonds in *trans*-polyacetylene.

The degree of dehydrochlorination increases with an increase in concentration of DBU and also with an increase in reaction time up to 40 h, reaching a value of 0.8 and then remaining constant (at a molar ratio of DBU:Cl = 4:1).[120]

A well-defined absorption band occurs at 605 cm^{-1} in the IR spectra of the films after the first stage of dehydrochlorination. This band is absent in the spectra of the initial PVC, whereas a band is clearly defined at 615 cm^{-1}. The absorption bands in the IR spectra at 605 and 615 cm^{-1} are attributed to stretching vibrations of C–Cl bonds in crystalline and amorphous PVC respectively. Thus, during dehydrochlorination at the first stage, elimination of HCl mainly occurs in the amorphous phase of PVC whereas the crystalline region does not change. Therefore, the maximum degree of dehydrochlorination attained at the first stage (0.8) is due to the presence in the initial PVC of about 20% as a crystalline fraction, which is more resistant to dehydrochlorination.[120]

After the first stage of the reaction the films became insoluble, which made it possible to use pure solvents at the second stage. For this second stage the reaction was carried out in pure DMF at 50 °C for 24 h in a current of nitrogen. The authors anticipated that at the second stage the crystalline regions of PVC would swell in the solvent and undergo further dehydrochlorination. In fact, the degree of dehydrochlorination increases to 0.95 at the second stage. The absorption band at 605 cm^{-1} in the IR spectra of the reaction products almost completely disappears, which suggests that the crystalline fraction undergoes dehydrochlorination. In the spectra of the products, absorption bands occur at 1665, 1720, and 3450 cm^{-1}. The bands at 1665 and 1720 cm^{-1} are attributed to the absorption of α,β-unsaturated and isolated keto groups respectively. The band at 3450 cm^{-1} is attributed to the absorption of hydroxyl and hydroperoxide groups. The appearance of oxygen-containing groups in the reaction products is attributed by the authors to a reaction between polymer and DMF. When dehydrochlorination was carried out under similar conditions in cyclohexanone, methyl ethyl ketone, and THF, bands in the IR spectra corresponding to the absorption of oxygen-containing groups were absent or very weak.[120]

An increase in reaction time from 36 to 67 h at the first stage and from 24 to 48 h at the second stage did not produce any substantial changes in the degree of dehydrochlorination or the IR spectra of the products.[121]

A study of the dehydrochlorination products of industrial PVC using X-ray diffractometry showed that the resulting polyenes were completely amorphous,[120] whereas in the dehydrochlorination of syndiotactic PVC obtained by low-temperature polymerisation polycrystalline films of a similar polyene structure were obtained.[121]

The dehydrochlorination of stereospecifically chlorinated polyacetylene by DBU in different solvents was studied by Akagi et al.[122] In the IR spectra of the reaction products there are strong absorption bands in the region of 1640 and 2130 cm^{-1}, attributed to stretching vibrations of carbon–carbon double and triple bonds respectively. With an increase in polarity of the solvent used, the absorption band due to the triple bonds shifts from 2140 cm^{-1} (for toluene) to 2121 cm^{-1} (for dimethyl sulphoxide) and the degree of dehydrochlorination increases (from 80.8 to 100%). In the Raman spectra of the dehydrochlorination products, intense lines occurred in the region of 1550 and 1140 cm^{-1}, attributed to stretching vibrations of carbon–carbon double and single bonds respectively in conjugated *trans*-polyenes. The authors attribute the presence of these bands to incomplete chlorination of the initial polyacetylene. A line occurred at about 2150 cm^{-1} which was attributed by the authors to stretching vibrations of C≡C triple bonds in macromolecules of the polyyne modification of carbyne (α-carbyne). On increasing the wavelength of exciting light from 457.9 to 632.8 nm, the frequency of this line decreased from 2157 to 2113 cm^{-1} correspondingly. As a result of a numerical calculation from Raman spectroscopic data of the length n of the resulting polyynes using the empirical relationship

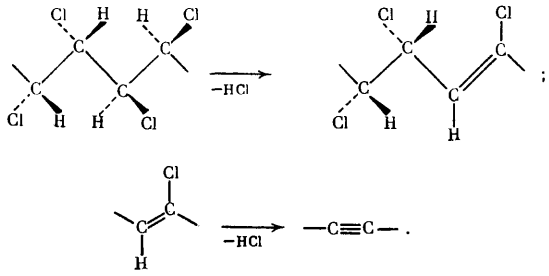
$$\nu_{C\equiv C} = 2104 + 698/(n_{C\equiv C} + 1)$$

values of n from 12 to 65 fundamental units were determined. Here $\nu_{C\equiv C}$ is the vibrational frequency of the C≡C bond in the Raman spectrum; n is the number of units of α-carbyne (–C≡C–).

In the UV spectra of the carbyne obtained there is a very broad absorption band from 350 to 700 cm^{-1}, which the authors attribute to overlap of the bands resulting from $\pi \rightarrow \pi^*$ excitations in the polyyne structures.[122]

The authors concluded from the IR and UV spectroscopic data that α-carbyne was formed and proposed a mechanism involving

two-stage *trans*-elimination:

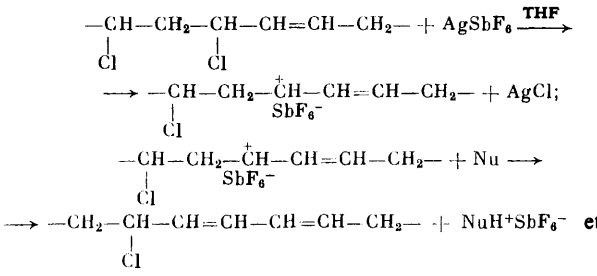


However, it should be noted that the results of vibrational spectroscopy alone are insufficient for an unequivocal conclusion about the type of bonding in the carbyne—polyyne or cumulene. Thus, according to calculated data which are good agreement with the experimental IR spectra, absorption bands in the region of 1600 and 2100–2200 cm^{-1} are characteristic of vibrations due to cumulene structures in β-carbyne molecules.[48] The absence of absorption bands at 1950 cm^{-1} in the IR spectra is not proof of the absence of a cumulene structure.[123,124] Moreover, assignment of the lines in the region of 1140 and 1550 cm^{-1} in the Raman spectra to vibrations of polyene structures[122] is only partly correct. Thus, while the line at 1140 cm^{-1} is due to the presence of polyacetylene residues in the sample, the intensity of the line in the region of 1550 cm^{-1} is disproportionately high for it to be assigned completely to vibrations of polyene structures.[125] The line in the region of 2150 cm^{-1} in the Raman spectrum was attributed by the authors to vibrations of the polyyne structures of α-carbyne. However, it was shown by Berdyugin et al.[54] that in the Raman spectra of β-carbyne obtained by dehydrohalogenation of poly(vinylidene halides) the lines in the region of 2150 and 1550 cm^{-1} correspond to vibrations of cumulated double bonds in the carbon chain. For a clear identification of the nature of the bonds in carbyne, a detailed study of its electronic structure is necessary.[33,41,42,51,52]

IX. Some other dehydrohalogenating agents

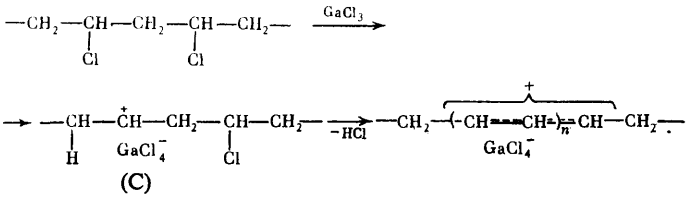
The chemical agents and systems that are widely used in the dehydrohalogenation of halogen-containing polymers are examined in Sections II–VIII. In the present section certain other chemical agents which are also active in hydrogen halide elimination reactions are described.

In the preparation of graft copolymers of isobutylene on PVC Kennedy and Davidson[126] found that organoaluminium compounds such as diethylaluminium chloride are able to dehydrochlorinate PVC to form a small quantity (2–5 mol%) of short $-(-CH=CH-)_n-$ polyene sequences, where $n \leqslant 5$ (according to UV spectroscopic data). In an attempt to obtain graft copolymers of THF on PVC it transpired that on treatment with silver hexafluoroantimonate dehydrochlorination of PVC occurred with the formation of polyene structures of 11 or more conjugated C=C double bonds,[127] while it was not possible to obtain graft copolymers. In the opinion of Kennedy[126] and Franta,[127] initiation of dehydrochlorination occurs at the sites of labile structures (mainly allylic chlorine atoms) present in the initial PVC. On replacement of the allylic chlorine atom by a SbF_6^- anion [or addition of a $(C_2H_5)_2AlCl$ molecule] a polymer carbocation is formed, which eliminates a proton by a β-elimination mechanism with reproduction of a chlorallylic structure, following which the process is repeated



where Nu is a nucleophile which can be a molecule of THF or another solvent.[127]

It was found by Myakov et al.[128] that PVC reacts with gallium trichloride with elimination of HCl at room temperature in the absence of a solvent. However, the degree of dehydrochlorination and the length of the resulting polyenes are small. Thus, for example, when the $GaCl_3$ content is 7.5%, the degree of dehydrochlorination only reaches 3%. With an increase in $GaCl_3$ content the degree of dehydrochlorination increases. In the UV spectra of the reaction products there are absorption bands at 317, 408, 470, and 535 nm, attributed to allylic, di-, tri- and tetra-enyl cations respectively. The formation of polyenyl cations in PVC macromolecules can be depicted by the following scheme:



(C)

The instability of PVC in the presence of $GaCl_3$ is due to the high ionising ability of $GaCl_3$ and also by the large energy gain in the elimination of HCl by the carbocation (C) through the formation of more stable allylic and polyenyl cations.[128]

On treatment of PVC in solution with different aromatic carbanions[129] obtained from organometallic compounds, the competing reactions of dehydrochlorination and nucleophilic substitution occur. The highest activity in dehydrochlorination was recorded for the phenylisopropyl carbanion $[C_6H_4(CH_3)_2C^-]$. According to UV spectroscopic data, the length of the resulting polyene sequences ranges from 5 to 12 conjugated C=C double bonds.[129]

When films of halogen-containing polymers under vacuum are brought into contact with antimony pentafluoride vapour, dehydrochlorination occurs vigorously to give long chains of conjugated double bonds.[130] On exposure of a PVDF film to SbF_5 vapour, the film darkens and then turns black. An increase of temperature was required in order to carry out the dehydrofluorination of polytrifluoroethylene, whereas a PVC flm turned black immediately on exposure to SbF_5 at room temperature. Taking into account the fact that SbF_5 is an effective dopant for polyacetylene,[86] it may be concluded that there is future potential in this method of dehydrohalogenation for obtaining organic semiconductor materials.

The reaction between PVC and the superoxide anion was studied by Osawa et al.[131,132] In order to achieve this, PVC in THF solution was treated with potassium superoxide in an atmosphere of nitrogen at 40 °C. In the IR spectra of the reaction products, absorption bands occur at 3300, 1680, 1620, and 765 cm^{-1}, attributed to hydroxyl groups, α,β-unsaturated keto groups, and polyene structures (1620 and 765 cm^{-1}) respectively. The UV spectroscopic data confirm the presence of conjugated polyene structures in the reaction products. According to the elemental analysis data, with an increase in the time of reaction between PVC and KO_2, the content of chlorine in the reaction products decreases while the oxygen content increases. In the opinion of the authors, initiation of the reaction between PVC and O_2^- occurs by a mechanism involving nucleophilic substitution of the chlorine atoms in chlorallylic groups present in the initial PVC.[131,132] The resulting peroxide macroradicals undergo secondary reactions to form α,β-unsaturated keto groups, hydroxyl groups, peroxide cross-linking, and also polymer alkoxy radicals. The alkoxy radicals can detach a proton from the polymer chain to form alkyl macroradicals which undergo further dehydrochlorination to form conjugated polyene structures.[131,132]

In these studies[79,80,133] a method was proposed for the dehydrohalogenation of halogen-containing polymers [poly(α-chloroacrylonitrile,[79,80,133] PVC, chlorinated polybutadiene, poly(2,3-dibromobutene) [133]] by alkali metal hydrides in DMF or dimethyl sulphoxide solution at 60–80 °C to form polymers with a system of conjugated double bonds.

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The dehydrohalogenation products of halogen-containing polymers, as in the majority of polymers with a system of conjugation, have semiconductive properties and are of interest for their use in electrical engineering (sources of a current),[58,134,135] microelectronics ($p-n$ transitions, Schottky barriers, photoelectric cells[136]) optics (polarising films[137–144]), and also for the preparation of electrodes and membranes in electrochemistry, protective films in microwave technology,[145,146] and antistatic materials.[146,147]

The electrophysical properties of polymers with a system of conjugation obtained by dehydrohalogenation have been investigated in a considerable number of studies.[20,22,26,40,58,75,79,80,99,113,114,119–122,145–157] The specific electrical conductivity of the dehydrohalogenation products varies over a wide range ($10^{-12}-10^{-7}$ Ohm^{-1} cm^{-1}) depending on the nature of the initial polymer, the dehydrohalogenating agent, and the reaction conditions. Alloying (doping) of the reaction products with different electron-donating or electron-withdrawing components results in an increase in the electrical conductivity by a factor of 10^5-10^8 ($10^{-6}-10^{-1}$ Ohm^{-1} cm^{-1}). Iodine[20,22,26,40,119,120,122,150–152,154], $FeCl_3$,[26,151] SO_3,[58,119] BF_3,[26] AsF_5,[119] and also $(C_2H_5)_4NBF_4$ [156] and copper phthalocyanine[155] have been used as dopants.

From an examination of the results of the studies cited above it may be concluded that chemical dehydrohalogenation of halogen-containing polymers is a practicable and convenient method of obtaining carbon-chain polymers with a system of conjugation in the main chain, which can be used to obtain even crystalline polyacetylene.[158,159] The most effective dehydrohalogenating agents are hydroxides, alkoxides, and alkali metal amides. Dehydrohalogenation by DBU and SbF_5 also appears to have future potential.

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Translated from *Uspekhi Khimii* **60** 799–834 (1991) U.D.C. 547.241

P-Halogen-substituted phosphorus ylids

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ABSTRACT. Literature data on methods of obtaining ylids containing halogen atoms on the phosphorus atom of the P=C group are arranged systematically and reviewed.

The bibliography contains 125 references.

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I. Introduction

Phosphorus ylids are important reactants and are widely used in organic synthesis.[1] Among the various types of these compounds synthesised in recent years there is significant interest in *P*-hetero-substituted phosphorus ylids,[2–4] particularly in ylids containing halogen atoms on phosphorus, or *P*-halogenated ylids as they are usually called. The presence of labile halogen atoms determines the properties of these compounds, which are interesting from theoretical and preparative aspects.[2–7] With the aid of *P*-halogenated ylids such valuable substances for organic synthesis as phosphorus-containing ketenes, thioketenes, vinylphosphine oxides, allylphosphine oxides, etc. have been obtained. *P*-Halogenated ylids participate in various cycloaddition and heterocyclisation reactions and possess high phosphorylating ability.

In addition *P*-halogenated ylids are also convenient subjects for studying important theoretical problems of structure and reactivity of organophosphorus compounds.

Recently published review papers on *P*-halogenated ylid chemistry comprise material from only the author's work.[2,8–10] Latterly a significant number of publications has appeared describing new methods of synthesis and disclosing interesting properties of *P*-halogenated ylids as a result of which there is a need to review all the available information on this important type of organophosphorus compound. Results of investigations on *P*-halogenated ylid chemistry published up to 1990 are correlated in this review.

II. Synthetic methods

Detailed investigations on *P*-halogenated ylids have enabled convenient methods for their synthesis to be devised based on the following conversions. 1. 'Oxidative ylidation' of compounds of trivalent phosphorus comprising increasing the phosphorus coordination number to four by adding halogen and forming a P=C bond.[2] Such reactions include 1,2(C→P)-halogenotropic rearrangements and reactions of tertiary alkylphosphines with carbon tetrahalides to form *P*-halogenated ylids containing one atom of chlorine or bromine on the phosphorus atom. 2. The formation of a P=C multiple bond in a halophosphorane or halophosphonium salt by an elimination reaction. Various *P*-chloro- and *P*-fluoroylids were synthesised by this means, including some containing several halogen atoms on phosphorus. 3. Reactions of *P*-halogenated ylids with chlorine-containing electrophiles which proceed with replacement of hydrogen atoms at the α-carbon by various groups.

The methods listed have enabled *P*-halogenated ylids of practically any strucure to be obtained by simple operations using starting materials available in the laboratory.

1. Rearrangement of α-haloalkylphosphines into *P*-halogenated ylids

A halogen atom at the α-position of tertiary alkylphosphines is distinguished by high lability as a result of which it may possibly migrate to the phosphorus atom [1,2(C→P)-halogenotropic shift]. The valency of the phosphorus atom is increased as a result of halogen atom migration, a P=C bond is formed and the α-haloalkylphosphines (A) are converted into *P*-halogenated ylids (B).

$$\underset{\text{(A)}}{R_2P(X)-CR_2'} \longrightarrow \underset{\text{(B)}}{R_2P(X)=CR_2'},$$

X = Br, Cl.

Halogenotropy in a P–C diad depends on the substituents R and R′ on the phosphorus and carbon atoms, which influence the thermodynamic stability of the halogenotropic isomers (A) and (B). Consequently not only 1,2(C→P) but also 1,2(P→C)-halogenotropic rearrangements (see below) are possible with a particular choice of substituents. However α-haloalkylphosphines containing electron-accepting substituents on the α-carbon atom, stabilising the ylid function as a rule, are readily converted into *P*-halogenated ylids and in this case a 1,2(C→P)-halogenotropic rearrangement is a reliable means of obtaining them.

Halo-bis-(benzenesulphonyl)methanes, being comparatively strong CH-acids, react with chlorodiphenylphosphine in the presence of triethylamine in tetrahydrofuran at 0 °C with the formation of tertiary α-haloalkylphosphines (I). Compounds (I) rearrange smoothly into *P*-halogenated ylids (II), which are isolated in good yield as stable crystalline compounds and are used as reagents in various chemical conversions.[11]

$$Ph_2PCl + XCH(SO_2Ph)_2 \xrightarrow[-Et_3N\cdot HCl]{Et_3N} \underset{\text{(I)}}{Ph_2PC(X)(SO_2Ph)_2} \longrightarrow \underset{\text{(II)}}{Ph_2P(X)=C(SO_2Ph)_2}$$

X = Br, Cl.

The reaction of di-organochlorophosphines with metallochloromethanes (III) or (V) stabilised by sulphonyl or trimethylsilyl groups proceeds readily.[2,11–13] The resulting α-chloroalkylphosphines (IV) and (VI) are very unstable and rearrange into *P*-chloroylids at low temperature. For example, α-chloroalkylphosphine (VI), which was observed by its ^{31}P NMR (signal at δ_P 86.1 p.p.m.), exists at −110 °C in toluene but even at −90 °C is converted quantitatively into ylid (VII) (δ_P 65.5 p.p.m.).[13]

$$R_2PCl + LiCHSO_2CF_3 \xrightarrow[-LiCl]{} \underset{Cl}{\underset{|}{R_2PCHSO_2CF_3}} \longrightarrow \underset{Cl}{\underset{|}{R_2P{=}CHSO_2CF_3}},$$

(III) (IV) 60—75%

R = Et, iso-Pr, Ph,

$$(Me_2N)_2PCl + LiCHSiMe_3 \xrightarrow[-LiCl]{} \underset{Cl}{\underset{|}{(Me_2N)_2PCHSiMe_3}} \longrightarrow$$

(V) (VI)

$$\longrightarrow \underset{Cl}{\underset{|}{(Me_2N)_2P{=}CHSiMe_3}}.$$

(VII), 64%

Compounds of trivalent phosphorus containing a trichloromethyl group are comparatively stable. Lutsenko and co-workers obtained bis-(dimethylamino)trichloromethylphosphine, which is stable at room temperature, by an exchange reaction of dichloro(trichloromethyl)phosphine with diethylamine. The product was purified by distillation in vacuum and was then converted into *P*-chloroylid (VIII) by boiling in dichloromethane.[14]

$$Cl_2PCCl_3 \xrightarrow[-Me_2NH\cdot HCl]{Me_2NH} (Me_2N)_2PCCl_3 \longrightarrow \underset{Cl}{\underset{|}{(Me_2N)_2P{=}CCl_2}}.$$

(VIII)

Pinchuk and co-workers have carried out the analogous rearrangement of bis-(diethylamino)trichloromethylphosphine (X) into ylid (XI).[15,16] Phosphine (X) was obtained by the reaction of chloro-bis-(diethylamino)phosphine with hexamethyltriaminophosphine and carbon tetrachloride. As was shown previously by Riesel[17] the ion pair (IX) is formed, containing the CCl_3^- anion, which is capable of reacting with chlorine-containing electrophiles. In this case the ion pair interacts with chloro-bis-(diethylamino)-phosphine with the formation of phosphine (X). Ylids (VIII) and (XI) were not isolated in a pure state. However their structures were confirmed spectroscopically and by hydrolysis.

$$(Me_2N)_3P + CCl_4 \longrightarrow \underset{(IX)}{[(Me_2N)_3\overset{+}{P}Cl\ CCl_3^-]} \xrightarrow{(Et_2N)_2PCl} \underset{(X)}{(Et_2N)_2PCCl_3} \longrightarrow$$

$$\longrightarrow \underset{(XI)}{(Et_2N)_2P(Cl){=}CCl_2} \xrightarrow{H_2O} (Et_2N)_2P(O)CHCl_2.$$

The *C*-silicon-substituted *P*-chloroylids (XIII) and (XIV) were obtained by reacting carbosilanes with lithio- or silylphosphines. α-Haloalkylphosphines (XII) rearrange into *P*-chloroylids extremely readily but they were not recorded spectroscopically. Nonetheless the formation of α-haloalkylphosphines is not in doubt as follows convincingly from the reaction scheme.[18,19]

$$Cl_{4-n}C(SiCl_3)_n \xrightarrow{Me_2PLi} Me_2PC(Cl_{3-n})(SiCl_3)_n \longrightarrow \underset{Cl}{\underset{|}{Me_2P{=}C(Cl_{2-n})(SiCl_3)_n}},$$

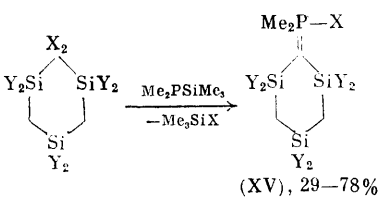
(XII) (XIII)

$n = 1, 2,$

$$Cl_2C(SiMe_3)_2 \xrightarrow[-Me_3SiCl]{Me_2PSiMe_3} Me_2PC(Cl)(SiMe_3)_2 \longrightarrow \underset{Cl}{\underset{|}{Me_2P{=}C(SiMe_3)_2}}.$$

(XIV)

The reaction of *C*-dihalo-1,3,5-trisilacyclohexanes with silylphosphines on boiling in dimethoxyethane gives *P*-halogenated ylids (XV) with fission of the Si—P bond. These are stable crystalline substances or liquids distillable in vacuum.[19] The structures of the *P*-chloroylids were proved by X-ray structural analysis. Compounds (XV) are molecules planar in structure with shortened lengths for the P=C and Si—C bonds as a result of delocalisation of the negative charge on the ylid carbon atom around the ring.[20]



(XV), 29—78%

X = Br, Cl; Y = Cl, F, Me.

In certain cases *P*-chloroylids (XVI) and (XVIII), formed by 1,2 (C→P)-chlorotropic rearrangement, then undergo a prototropic or silylotropic rearrangement being converted into imidophosphonic chlorides (XVII) and (XIX).[21–24]

$$Cl_2PCHCl_2 \xrightarrow{RNH_2 + Et_3N} (RNH)_2PCHCl_2 \longrightarrow$$

$$\longrightarrow \underset{Cl}{\underset{|}{[(RNH)_2P{=}CHCl]}} \longrightarrow \underset{Cl}{\underset{|}{RNH{-}\overset{\overset{NR}{\|}}{P}CH_2Cl}},$$

(XVI) (XVII)

R = Alk,

$$\underset{Cl}{\underset{|}{Et_2NPCHCl_2}} \xrightarrow{(Me_3Si)_2NLi} \underset{(Me_3Si)_2N}{\underset{|}{Et_2NPCHCl_2}} \longrightarrow \left[\underset{(Me_3Si)_2N}{\underset{|}{\overset{Cl}{\overset{|}{Et_2NP{=}CHCl}}}}\right] \longrightarrow$$

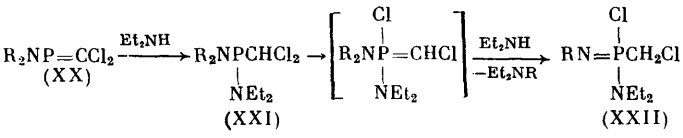
(XVIII)

$$\longrightarrow \underset{Me_3SiN}{\underset{\|}{\overset{Cl}{\overset{|}{Et_2NPCH(Cl)SiMe_3}}}}$$

(XIX)

The phospha-ethylene (XX) is converted into trimethylsilylimidophosphonic chloride (XXII) on boiling in tetrahydrofuran with an excess of diethylamine. Seemingly diethylamine adds to the phospha-ethylene with the formation of dichloromethylphosphine (XXI) which rearranges to an unstable *P*-chloroylid. The latter gives

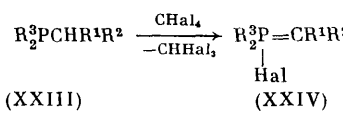
ylid (XXII) as a result of a silylotropic rearrangement and desilylation.[25,26]



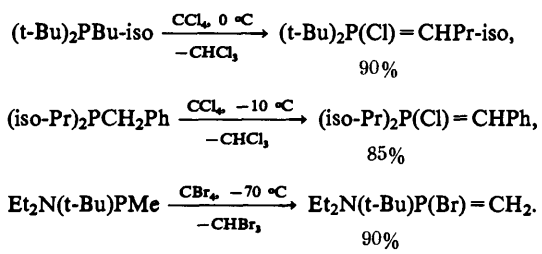
R = Me_3Si.

2. Reactions of tertiary alkylphosphines with carbon tetrahalides

The reaction of tertiary alkylphosphines with carbon tetrahalides was first studied in the last century.[27,28] However *P*-halogenated ylids were not obtained from this reaction for a long time.[29–32] The reaction, which is very sensitive to conditions, proceeded only to the formation of a mixture of compounds difficult to identify.[32] Only in 1975–1977 was it established that by observing an appropriate temperature regimen and choice of solvent, tertiary alkylphosphines (XXIII) react with carbon tetrachloride or tetrabromide with the formation of *P*-halogenated ylids (XXIV).[33–36]

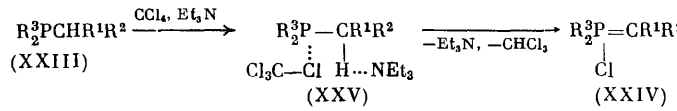


The interaction of compounds (XXIII) with carbon tetrahalides (CCl_4,[33,34] $CBrCl_3$, CBr_4 [34–37]) is usually carried out in pentane, diethyl ether[33–37] or dichloromethane[39] below 0 °C. Reaction with carbon tetrachloride occurs below 0 °C, and with CBr_4 and $CBrCl_3$ at −70 °C. The yields of *P*-halogenated ylids are high as a rule. *P*-Halogenated ylids are not isolated from the reaction mixture for preparative work, which appreciably simplifies handling. In this event it is sufficient to add carbon tetrachloride to the alkylphosphine in ether in order to obtain a reagent which is very reactive and ready to use.[9] However where necessary (for example for spectroscopic investigations) *P*-halogenated ylids may be purified by distillation in vacuum or by crystallisation from inert solvents.[9,40–43]

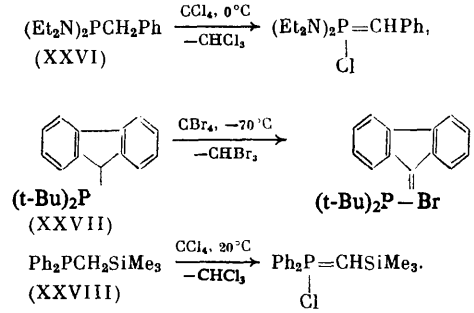


The substituents R^1 and R^2 in compound (XXIII) may be electron acceptors, groups, increasing the CH-acidity,[35–37,39–41] electron-neutral or electron-donating groups.[33,34,37,38] Compounds of trivalent phosphorus, containing at the α-carbon atom, alkyl groups, hydrogen atoms or trimethylsilyl or phenyl groups, which stabilise the ylid function, interact most actively with carbon tetrahalides. Yields of ylids obtained in this way are very high.[34,38,43–45] Strong electron-accepting groups at the α-carbon atom may reduce the nucleophilicity of the trivalent phosphorus atom since the rate of their interaction with carbon tetrahalides is reduced. For example, the introduction of one, two or three atoms of chlorine or bromine at the α-carbon atom of tertiary alkyl phosphines successively slows the reaction with carbon tetrachloride down to a complete stop. Electronegative alkoxycarbonyl or arylsulphonyl groups at the α-carbon atom of tertiary alkylphosphines also reduce the rate of interaction of the trivalent phosphorus atom with carbon tetrachloride.[35,40] However the reaction rate may in this case be increased by the addition to the reaction medium of tertiary amines the catalytic action of which is explained by participation in the formation of an intermediate reaction complex (XXV) (Scheme 1).[35,44] For example, compounds (XXIII) react readily with carbon tetrachloride in the presence of triethylamine in ether below 0 °C being converted in high yield into *P*-chloroylids (XXIV). In the absence of triethylamine at 20 °C the interaction is effected extremely slowly.[35]

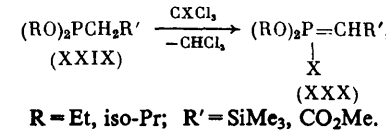
Scheme 1



Among tertiary alkylphosphines, compounds of the type of (XXVI)–(XXVIII) containing alkyl, phenyl or dialkylamino groups on the trivalent phosphorus atom react readily with carbon tetrahalides.[38,39,43–46]

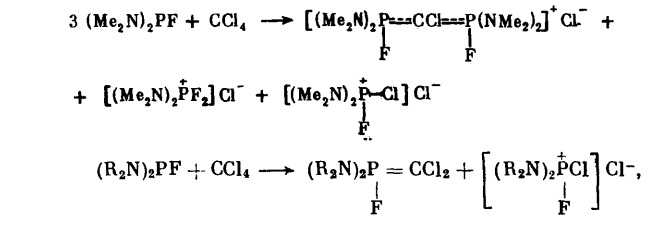


Esters of alkylphosphonous acids (XXIX) react slowly even with an excess of carbon tetrachloride at 20 °C (R′ = $SiMe_3$, 14 h) while with CBr_4 or $CBrCl_3$ they react in ether at −70 °C and give high yields of *P*-bromoylids (XXX).[35–37,40,44]



Acid chlorides and bromides of trivalent phosphorus do not react directly with carbon tetrahalides although fluorotetraalkyldiamino-phosphines react slowly with carbon tetrachloride at a ratio of 1:3

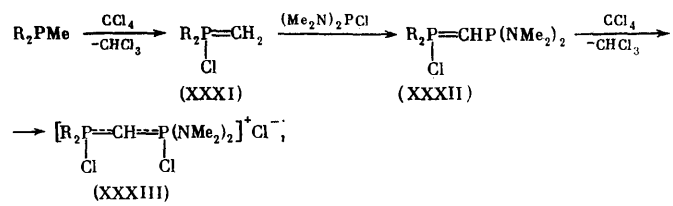
(R = Me) or 2:1 (R = Et, n-Pr) giving *P*-fluoroylids and phosphonium salts.[47]



R = Et, iso-Pr.

Tertiary alkylphosphines give *P*-chloroylids (XXXIII) in high yield with an excess of carbon tetrachloride in the presence of chloro-bis-(dimethylamino)phosphine. As shown in Scheme 2 ylids (XXXI) are formed initially and are converted by reaction with the chlorophosphine into ylids (XXXII) containing a trivalent phosphorus atom. Reaction of the latter with CCl_4 gives *P*-chloroylid (XXXIII).[34]

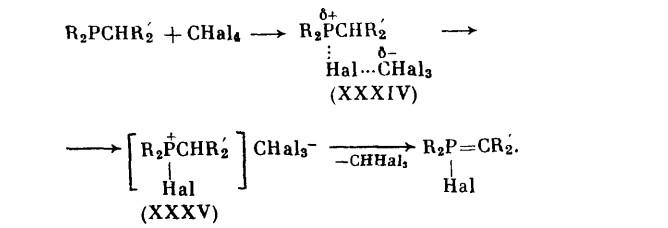
Scheme 2



R = t-Bu, Et_2N.

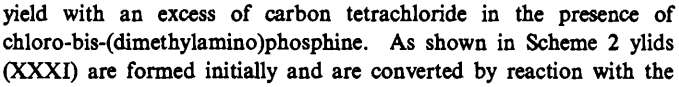
It is assumed at present that the mechanism of the reaction of trivalent phosphorus compounds with carbon tetrahalides with few exceptions[48,49] has an ionic character.[50,51] The mechanism of the reaction of tertiary alkylphosphines with $CHal_4$ is not exceptional in this regard, although the presence of a labile hydrogen atom on the α-carbon determines some of its special features (Scheme 3).[34]

Scheme 3



Nucleophilic attack of the trivalent phosphorus by a halogen atom of the carbon tetrahalide leads through the intermediate formation of complex (XXXIV) to heterolytic fission of the readily polarised bond of $CHal_4$ and the formation of an ion pair (XXXV) containing trichloromethyl anion (Scheme 3). The highly basic $CHal_3$ anion deprotonates the α-carbon atom of the intermediate, the CH-acidity of which is fairly high due to the strong positive inductive effect of the phosphonium group, as a result of which halogenoform is eliminated and a *P*-halogenated ylid is formed.[9,34,52]

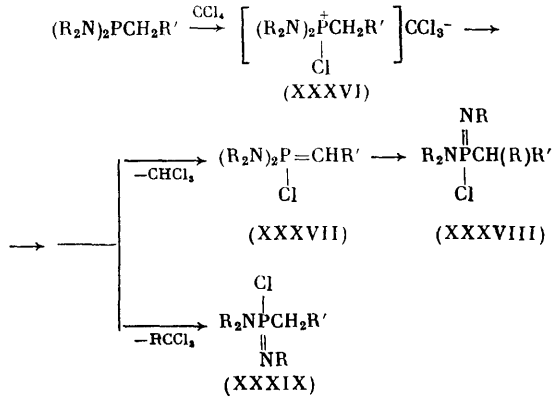
Scheme 3 demonstrates the reaction of sterically hindered trialkylphosphines with carbon tetrabromide as a result of which phosphonium salts containing tribromomethyl anion and stable at low temperature (−120 °C in pentane) are formed. The stability of the phosphonium salt is explained by steric hindrance to nucleophilic attack by the tribromomethyl anion on the phosphonium cation or on the α-proton. On increasing the temperature to −60 °C the phosphonium salts are converted into the corresponding *P*-bromoylids with elimination of chloroform. The structure of the phosphonium salts, particularly the presence in them of CBr_3 anion, was demonstrated by chemical reactions. Deuterobromoform was obtained on reacting the salts with deuterium chloride and tribromotrimethylsilylmethane was formed with chlorotrimethylsilane.[34]



R = D, Me_3Si.

The route of the reaction of compounds of trivalent phosphorus (XXIII) with carbon tetrahalides and the character of the resulting products depends on the solvent.[53] Neilson and co-workers have shown that on reacting aminoalkyl-bis-(trimethylsilyl)phosphines with carbon tetrachloride in nonpolar solvents, chloroform is eliminated and *P*-chloroylids (XXXVII) are formed which then rearrange into iminophosphoranes (XXXVIII). However on carrying out the reaction in dichloromethane, trichlorotrimethylsilylmethane is eliminated and iminophosphoranes (XXXIX) are formed (Scheme 4). The dependence of the reaction route on the nature of the solvent is determined by the polarity of the medium on ion pair (XXXVI). In a polar solvent the ion pair separates and consequently the CCl_3^- anion attacks the exposed trimethylsilyl group. On the other hand in a nonpolar solvent a tighter ion pair (XXXVI) exists and consequently reaction of CCl_3 anion with the neighbouring hydrogen on the α-carbon atom and elimination of chloroform are readily effected.[54]

Scheme 4

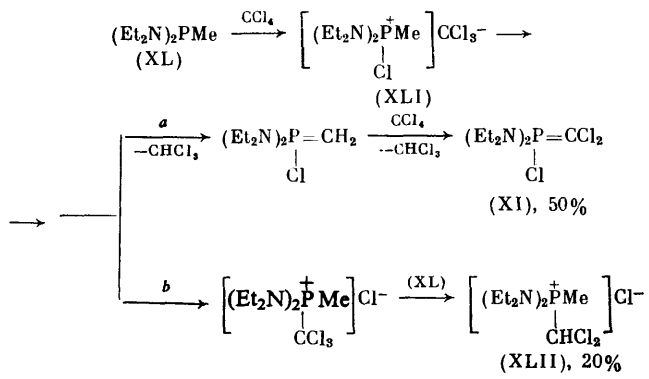


R = Me_3Si; R′ = H, Alk.

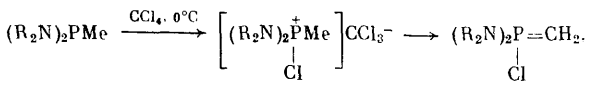
The reaction of compounds of trivalent phosphorus with carbon tetrahalides may under certain conditions occur with no elimination of halogenoform and no *P*-halogenated ylid formation but with attack of the trichloromethyl anion on the phosphonium cation and

formation of trichloromethylphosphonium salts.[55–57] The first reaction route occurs more frequently than the relatively rare second. As shown in Scheme 5, the reaction of bis-(diethylamino)methylphosphine (XL) with an excess of carbon tetrachloride occurs simultaneously in the two directions *a* and *b*, as a result of which a certain quantity of phosphonium salt (XLII) is formed in addition to ylid (XI).[57]

Scheme 5

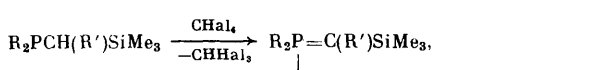


Branched groups on the phosphorus atom, which cause steric hindrance, hinder attack to $CHal_3^-$ on the phosphonium cation of ion pair (XLI). Consequently, in contrast to compound (XL), the reaction of bis-(diisopropylamino)methylphosphine with carbon tetrachloride in ether at 0 °C at a reactant ratio of 1:1 gives *P*-chloroylid (XLIII) in quantitative yield.[58] Tertiary alkylphosphines containing bulky t-butyl or isopropyl groups are smoothly converted into *P*-chloroylids. The groups mentioned not only facilitate ylid formation but also increase their stability.[9,33,34]



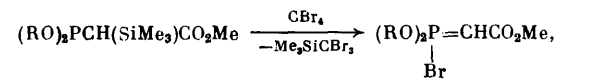
R = iso-Pr.

Tertiary alkylphosphines containing trimethylsilyl groups on the α-carbon atom very often react with carbon tetrahalides and are usually converted into ylids (XLIV).[20,34,37–40,46]

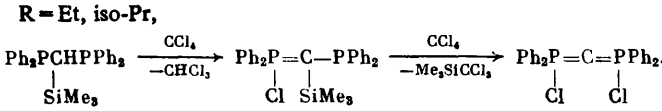


Hal = Br, Cl; R = Me_2N, Et_2N, $(iso\text{-}Pr)_2N$, Me, t-Bu, Ph, EtO, iso-PrO; R′ = $SiMe_3$, Ph.

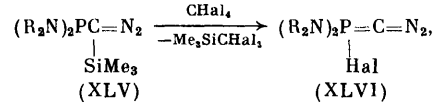
In certain cases trivalent phosphorus compounds containing trimethylsilyl groups on the α-carbon atom react with carbon tetrahalides with elimination of trihalotrimethylsilylmethane and not haloform. Trivalent phosphorus compounds containing a trimethylsilyl group at the sp^2-hybridised carbon atom are particularly readily desilylated.[59,60]



R = Et, iso-Pr,

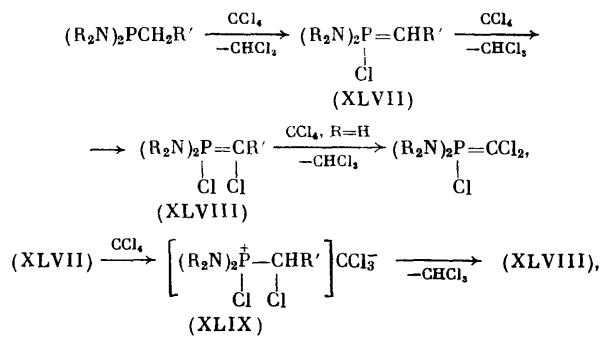


Compound (XLV) eliminates trihalotrimethylsilylmethane on reaction with carbon tetrahalides being converted into *P*-halogenated ylids (XLVI) containing a diazo group on the ylid carbon atom.[61,62] Ylids (XLVI) are hygroscopic red oily liquids containing an absorption band at 2035 cm^{-1} in the IR spectrum. They are stable in solution for several days and are very reactive (see below).



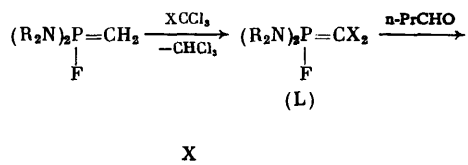
Hal = Br, Cl, R = iso-Pr.

P-Chloroylids formed by reaction of trivalent phosphorus compounds with carbon tetrachloride may react with a second molecule of CCl_4, exchanging a hydrogen atom on the α-carbon atom by an atom of chlorine. Thus reaction of bis-(dialkylamino)-alkylphosphines with an excess of carbon tetrachloride gives *C*-chloro-substituted *P*-chloroylids in yields of 70–80%.[57,63] Nucleophilic removal of a chlorine atom from carbon tetrachloride by the ylid carbon atom with the formation of ion pair (XLIX) is proposed, which is then converted into ylid (XLVIII) by elimination of chloroform.



R_2N = Et_2N, $C_5H_{10}N$; R′ = H, Me, n-Pr, iso-Pr, Cl.

Exchange of hydrogen atoms on the ylid carbon atom by chlorine or bromine occurs on reaction of *P*-fluoroylids with carbon tetrachloride or tetrabromide in ether at −10 to +20 °C. *C*-Halogen-substituted ylids (L) are used in the synthesis of 1,1-dihaloolefins.[57]



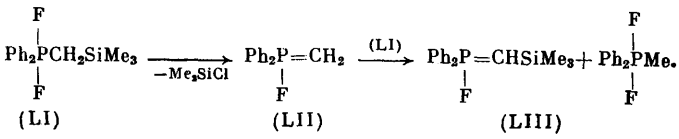
X = Br, Cl; R = Et, $C_5H_{10}N$.

The ability of *P*-halogenated ylids to react with carbon tetrachloride is appreciably reduced on introducing electron-accepting groups onto the ylid carbon atom thus reducing its nucleophilicity.[57]

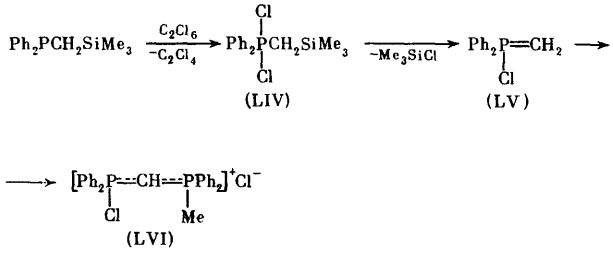
3. Synthesis of *P*-halogenated ylids from halophosphoranes

A comparatively simple method of obtaining *P*-halogenated ylids is the elimination of X—Hal (X = H, Hal, Me_3Si) from halophosphoranes or halophosphonium salts.[44–47]

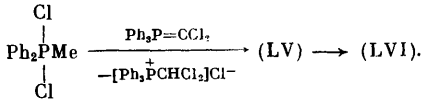
Difluorotrimethylsilylphosphorane (LI) eliminates fluorotrimethylsilane at room temperature with the formation of *P*-fluoroylid (LII) which enters into a transylidation reaction with difluorophosphorane (LI) being converted into *C*-silicon-substituted *P*-fluoroylid (LIII).[64]



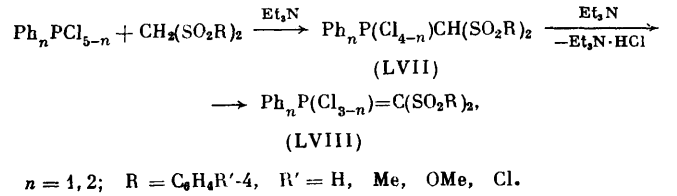
The dichlorophosphorane (LIV) formed from the reaction of diphenyltrimethylsilylmethylphosphine with hexachloroethane is converted into ylid-phosphonium salt (LVI). It is proposed that elimination of chlorotrimethylsilane from the dichlorophosphorane (LIV) gives *P*-chloroylid (LV) which dimerises and forms salt (LVI).[65] The difference in behaviour of *P*-chloro- and *P*-fluoroylids (LII) and (LV) is seemingly explained by the instability of the *P*-chloroylid.[65]



The dimerisation of ylid (LV) resulting on dehydrochlorination of dichloromethyldiphenylphosphorane with triphenylphosphonium-dichloromethylylid proceeds in a similar manner.[66]

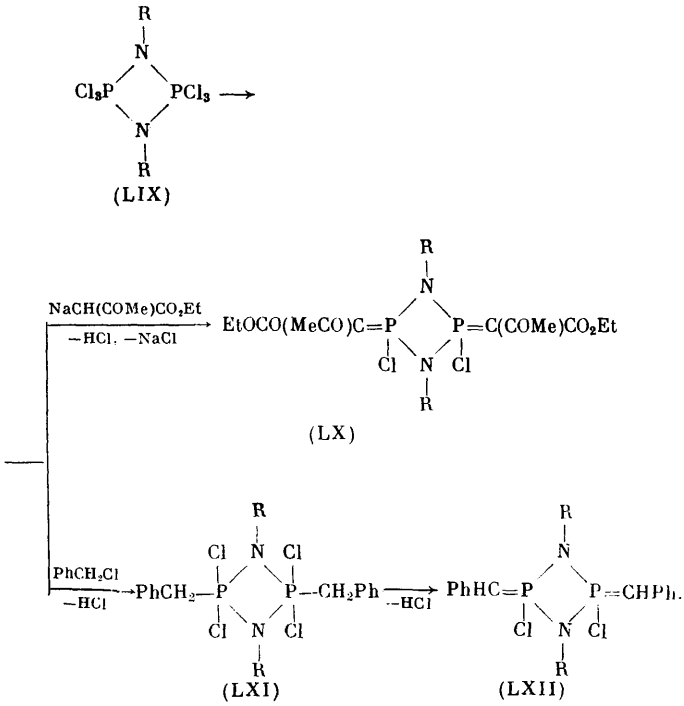


Polychlorophosphoranes react with bis-(arylsulphonyl)methanes in the presence of triethylamine through the formation of phosphonium salts (LVII) to give *P*-chloroylids with one or two chlorine atoms on phosphorus (LVIII).[67,68]

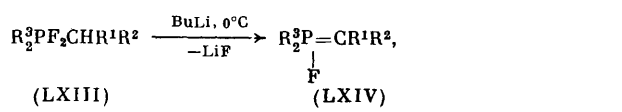


$n = 1, 2$; $R = C_6H_4R'$-4, $R' = H$, Me, OMe, Cl.

The reaction of dimers of trichlorophosphazo compounds (LIX) with sodio acetoacetic ester in boiling benzene as reported by Salman and co-workers proceeds with separation of hydrogen chloride and gives *P*-chloroylids with exocyclic P=C bonds (LX) in 4–56% yield. In precisely the same way the *P*-chloroylids (LXII) are formed in 12–48% yield on extended boiling in benzene of compounds (LIX) with an exess of benzyl chloride, hydrogen chloride being eliminated. It was proposed that phosphonium salts (LXI) are formed initially, which spontaneously eliminate hydrogen chloride, and are converted into *P*-chloroylids (LXII). The formation of ylids in the presence of HCl is remarkable, since these compounds are strong bases readily adding and firmly retaining hydrogen chloride.[69]



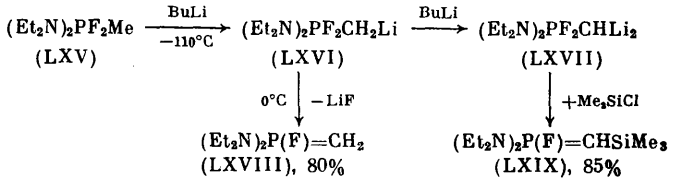
In several cases dihalophosphoranes were not converted into *P*-halogenated ylids on treatment with organometallic compounds. The main obstacle to successfully obtaining *P*-halogenated ylids in this way is the competing substitution of the halogen at phosphorus by an alkyl group. Nonetheless dehydrohalogenation of difluorophosphoranes (LXIII) with butyllithium or lithium hexamethyldisilazane proceeded quite smoothly and enabled the preparation of *P*-fluoroylids (LXIV) containing various substituents R^1, R^2 and R^3 on the phosphorus and carbon atoms of the P=C bond. To achieve high yields of *P*-fluoroylids (LXIV) it was necessary to carry out the reaction in ether at 0 °C, since a reduction of temperature down to −60 to −80 °C strongly reduced the yields and purity of the compounds.[64,70]



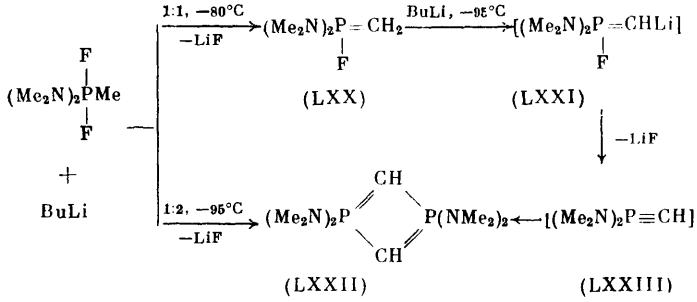
R^1, R^2 = H, Me, n-Pr, iso-Pr; R^3 = t-Bu, Et_2N.

Reaction of the difluorophosphorane (LXV) with butyllithium gives the *C*-substituted difluorophosphorane (LXVI) which eliminates lithium fluoride at −20 to 0 °C but is stable at lower temperatures. At −60 °C and below, compound (LXVI) is readily

metallated by a second molecule of butyllithium with the formation of the dilithio-substituted difluorophosphorane (LXVII). On reaction of the difluorophosphorane with one equivalent of butyllithium a mixture is formed of mono- and dilithio-substituted difluorophosphoranes (LXVI) and (LXVII). In addition a portion of the difluorophosphorane (LXV) remains unreacted and after elimination of lithium fluoride leads to a complex mixture of final reaction products. On reacting difluorophosphorane (LXV) with two equivalents of chlorotrimethylsilane the *C*-silylated *P*-fluoroylid (LXIX) is obtained in high yield.[64]



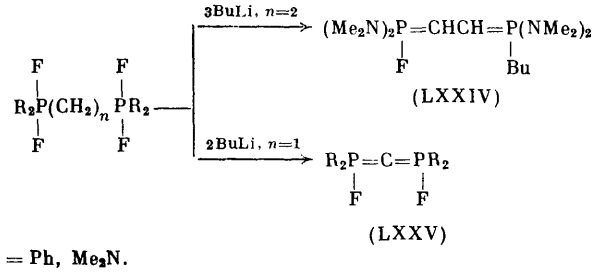
At a reactant ratio of 1:1 butyllithium dehydrofluorinates bis-(dimethylamino)methyldifluorophosphorane in pentane at −80 °C giving the *P*-fluoroylid (LXX) in 61.2% yield,[71,72] while on reacting the difluorophosphorane with two equivalents of butyllithium in pentane at −95 °C the diphosphacyclobutadiene (LXXII) is formed.[6,73,74]



It is proposed that butyllithium metallates the ylid carbon atom of the *P*-fluoroylid (LXX) with formation of compound (LXXI) which eliminates lithium fluoride and is converted into the phospha-acetylene (LXXIII). Dimerisation of the phospha-acetylene gives the diphosphacyclobutadiene.[72] It should be noted however that exchange of a hydrogen atom on the α-carbon of the P=C bond by lithium is achieved with great difficulty even at +20 °C or on heating. This is even less probable at −90 °C. The constitution of the diphosphacyclobutadiene was confirmed by X-ray structural analysis which showed particularly the planar structure of the cyclic portion of the molecule with completely uniform P−C bonds, the length of which were 172.5 pm.[72]

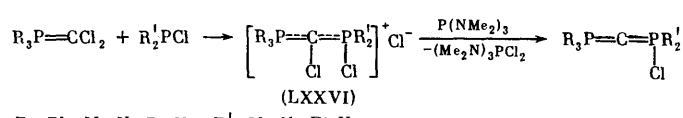
Diphosphacyclobutadiene (LXXII) is a reactive compound and readily participates in various cycloaddition reactions.[75−78]

The reaction of bis-(difluorophosphoranyl)ethane with butyllithium proceeds with dehydrofluorination of one difluorophosphorane group and replacement of a fluorine atom by a butyl group at the other, as a result of which the bis-ylid (LXXIV) is formed in good yield.[79] At the same time carbodiphosphoranes (LXXV) are obtained on reaction of bis-(difluorophosphoranyl)methane with butyllithium, the structure of which was shown by X-ray structural analysis.[80,81]



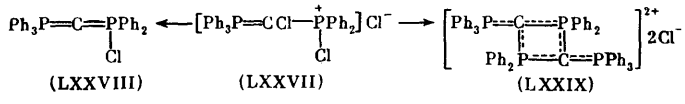
R = Ph, Me_2N.

Phosphoric acid triamides, possessing high dehalogenating ability, were used with success for converting halogenalkylphosphonium salts into *P*-halogenated ylids. For example, the dechlorination of the phosphonium salts (LXXVI) with tris-(dimethylamino)phosphine in dichloromethane at room temperature gives carbodiphosphoranes in high yield.[82]

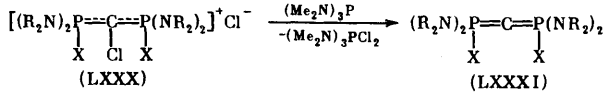


R = Ph, Me_2N, Et_2N ; R' = Me_2N, Et_2N.

The initial reaction conditions influence its course. Appel and co-workers established that the dechlorination of the salt (LXXVII) with tris-(dimethylamino)phosphine in toluene at −78 °C gives the chloropentaphenylcarbodiphosphorane (LXXVIII),[83] while in dichloromethane at room temperature the dimer of product (LXXVIII), viz. diphosphacyclobutadiene, is formed.[84] The structure of dimer (LXXIX) was established by X-ray structural analysis. Compound (LXXIX) contains a centrosymmetric cation with uniform endocyclic and exocyclic P−C bonds because all four phosphorus atoms participate in the delocalisation of the negative charge of the ylid carbon atom.[85]

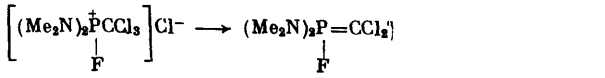


Symmetrical *P*-halogen-substituted carbodiphosphoranes (LXXX) were obtained by the dechlorination of the halogenophosphonium salts (LXXXI) and tris-(dimethylamino)phosphine.[86−88]



R = Me, X = F; R = Me, Et, n-Pr, X = Cl.

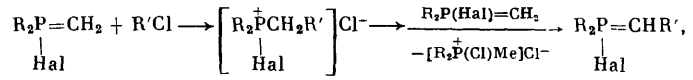
The dehalogenation of trichloromethylphosphonium salts with tris-(dimethylamino)phosphine gives *P*-halogenated ylids, containing a dichloromethylene group, in good yield.[47]



4. Other methos of synthesising *P*-halogenated ylids

Hydrogen atoms and trimethylsilyl groups on the α-carbon atom of *P*-halogenated ylids are distinguished by a high lability and are readily replaced by various groups on interaction with electrophiles. Consequently reactions of *P*-halogenated ylids, having hydrogen or silicon on the α-carbon atom, with various chlorine-containing electrophiles is a convenient means of obtaining new *C*-substituted *P*-halogenated ylids of more complex structure than the starting materials.

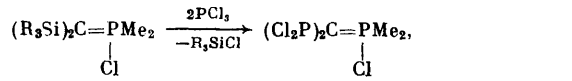
The reaction of *P*-chloro- and *P*-fluoroylids with chlorotrimethylsilane and with acid chlorides of carboxylic, carbonic and phosphoric acids proceeds readily. Intermediate phosphonium salts (LXXXII) substituted at the α-carbon atom are formed in this way, the dehydrochlorination of which with a second molecule of the starting ylid gives new *P*-halogenated ylids (LXXXIII).[2,9] Dehydrochlorination of the phosphonium salt (LXXXII) occurs more readily the greater the electron-accepting ability of the group R′. Yields of *P*-halogenated ylids (LXXXII) containing trimethylsily, acyl, alkoxycarbonyl or phosphino groups at the α-carbon atom are between 50–85%.[9,34,71,89]



(LXXXII) (LXXXIII)

Hal = Cl, F; R′ = Me_3Si, $R_2''P$, R″C(O), AlkOCO.

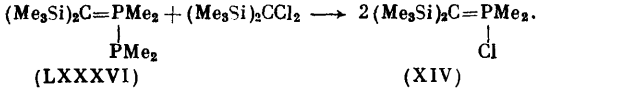
On reacting ylids (LXXXIV) with phosphorus trichloride in benzene at room temperature the Si–C bond is readily broken and *P*-chloroylids with two dichlorophosphine groups on the phosphorus atom (LXXXV) are formed in good yield.[90]



(LXXXIV) (LXXXV)

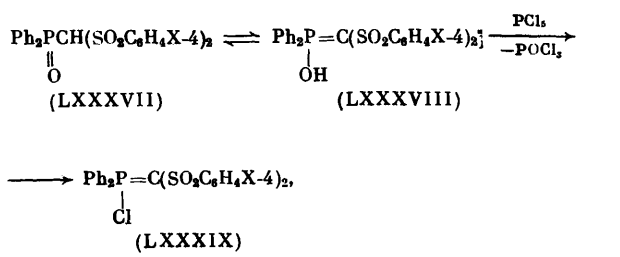
R_3Si = Cl_3Si, $Cl_2Si(CH_2SiCl_2)_2C$, $Me_2Si(CH_2SiMe_3)_2C$.

The ylid (LXXXVI) containing a very labile P–P bond is converted in good yield into the *P*-chloroylid (XIV) on reaction with dichloro-bis(trimethylsilyl)methane.[19]



(LXXXVI) (XIV)

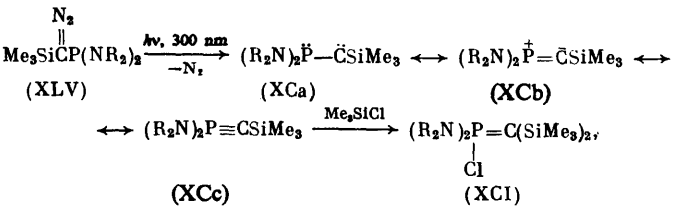
Ylids with OH groups on phosphorus (LXXXVIII), which are prototropic isomers of bis-(arylsulphonyl)methylphosphine oxides (LXXXVII), form *P*-chloroylids (LXXXIX) on boiling with phosphorus pentachloride in benzene.[68]



(LXXXVII) (LXXXVIII) (LXXXIX)

X = H, Me, OMe, Cl.

It has been reported that photolysis of phosphinodiazomethane (XLV) in benzene solution at room temperature in the presence of an excess of chlorotrimethylsilane gives the *P*-chloroylid (XCI) in almost quantitative yield.[91–94]

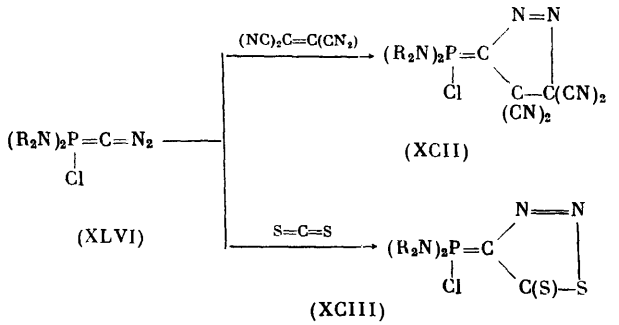


(XLV) (XCa) (XCb) (XCc) (XCI)

R = iso-Pr.

The carbene (XCa) is formed on photolysis of phosphinodiazomethane and has a certain degree of 'phospha-acetylene' character as a result of the contribution of resonance structures to the ground state of the molecule. The presence of an electron-rich trivalent phosphorus atom on the electron-deficient carbon atom determines the displacement of the lone pair of electrons on the phosphorus atom towards the carbon atom with addition of its electrons to the octet and formation of the dipolar structure (XCb), which makes the 1,2-addition of trimethylchlorosilane possible. Recently Bertrand and co-workers succeeded in obtaining the phosphinocarbene (XC) in stable form by flash photolysis of the phosphinodiazomethane (XLV) at 250 °C in vacuum and purified it by vacuum distillation [b.p. 75–80 °C (0.01 mmHg)].[94,95] According to its NMR spectrum the phosphinocarbene (XCI) partially possesses the structure of a phosphorovinyl-ylid and consequently enters into the various addition and cycloaddition reactions typical of a multiple bond. A characteristic is the low field ^{13}C chemical shift, δ_C 142.754 p.p.m., a doublet with $^1J_{CP}$ 159.3 Hz belonging to a two-coordinated carbon atom.

The phosphacumulene-ylid (XLVI) reacts with tetracyanoethylene and also with carbon disulphide forming *P*-chloroylids (XCII) and (XCIII) in quantitative yield. These are products of [2+2]-cycloaddition at the diazo group.[61,62]

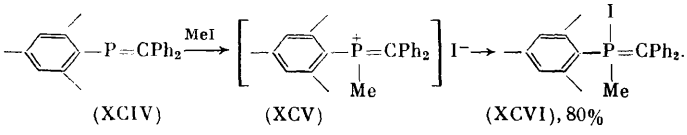


(XLVI) (XCII) (XCIII)

R = iso-Pr.

Bickelhaupt and co-workers have shown that phospha-ethylene (XCIV) is converted into β-iodoylid (XCVI) in 80% yield on heating with an excess of methyl iodide in the dark. The reaction occurs by 1,1-addition of methyl iodide to the phosphorus atom. They

proposed that the phosphoniumalkene (XCV) is formed by nucleophilic attack of methyl iodide at the two-coordinated phosphorus atom and is then converted into the ylid (XCVI).[96]



(XCIV) (XCV) (XCVI), 80%

III. Physical and spectral properties

P-Halogenated ylids are crystalline substances or liquids. The majority of *P*-halogenated ylids are colourless and only some of them are coloured. For example, fluorenylids are intensely red and diphenylmethylids are an orange colour.[34]

The stability of *P*-halogenated ylids to heat depends on their structure. The most stable *P*-halogenated ylids store well in an inert atmosphere and are distillable in vacuum without decomposition. The less stable *P*-chloroylids can be distilled in vacuum in many cases and store well in an inert atmosphere at 0 °C. The still less stable *P*-bromoylids are successfully isolated and purified only in those cases when they contain electron-accepting groups at the α-carbon atom. The *P*-iodoylids are unstable compounds. Possibly for this reason only one stable *P*-iodoylid (XCV) is known which has been isolated and identified.[96] The stability of *P*-halogenated ylids is increased with increasing electron-accepting properties of the substituents at the α-carbon atom, reducing the negative charge centred on this atom, and also by introducing bulky substituents (e.g. t-butyl, isopropyl, diisopropylamino groups, etc.) at the phosphorus and carbon atoms, creating steric hindrance. Such substituents screen the P=C bond and hinder nucleophilic attack of the ylid carbon atom onto the positively charged phosphorus atom.

The structure of *P*-halogenated ylids has been investigated in detail by various spectroscopic methods including IR, UV, ^{1}H, ^{13}C, ^{31}P, and ^{19}F NMR and also by X-ray structural analysis.[18,19,72,80,85]

The ^{31}P chemical shifts for *P*-halogenated ylids are very close to the δ_P values of the corresponding phosphonium salts and depend on the substituents at phosphorus (to a larger degree) and carbon (to a lesser degree), viz. δ_P 50–70 (R = Alk_2N), 40–60 (R = Me), 90–100 (R = iso-Pr), 95–110 (R = t-Bu), 55 (R = Ph), 60 p.p.m. (R = AlkO). Signals of phosphorus nuclei of *P*-halogenated ylids are doublets, $^{1}J_{PF}$ 1000–1100 Hz.

The ^{13}C chemical shifts of the P=C carbon atom are in the region of δ_C 20–80 p.p.m. and are doublets with large values of the $^{1}J_{CP}$ constant of 150–200 Hz, which is in agreement with the carbanion character of the ylid carbon atom.

X-Ray structural analysis shows the effective delocalisation of the negative charge of the ylid carbon atom of *P*-halogenated ylids with atoms or groups of atoms added to it. The ylid portion of the majority of molecules studied has a planar structure. For example, in the molecule of (LXXV) the N–P–C–P–N bond system lies in one plane and the C–P–C angle is 134.8°.[80] The lengths of phosphorus–carbon multiple bonds of *P*-halogenated ylids are shortened.

IV. Chemical properties

P-Halogenated ylids are highly reactive entering into numerous conversions. The chemical properties of *P*-halogenated ylids are very unusual due to the presence in the molecule of a highly polar P=C bond and a labile halogen atom. Characteristic reactions for *P*-halogenated ylids occur with carbonyl compounds, proceeding with retention of the phosphorus–carbon bond, chlorotropic rearrangements in the P–C diad, conversions with reduction in the phosphorus coordination number and several other properties not met in the case of triphenylphosphonium ylids.

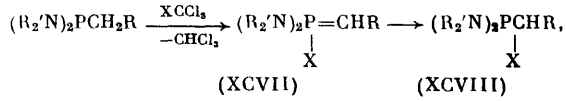
1. Conversions of *P*-halogenated ylids proceeding with a reduction in the phosphorus coordination number

A significant negative charge is centered on the α-carbon atom of *P*-halogenated ylids weakening the P–Hal bond. Consequently transition of a tetracoordinated into a tricoordinated phosphorus atom, which is extremely rare in organophosphorus chemistry, becomes possible.

a) Halogenotropy in the P–C diad

Halogen atoms in the P–C diad are capable of migrating between the phosphorus and carbon atoms as a result of which the interconversion of *P*-halogenated ylids and α-haloalkylphosphines may be effected. Various examples were shown in section II of conversions of α-haloalkylphosphines into *P*-halogenated ylids which were accompanied by the transition of three-coordinated into four-coordinated phosphorus and, as is known, give a significant energy gain.[97] It must be borne in mind that in this the electrically neutral four-coordinated α-carbon atom is converted into a negatively charged three-coordinate ylid carbon atom. But such a transition is one the other hand energetically unprofitable. Consequently changes in energies of coordination transitions of phosphorus and carbon atoms are mutually counterbalanced by one another. Therefore by varying the substituents on the phosphorus and carbon atoms of the P–C diad it is possible to influence the thermodynamic stability of the halogenotropic isomers and to create conditions for 1,2(C→P)- or 1,2(P→C)-migrations of halogen atoms.

1,2(P→C)-Chlorotropic rearrangements have been detected in the case of *P*-chloroylids containing diisopropylamino groups on the phosphorus atom. Bis-diisopropylamides of alkylphosphonous acids react with carbon tetrachloride with the formation of *P*-chloroylids (XCVII) stable in solution below 0 °C, which were observed by ^{13}C and ^{31}P NMR spectra. Above 0 °C, ylids (XCVII) are converted quantitatively into α-chloroalkylphosphines (XCVIII).[57,99] The reaction of bis-(diisopropylamino)alkylphosphines with bromotrichloromethane proceeds analogously. The resulting *P*-bromoylids (XCVII) are converted into the α-bromoalkylphosphines (XCVIII) significantly more rapidly than are the corresponding *P*-chloroylids. Nonetheless they were observed by ^{31}P NMR. α-Haloalkylphosphines (XCVIII) were isolated as crystalline substances in good yield.



(XCVII) (XCVIII)

X = Br, Cl; R = H, Me, n-Pr, iso-Pr, R′ = iso-Pr.

Bis-(diisopropylamino)methylphosphines with an excess of CCl_4 or $CBrCl_3$ in ether at 0 °C give *P*-halogenated ylids (XCIX) which readily rearrange into dihalomethylphosphines (C).[57]

$$(R_2N)_2PMe \xrightarrow[-CHCl_3]{XCCl_3} (R_2N)_2P(X)=CH_2 \xrightarrow[-CHCl_3]{XCCl_3} (R_2N)_2P(X)=CHX \longrightarrow$$

(XCIX)

$$\longrightarrow (R_2N)_2PCHX_2,$$

(C)

X = Br, Cl, R = iso-Pr.

Chlorotropic migrations (CI)⇄(CII) depend on the substituent at the carbon atom of the P–C diad in such a way that electron-accepting substituents (Ph, $SiMe_3$) favour a displacement of the chlorotropic equilibrium to the side of *P*-chloroylids (CI) but electron-donors (H, Me, n-Pr, iso-Pr) favour the side of chloroalkylphosphines (CII).[98–101]

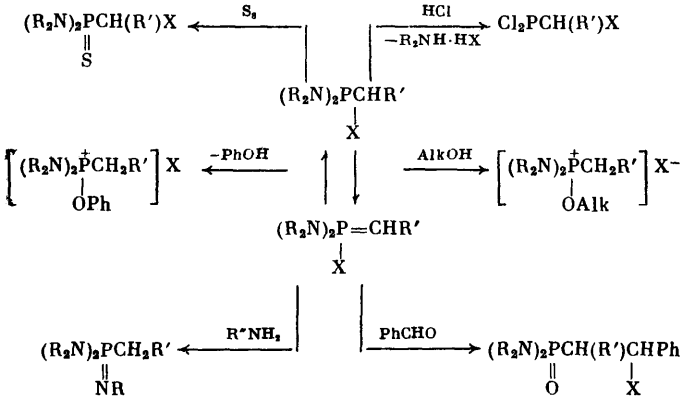
$$(R_2N)_2P(Cl)=CHR' \rightleftharpoons (R_2N)_2PCl(CHR')$$

(CI) (CII)

R = iso-Pr; R' = H, Me, n-Pr, iso-Pr, Cl, Br, Ph, $SiMe_3$.

The α-chloroalkylphosphines (CII) display chemical properties characteristic of both compounds of trivalent phosphorus and of *P*-halogenated ylids, as a result of which they are considered as 'masked' *P*-chloroylids.[58,98] The chemical properties of α-chloroalkylphosphines (CII) correspond to the existence of a reversible phosphorus–carbon diad chlorotropy (C)⇄(CII). As is shown in Scheme 6, the α-haloalkylphosphines (CI), being compounds of trivalent phosphorus, add sulphur with the formation of α-haloalkylthiophosphonic acid derivatives and are split at the P–N bond by hydrogen chloride giving acid chlorides of phosphonic acid.[58] Like *P*-halogenylids, the α-haloalkylphosphines (CI) add alcohols and phenols with the formation of R-oxyphosphonium salts, they react with primary alkylamines and aniline being converted into imidophosphonic acid derivatives and give 2-chloroalkylphosphonic acid derivatives on reaction with carbonyl compounds.[58,98,101]

Scheme 6



X = Br, Cl; R = iso-Pr; R' = H, Alk, Cl, Br.

Kinetic measurements, carried out with ^{31}P NMR, showed that the 1,2(P→C)-chlorotropic rearrangement obeyed a first order reaction rate equation exactly at various concentrations of *P*-chloroylid and at various temperatures. The rate constant for the rearrangement increased in proportion to the increase in ionising ability of the solvent: $CH_3CN > Cl_2CHCHCl_2 > CHCl_3 > CH_2Cl_2 \gg C_6H_6 > C_6H_{14}$. Based on the kinetic characteristics and on the activation parameters, it was established that the 1,2(P→C)-chlorotropic rearrangement proceeds through the formation of phosphonium cation (CIII) resulting from dissociation of the ylid at the P–Cl bond. Stabilisation of the phosphonium cation was achieved by effective delocalisation of the positive charge by branched diisopropylamino groups.[58,100]

$$(R_2N)_2P(Cl)=CHR \longrightarrow [R_2N)_2P^+=CHR\ Cl^-] \longrightarrow (R_2N)_2PCl(CHR),$$

(CIII)

R = iso-Pr.

Kinetic investigations of the reverse 1,2(C→P)-chlorotropic rearrangement have been carried out using the chloromethylphosphine (CIV) as an example.

$$t\text{-}Bu(R_2N)PCH_2Cl \rightarrow t\text{-}Bu(R_2N)P(Cl)=CH_2$$

(CIV) (CV)

R = n-Bu.

Compound (CIV) is stable in nonpolar solvents (diethyl ether, hexane) however it is readily converted into ylid (CV) in dissociating solvents of the type of acetonitrile > tetrachloroethane > chloroform > dichloromethane. Kinetic investigations showed that the 1,2(C→P)-chlorotropic rearrangement of (CIV)→(CV), just like the 1,2(P→C)-chlorotropic rearrangement, obeyed a first order reaction rate equation. Analysis of the activation parameters for the rearrangement (E_a 77 kJ mol^{-1} and $\Delta S^{\neq}$ −67 kJ K mol^{-1}, at 30 °C in benzene + 15% chloroform) and the dependence of the rate constants on the dissociating ability of the solvent enabled a conclusion to be drawn on the decisive effect of solvolysis on the rearrangement, under the influence of which there was heterolytic fission of the C–Cl bond of chloromethylphosphine (Scheme 7).

Scheme 7

$$(R_2PCH_2Cl)_{solv} \rightleftharpoons (R_2PCH_2^+Cl^-)_{solv} \rightleftharpoons \left(R_2\overset{+}{P}=CH_2\ Cl^-\right)_{solv} \rightleftharpoons \left(R_2P(Cl)=CH_2\right)_{solv}$$

The values of the main kinetic characteristics and activation parameters for the 1,2(P→C)- and 1,2(C→P)-chlorotropic rearrangements proceeding through the same phosphonium intermediates and having a reversible character, were very close.

Dissociation of chloromethylphosphines at the C–Cl bond with the formation of phosphonium chlorides recalls the behaviour of chloromethylamines, existing in the ionised state as iminium

chlorides,[102] with the only difference that chloromethylphosphines are not as strongly ionised as chloromethylamines.

$$R_2NCH_2Cl \rightleftharpoons [R_2N{=}CH_2]Cl^-,$$

$$R_2PCH_2Cl \rightleftharpoons [R_2\overset{+}{P}{=}CH_2]Cl^-.$$

The formation of phosphinium salts from *P*-halogenated ylids is confirmed by various experimental data. *P*-Chloroylids (CVI) containing an alkoxy group on the α-carbon atom as a result of a 1,2(P→C)-migration of chlorine rearrange to α-chloroalkylphosphines or are converted into acylphosphines with loss of alkyl chloride. The structure of ylids (CVI) existing in solution below 0 °C was demonstrated by NMR and by chemical methods.[8,103]

$$(t\text{-Bu})_2PCH(R)OAlk \xrightarrow[-CHCl_3]{CCl_4} (t\text{-Bu})_2P(Cl){=}C(R)OAlk \rightarrow$$

(CVI)

$$\rightarrow \begin{cases} \xrightarrow{R=H} (t\text{-Bu})_2PCH(Cl)OAlk \\ \xrightarrow{R=Ph} (t\text{-Bu})_2PC(=O)Ph \end{cases}$$

Conjugation of the free electron pairs of oxygen with the P=C multiple bond stimulates fission of chloride ion and favours the formation of an intermediate phosphinium cation (CVII) which, depending on attack by chloride ion on the α-carbon or on the alkoxy group, is converted into an α-chloroalkylphosphine or eliminates alkyl chloride with the formation of acylphosphine. The formation of the cation is facilitated by effective delocalisation of the positive charge in the P–C–O triad.[8]

$$R_2P(Cl){=}C(R')-OAlk \longrightarrow \left[R_2\overset{+}{P}{=}C(R')-OAlk \leftrightarrow R_2P-C(R'){=}\overset{+}{O}Alk \right] Cl^-$$

(CVII)

b) Conversion into compounds of three-coordinate pentavalent phosphorus and two-coordinate phosphorus

Precisely the same as ylids with alkoxy groups (CVI) the *P*-chloroylids (CVIII) containing a dialkylamino group at the α-carbon atom are ionised with fission of the P–Cl bond. However in this case, as a result of more effective delocalisation of the positive charge in the P–C–N triad, stable phosphonium cations (CIX) are formed and were isolated as crystalline compounds.[104]

$$(t\text{-Bu})_2PCH_2NAlk_2 \xrightarrow[-CHCl_3]{CCl_4} (t\text{-Bu})_2P(Cl){=}CHNAlk_2 \rightarrow (t\text{-Bu})_2\overset{+}{P}{=}CH-NAlk_2\ Cl^-$$

(CVIII) (CIX)

Alk = Me, Et.

Compounds (CIX) are very soluble in polar and with difficulty in nonpolar solvents. They readily exchange chloride anion for perchlorate anion on reaction with sodium perchlorate in aqueous solution. The structure of phosphonium cations (CIX) was confirmed by the NMR spectroscopy. The values δ_P 21 p.p.m. corresponds to a three-coordinate phosphorus atom, and δ_C 207 p.p.m., a doublet with $^1J_{CP}$ 14 Hz to a sp^2-hybridised carbon atom on phosphorus. The δ_H signal at 10.5 p.p.m., a doublet with $^1J_{HP}$ 3 Hz, belongs to a proton on carbon in a P=C group.[8]

The synthesis of another phosphonium cation (CX) has been reported recently.[95]

$$\underset{(XC)}{(R_2N)_2\overset{+}{P}{=}\overline{C}SiMe_3} \xrightarrow{CF_3SO_2OSiMe_3} \underset{(CX)}{[(R_2N)_2\overset{+}{P}{=}C(SiMe_3)_2]CF_3SO_3^-},$$

R = iso-Pr.

On adding an excess of trimethylsilyl triflate to an ethereal solution of the carbene (XC) a salt-like product (CX) was isolated as a yellow crystalline substance. The ^{31}P chemical shift δ_P 76.5 p.p.m., a doublet with $^1J_{CP}$ 87.6 Hz, is in agreement with the proposed structure. The structure of the phosphinium cation (CX) was confirmed by X-ray structural analysis.

Various types of cations of three-coordinate pentavalent phosphorus are known which are obtained by the action of aluminium chloride on the acid chlorides of oxo-, thiono-, seleno- and iminophosphoric acids. Certain of them exist in the crystalline state as dimers as shown by X-ray structural analysis.[105]

$$Y_2P(Cl){=}X \xrightarrow{AlCl_3} [Y_2\overset{+}{P}{=}X]AlCl_4^- \rightleftharpoons \left[Y_2P\begin{smallmatrix} X \\ \diagup\diagdown \\ X \end{smallmatrix}PY_2 \right] AlCl_4^-,$$

Y = Cl, NMe_2, NEt_2; X = O, NR, CR_2, S, Se.

It is assumed that phosphinium cations are generated by fission of the P–Cl bond in *P*-chloroylids by aluminium chloride. However this idea, with the exception of a short communication,[106] has not yet been developed.

$$(R_2N)_2P(Cl){=}CHSiMe_3 \xrightarrow{AlCl_3} [(R_2N)_2PCH(SiMe_3)]^+AlCl_4^-,$$

R = iso-Pr.

Appel obtained bis-(methylene)phosphoranes by dehalogenation of *P*-chloroylid (CXI) with a lithio-organic compound. These are compounds of three-coordinate pentavalent phosphorus containing two P=C multiple bonds. Bis-(methylene)phosphoranes (CXII) are stable compounds which enables their purification by crystallisation from inert solvents or by vacuum distillation.[107,108]

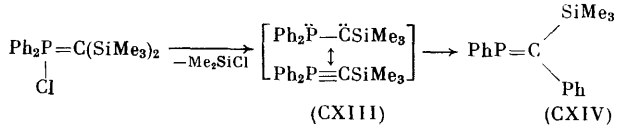
$$RPCl_2 \xrightarrow{LiCCl(SiMe_3)_2} RP[CCl(SiMe_3)_2]_2 \longrightarrow \underset{(CXI)}{RP(Cl)(Cl){=}C(SiMe_3)_2} \longrightarrow$$

$$\xrightarrow{LiCCl(SiMe_3)_2} \underset{(CXII)}{RP{=}C(SiMe_3)_2}$$

R = Alk, Ph, AlkO, AlkS, Alk_2N.

Conversions of *P*-chloroylids are also known which occur with reduction of the phosphorus coordination number to two. Thermolysis of a *P*-chloroylid containing two trimethylsilyl groups

on the α-carbon led to the formation of the phospha-alkene (CXIV). It was proposed that elimination of trimethylchlorosilane from the *P*-chloroylid initially gave a compound of three-coordinate pentavalent phosphorus, viz. the phospha-acetylene (CXIII), which was converted into a compound of two-coordinate phosphorus (CXIV) by migration of a phenyl group to the α-carbon atom (by a type of Curtius rearrangement).[5]



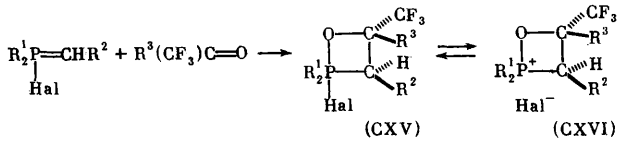
(CXIII) (CXIV)

2. Reactions of *P*-halogenated ylids with carbonyl compounds

The reactions of *P*-halogenated ylids with carbonyl compounds are highly original. *P*-Halogenated ylids react with carbonyl compounds 'anomalously' without fission of the phosphorus–carbon bond, which opens wide possibilities for the synthesis of every kind of phosphorus-containing alkene. In addition *P*-halogenylids form comparatively stable products by [2+2]-cycloaddition of the C=O group to the P = C$^-$ bond.

a) [2+2]-Cycloaddition reactions

P-Chloro- and *P*-bromoylids with ketones containing a trifluoromethyl group with the formation of stable [2+2]-cycloaddition products, 2-chloro- or 2-bromo-1,2λ^5-oxaphosphetanes (CXV) which were isolated in yields close to quantitative as crystalline substances or as liquids distillable in vacuum.[8,42,109,110]



(CXV) (CXVI)

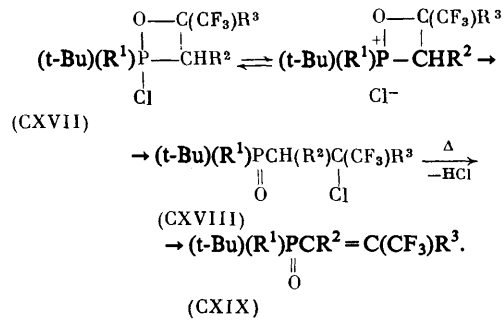
Hal = Br, Cl; R^1 = iso-Pr, t-Bu, Et$_2$N; R^2 = H, Me, Ph; R^3 = Ph, C$_6$H$_4$OMe-4, C$_6$H$_4$F-4.

The [2+2]-cycloaddition of *P*-halogenated ylids to ketones proceeds stereoselectively and leads predominantly to the formation of one of the possible diastereomers of 2-halooxaphosphetanes (CXV). It was established by NMR that the ratio of diastereoisomers of 2-halooxaphosphetanes containing asymmetric atoms at C(3) and C(4) was within the limits 95:5 to 90:10. If phosphorus is one of the asymmetric atoms in the molecule then the stereoselectivity of the reaction is low. The ratio of disastereomers after completion of the reaction was approximately 6:4. However on heating, as a result of permutational changes in the molecule, the ratio of diastereomers grew to a value of 95:5 in favour of the thermodynamically more stable diastereomer.[109,110]

2-Halo-1,2λ^5-oxaphosphetanes (CXV) dissociate in solution at the P–Hal bond with the formation of cyclic phosphonium salts (CXVI), as a result of which an equilibrium is established between the forms (CXV) ⇄ (CXVI) with five- and four-coordinate phosphorus atoms. Dissociation of 2-halooxaphosphetanes is enhanced with a reduction of the electron-accepting properties of substituents R^3 and also with a growth in solvent polarity.[110]

The stability of 2-halooxaphosphetanes changes in the same sequence of substituents R^3 at the endocyclic carbon atoms at position 4. The most stable are compounds, containing strong electron-accepting groups at C(4), drawing off electron density from the oxygen atom as a result of which the three-centre apical bond O–P–Hal is strengthened. 2-Chlorooxaphosphetanes (CXVII) containing two CF$_3$ groups at the α-carbon atom, are converted into vinylphosphonates (CXIX) with elimination of hydrogen chloride only at a temperature of 160–190 °C.[42,110]

2-Chloroxaphosphetanes, having less electron-accepting substituents at C(4), are dissociated to a large extent and correspondingly are converted into vinylphosphine oxide at a lower temperature. The 2-chlorooxaphosphatane (CXVII) (R^1 = t-Bu, R$_2$ = H, R^3 = C$_6$H$_4$OMe-*p*) is transformed quantitatively into the 2-chloroalkylphosphine oxide (CXVIII) at 20 °C in the course of several days. On heating compound (CXVIII) elimination of hydrogen chloride was observed and the (*E*)-olefin (CXIX) was obtained in high yield.[42]



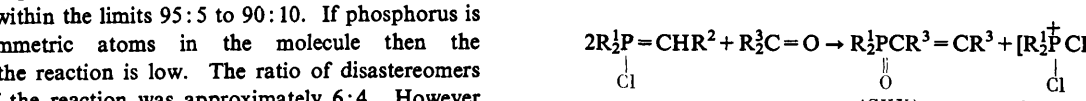
(CXVII) (CXVIII) (CXIX)

2-Bromooxaphosphetanes are more strongly dissociated at the phosphorus–halogen bond than 2-chlorooxaphosphetanes and consequently are less stable. Usually they are gradually converted at room temperature into vinylphosphine oxides.[110]

b) Synthesis of phosphorus-containing alkenes

P-Chloroylids are more reactive than triphenylphosphonium ylids. Unstabilised *P*-chloroylids (R^2 = H, Alk) are particularly reactive and react readily with alkyl- and arylaldehydes below 0 °C with the formation of various types of phosphorus-containing alkenes.[8]

The reaction of *P*-chloroylids with aldehydes or ketones proceeds at a ratio of starting materials of 2:1. In this one molecule of *P*-chloroylid is consumed in binding hydrogen chloride isolated in the reaction process, as a result of which a phosphonium salt (CXXI) is formed in addition to olefins (CXX) and is separated in solid form and is readily removed by filtration.[8,42]

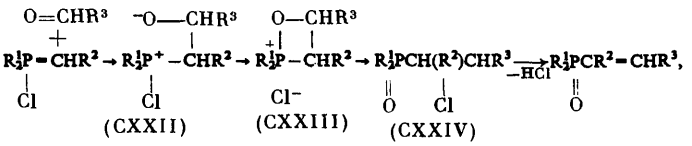


(CXX) (CXXI)

R^1 = Alk, Alk$_2$N; R^2 = H, Me, Ph; R$^3_2$C = Ph$_2$C, Ar(CF$_3$)C.

It was established by NMR spectroscopy at low temperature that *P*-chloroylids add aldehydes with the formation of zwitter-ions (CXXII), which are then converted into 2-chlorooxaphosphetanes (CXXIII). Compound (CXXIII) is strongly dissociated at the P–Cl bond and exists predominantly as cyclic phosphonium salt. They are stable in solution at −60 °C, but on increasing the temperature are

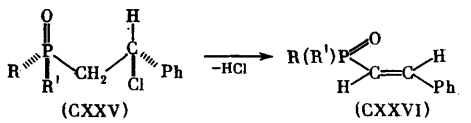
readily rearranged into 2-chloroalkylphosphine oxides (CXXIV). Compounds (CXXIV) are dehydrochlorinated by an excess of the initial *P*-chloroylid with the formation of vinylphosphine oxides.



(CXXII) (CXXIII) (CXXIV)

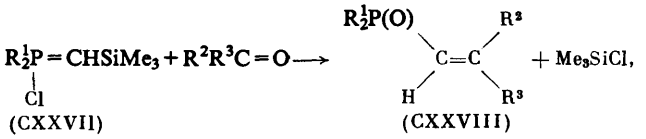
R^1 = Alk, Alk_2N; R^2 = H, Alk, Ph; R^3 = Alk, Ar.

In several cases the reaction of *P*-chloroylids with aldehydes occurs with the formation of 2-chloroalkylphosphine oxides (CXXIV) which are stable at room temperature and were purified by crystallisation from nonpolar solvents. On heating they lose hydrogen chloride and are converted in high yield into vinylphosphine oxides of (*E*)-configuration. 2-Chloroalkylphosphine oxides (CXXV) are usually obtained as *threo*-diastereomers and only in comparatively rare cases was a mixture of two diastereomers formed.[111] However elimination of HCl from these diastereomers occurs stereoselectively with the formation of only (*E*)-vinylphosphine oxides (CXXVI).



(CXXV) (CXXVI)

C-Silicon-containing *P*-chloroylids (CXXVII) react with aldehydes and ketones with elimination of chlorotrimethylsilane. The reaction proceeds at a ratio of initial reactants of 1:1 and gives vinylphosphine oxides (CXXVIII) in high yield.[112]

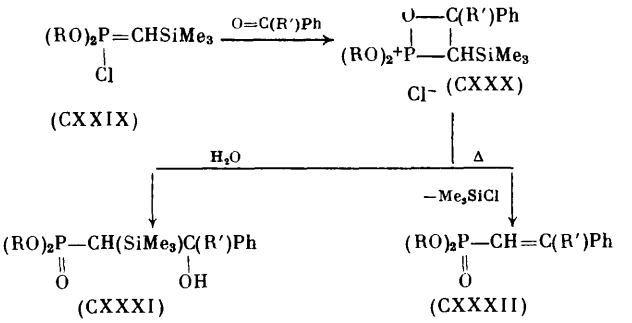


(CXXVII) (CXXVIII)

R^1 = Alk, AlkO, Alk_2N; R^2 = H, CF_3; R^3 = Alk, $C_6H_4R^4$-*p*; R^4 = H, OAlk, Cl, Br, CHO, CH=CHP(O)R_2.

Various aldehydes and ketones and dialdehydes react with *P*-chloroylids (CXXVII). On reacting *P*-chloroylids (CXXVII) with dialdehydes, one or two carbonyl groups were successfully 'olefinated' depending on the initial ratio of reactants. In all cases olefins of (*E*)-configuration were obtained with a high degree of stereoselectivity.[8,112]

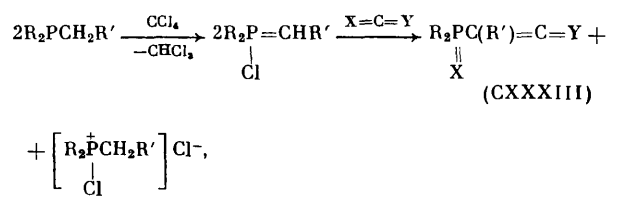
The cyclic phosphonium salts (CXXX) were obtained by reacting *P*-chloroylids (CXXIX) with aldehydes and ketones. Compounds (CXXX) were hydrolysed with the formation of 2-hydroxyalkylphosphine oxides (CXXXI) and on heating were converted into (*E*)-vinylphosphine oxides (CXXXII).[40]



(CXXIX) (CXXX) (CXXXI) (CXXXII)

R = Et, iso-Pr; R′ = H, CF_3.

There is significant preparative interest in the reaction of *P*-chloroylids with carbon dioxide, carbon disulphide and isocyanates leading to the formation of phosphorus-containing ketenes, thioketenes and ketenimines.[33,42] The reaction of *P*-chloroylids with CO_2, CS_2 and RNCO proceeds at an initial ratio of starting materials of 2:1 and leads to the formation of phosphorus-containing heterocumulenes and chlorophosphonium chlorides. Phosphorus-containing heterocumulenes (CXXXIII) are conveniently obtained preparatively by a 'one-pot' method without isolating *P*-chloroylids by sequentially treating tertiary alkylphosphines with CCl_4 initially and then with CO_2, CS_2 or RNCO.[9,33,42,113]

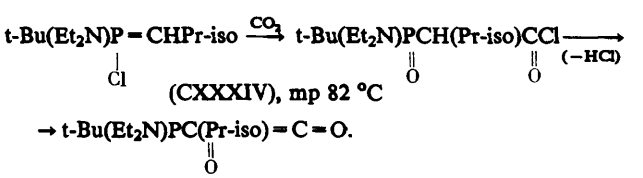


(CXXXIII)

X = O, S; Y = O, S, NPh; R = t-Bu, Et_2N; R′ = H, Me, n-Pr, iso-Pr.

The phosphorus-containing heterocumulenes (CXXXIII) are distinguished by high stability on storage and on vacuum distillation, which is explained by the steric and electronic influence of the phosphoryl grouping. For example, thioketenes are unchanged on storage for several years.

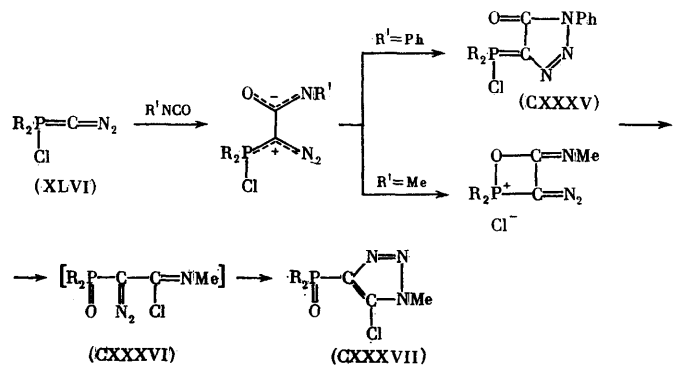
It was established that the reaction of *P*-chloroylids with CO_2 proceeds through the formation of acid chlorides (CXXXIV) of carboxylic acids which were isolated in a pure state and were then converted by the action of triethylamine into phosphorus-containing ketenes.[9]



(CXXXIV), mp 82 °C

Phosphorus-containing ketenes and thioketenes are very reactive and enter into a variety of addition and cycloaddition reactions.[113]

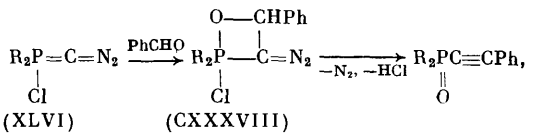
Phosphacumulene-ylids (XLVI) give addition products at the diazo group with isocyanates, the *P*-chloroylid (CXXXV) being formed with phenyl isocyanate and the triazenophosphonate (CXXXVI) with methyl isocyanate. It was proposed that initially nucleophilic attack of the ylid carbon atom on the carbonyl carbon gives a betaine, which depending on the relationship of the oxygen atom (or NR group) to nitrogen or phosphorus, is converted into products of 1,4- and 1,5-cyclisation. The unstable 1,4-cycloadduct is transformed initially into an α-diazoimine as a result of a 1,3-halogenotropic shift and then into the triazenophosphonate (CXXXVII).[61]



(XLVI) (CXXXV) (CXXXVI) (CXXXVII)

R = (iso-Pr)$_2$N.

Benzaldehyde gives the 2-chlorooxaphosphetane (CXXXVIII) with the ylid (XLVI) which readily eliminates hydrogen chloride and a molecule of nitrogen being converted into an acetylene phosphonate. This reaction is the first example of the direct formation of a carbon–carbon triple bond under the conditions of the Wittig reaction.[61]



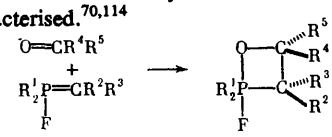
(XLVI) (CXXXVIII)

R = iso-Pr.

c) Reaction of *p*-fluoroylids with carbonyl compounds

P-Fluoroylids add carbonyl compounds with the formation of 2-fluoro-1,2λ^5-oxaphosphetanes (CXXXIX) which are distinguished by their higher stability compared with 2-chlorooxaphosphetanes. Usually 2-fluorooxaphosphetanes are successfully isolated without difficulty and are purified by vacuum distillation. The stability of 2-fluorooxaphosphetanes is explained by the higher electronegativity of the fluorine atom in comparison with the electronegativities of chlorine and bromine. Consequently the P–F bond of 2-fluorooxaphosphetanes is stable and they do not dissociate with the formation of cyclic phosphonium salts as do the 2-chlorooxaphosphetanes.[70]

Various stable products of [2+2]-cycloaddition of 2-fluoroylids with alkyl and aryl isocyanates, alkyl and aryl ketones, carbon dioxide and isocyanates have been synthesised and characterised.[70,114]

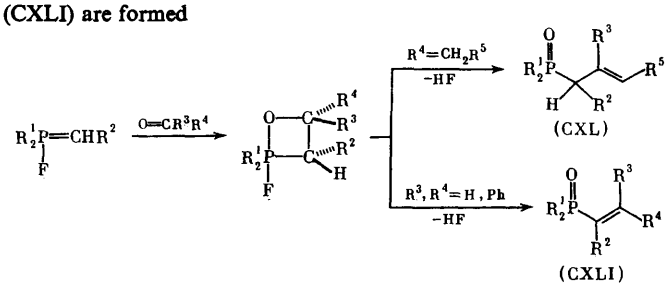


(CXXXIX)

R^1 = Alk, Ph, Alk$_2$N; CR^{2}R^3=CH$_2$, CHAlk, CAlk$_2$, CHPh, CHSiMe$_3$, CCl$_2$, CBr$_2$; CR^{4}R^5=C=O, C=NPh, CHAlk, CAlk$_2$, CHPh, CPh$_2$, CH$_2$CH=CR$_2$.

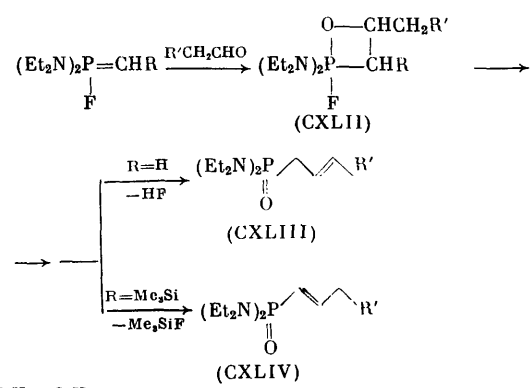
The reaction of *P*-fluoroylids with aldehydes and ketones is stereoselective and gives predominantly *threo*-diasteroisomers of 2-fluorooxaphosphetanes (CXXXIX),[64,70] the structure of which was demonstrated by spectroscopic methods. The content of *erythro*-diastereomers was small and did not exceed 5–10%.

On heating, 2-fluorooxaphosphetanes lost hydrogen fluoride and depending on structure were converted into allyl- or vinylphosphine oxides.[64,70,114,115] Allylphosphine oxides (CXL) are formed when there are hydrogen atoms on the carbon atom next to C(4) and a 1,4-elimination of HF can take place. If 1,4-elimination of HF cannot be effected because of structural features of the molecule than a 1,2-elimination of HF occurs and vinylphosphine oxides (CXLI) are formed



(CXL) (CXLI)

The reaction usually leads to the formation of isomers of allylphosphine oxides containing the maximum number of alkyl groups on the multiple C=C bond and is a convenient means of obtaining them. The route of the reaction may be guided in the direction of forming vinylphosphine oxides (CXLIV), which are isomers of the allylphosphine oxides (CXLIII), if a trimethylsilyl group is introduced at position C(3) of the oxaphosphetane ring. Silicon-containing 2-fluorooxaphosphetanes (CXLII) are obtained by the reaction of *C*-silyl-substituted *P*-fluoroylids with aldehydes. 1,2-Elimination of Me$_3$Si from fluorooxaphosphetanes (CXLII) proceeds with the formation of stereochemically pure (*E*)-vinylphosphine oxides (CXLIV).[64,114]

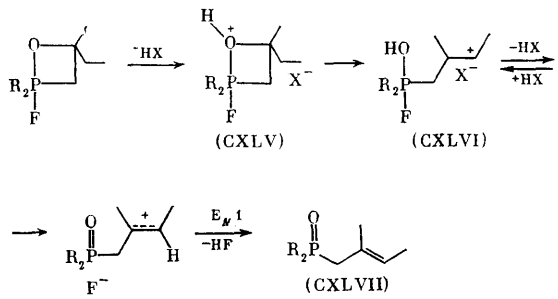


(CXLII) (CXLIII) (CXLIV)

R = C$_6$H$_{11}$, C$_6$H$_{13}$.

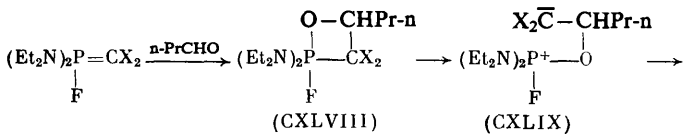
Lewis and Brønsted acids actively catalyse the conversion of 2-fluorooxaphosphetanes into allylphosphine oxides. In addition the reaction is autocatalytic since the hydrogen fluoride eliminated catalyses the transition of 2-fluorooxaphosphetanes into allylphosphine oxides.[114] Acids protonate the oxygen atom of 2-fluorooxaphosphetanes with the formation of oxonium salts (CXLV), which readily convert into carbenium intermediates (CXLVI), the deprotonation of which under E_N 1 elimination conditions gives allylphohphine oxides (CXLVII) (Scheme 8). The formation of carbenium intermediates (CXLVI) was shown by chemical methods.[64,115]

Scheme 8



(CXLV) (CXLVI) (CXLVII)

P-Halogenated ylids react with carbonyl compounds with the formation of phosphorus-containing alkenes as a rule. There is a single exception. 2-Fluorooxaphosphetanes (CXLVIII), containing chlorine or bromine atoms at C(3), decompose on heating with fission of the P–C bond and the formation of 1,1-diahloalkenes and fluorophosphine oxides. It is proposed that the electronegative halogen atoms favour transfer of the CX_2 group to an axial position as a result of which the phosphorus–carbon bond is broken and anion (CXLIX) is formed.[63,64]



(CXLVIII) (CXLIX)

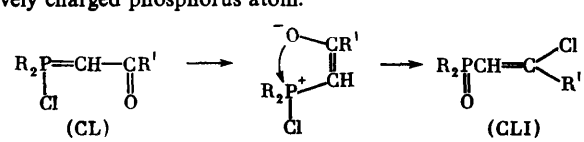
→ $X_2C{=}CHPr\text{-}n + (Et_2N)_2P(O)F$,

X = Br, Cl.

3. Conversions of *P*-halogenated ylids, containing C=O groups on the α-carbon

Conversions accompanied by transfer of the carbonyl oxygen to the phosphorus atom are characteristic of *P*-chloro- and *P*-bromoylids containing a carbonyl group at the α-carbon.

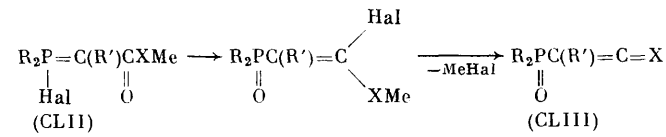
P-Chloroylids (CL) in which there is an acyl group at the α-carbon rearrange on heating into β-chlorovinylphosphine oxides (CLI). The rearrange-ments are effective intramolecularly by attack of the negatively charged oxygen atom of the C=O group on the positively charged phosphorus atom.[116]



(CL) (CLI)

R = t-Bu, Alk_2N; R′ = Alk.

The conversion of *P*-halogenated ylids (CLII) containing an alkoxycarbonyl group at the α-carbon proceeds by an analogous reaction scheme. They are converted at room temperature or on gentle heating into phosphorylated ketenes with separation of alkyl halide.[39,41,117] *P*-Bromoylids (CLII) with a dimethylaminocarbonyl group at the α-carbon are more stable. However they also split off methyl bromide on heating to 100 °C and phosphorus-containing ketenimines are formed in good yield.[116]



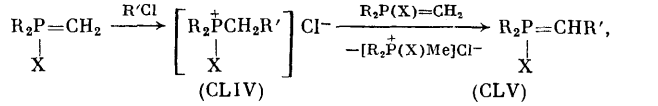
(CLII) (CLIII)

Hal = Br, Cl; X = O, NMe; R = iso-Pr, t-Bu, EtO, iso-PrO, Me_2N, Et_2N; R′ = Ph, CO_2Me.

4. Reactions of *P*-chloroylids with electrophiles

The P=C bond of *P*-halogenated ylids is strongly polarised as a result of which a significant negative charge is centred on the carbon atom. Consequently *P*-halogenated ylids readily add various electrophiles with the formation of the corresponding phosphonium salts or betaines.

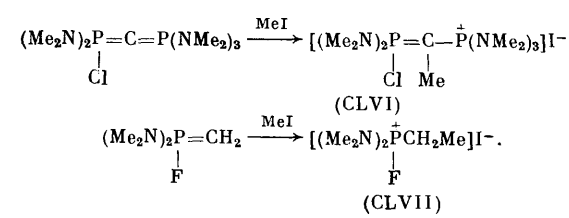
Phosphonium salts (CLIV) formed by reaction of *P*-halogenated ylids with such electrophiles as chlorotrimethylsilane, chloroformates, or acid chlorides of carboxylic and phosphoric acids and having an electron-accepting substituent R′ at the α-carbon are readily dehydrochlorinated by the initial *P*-halogenated ylid, being converted into *C*-substituted *P*-halogenated ylids (CLV).[8,33,71]



(CLIV) (CLV)

X = Cl, F; R = Alk, Alk_2N; R′ = Me_3Si, RP(Cl), $(Me_2N)_2P$, $CF_3C(O)$, MeOCO, EtOCO.

At the same time the phosphonium salts (CLVI) and (CLVII) formed by the interaction of *P*-halogenated ylids with alkyl halides are not dehydrohalogenated by the initial ylid even in excess because the alkyl group reduces the lability of the hydrogen atoms at the α-carbon.[75,84,118]



(CLVI) (CLVII)

P-Halogenated ylids usually add Lewis acids (boron trifluoride, aluminium chloride) with the formation of betaines (CLVIII).[33] It has however been reported that phosphinium cations may be

formed by this.[100] The reaction of *P*-chloroylids with gaseous chlorine leads to the formation of phosphonium salts (CLIX).[88]

$$\underset{\underset{X}{|}}{R_2P{=}CHR'} \xrightarrow{MX_3} \underset{\underset{X}{|}}{R_2\overset{+}{P}CH(R')}\bar{M}X_3,$$

(CLVIII)

$$\underset{\underset{Cl}{|}}{(R_2N)_2P{=}CCl_2} \xrightarrow{Cl_2} \left[\underset{\underset{Cl}{|}}{(R_2N)_2\overset{+}{P}CCl_3}\right]Cl^-,$$

(CLIX)

X = Cl, F.

5. Reactions of *P*-halogenated ylids with nucleophilic reagents

a) Nucleophilic replacement of the halogen atom

The labile halogen atom of *P*-halogenated ylids, located on the electrophilic, positively charged phosphorus atom is capable of ready replacement by various groups on interaction with nucleophiles. Preparatively these reactions are very simple and open wide possibilities for the synthesis of ylids containing practically any substituent at phosphorus.

P-Chloro- and *P*-bromoylids react smoothly with lithium and magnesium alkyls in organic solvents below 0 °C and form *P*-alkyl-substituted phosphorus ylids in good yield.[18,35,116]

$$\underset{\underset{X}{|}}{R_2P{=}CR_2'} \xrightarrow[-MX]{AlkM} \underset{\underset{Alk}{|}}{R_2P{=}CR_2'},$$

R = Ph, Me, t-Bu; CR_2' = $CHSiMe_3$, $C(SiCl_3)_2$, $C(SO_2Ph)_2$; M = Li, MgBr.

The reaction of *P*-chloroylids with lithium phosphides proceeds readily. The *p*-chloroylid (XIV) containing trichlorosilyl groups on the α-carbon selectively exchanges the chlorine atom on phosphorus for a dimethylphosphine group on interaction with lithium dimethylphosphide. The trichlorosilyl groups are unaffected by this. In addition, during reaction of ylid (XIV) with lithium trimethylsilylmethylphosphide, the P–P-ylid (CLX) is formed which readily reacts with a second molecule of P–Cl-ylid and is converted into a double ylid with a P–P bond (CLXI).[119]

$$\underset{\underset{Cl}{|}}{Me_2P{=}C(SiCl_3)_2} \xrightarrow{R(Me)PLi}$$

(XIV)

$$\longrightarrow R(Me)P{-}P(Me)_2{=}C(SiCl_3)_2 \xrightarrow[-Me_3SiP(Me)Cl]{R = Me_3Si} (Cl_3Si)_2C{=}\underset{\underset{Me}{|}}{\overset{\overset{Me}{|}}{P}}{-}\underset{\underset{Me}{|}}{\overset{\overset{Me}{|}}{P}}{=}C(SiCl_3)_2,$$

(CLX) (CLXI)

R = Me, Me_3Si.

P-Chloroylids exchange the chlorine atom for an amino group on interaction with primary and secondary alkylamines, ammonia or aniline. Ylids (CLXII) containing a hydrogen atom at nitrogen exist in a state of prototropic tautomeric equilibrium with the corresponding iminophosphoranes (CLXIII).[9,43,120–122]

$$\underset{\underset{Cl}{|}}{R_2P{=}CR_2'} \xrightarrow[-Alk_2NH\cdot HCl]{Alk_2NH} \underset{\underset{Alk_2N}{|}}{R_2P{=}CR_2'}$$

$$\underset{\underset{Cl}{|}}{R_2P{=}CR_2'} \xrightarrow[-R''NH_2\cdot HCl]{R''NH_2} \underset{\underset{R''NH}{|}}{R_2P{=}CR_2'} \rightleftharpoons \underset{\underset{R''N}{||}}{R_2PCHR_2'}$$

(CLXII) (CLXIII)

Symmetrically substituted hexa(dimethylamino)carbodiphosphorane (CLXV) is obtained in high yield by the reaction of *P*-chlorocarbodiphosphorane (CLXIV) with lithium dimethylamide in toluene at 20 °C.[84]

$$\underset{\underset{Cl}{|}}{(Me_2N)_2P{=}C{=}P(NMe_2)_3} \xrightarrow[-LiCl]{Me_2NLi} (Me_2N)_3P{=}C{=}P(NMe_2)_3.$$

(CLXIV) (CLXV)

The labile halogen atom of *P*-chloro- or *P*-bromoylids are successfully replaced by alkoxyl, phenoxyl or thioalkyl groups by the action of alcohols, phenols or mercaptans in the presence of triethylamine, which leads to various types of *P*-substituted phosphorus ylids (CLXVI). Ylid (XIII, n = 2) exchanges the chlorine atom on phosphorus and one chlorine atom on silicon by methoxyl groups on reaction with methanol in the presence of diethylamine with the formation of ylid (CLXVII).[18]

$$\underset{\underset{Hal}{|}}{R_2^1P{=}CR_2^2} \xrightarrow[-Et_3N\cdot HHal]{R^3XH+Et_3N} \underset{\underset{R^3X}{|}}{R_2^1P{=}CR_2^2},$$

(CLXVI)

R^1 = Alk, AlkO, Ph; CR_2^2=$C(CO_2Me)_2$, $CHCO_2Me$, $C(SO_2Ph)_2$;

R^3 = Alk, Ph; Hal = Br, Cl; X = O, S,

$$\underset{\underset{Cl}{|}}{Me_2P{=}C(SiCl_3)_2} \xrightarrow[-Et_2NH\cdot HCl]{MeOH+Et_2NH} \underset{\underset{MeO}{|}}{\overset{\overset{SiCl_3}{|}}{Me_2P{=}C{-}Si(OMe)Cl_2}}.$$

(XIII) (CLXVII)

Ylids (CLXVII) are formed in high yield on interacting *P*-chloroylids with sodium alkoxides or phenoxides. It is necessary to carry out the reaction at an equimolar reactant ratio since an excess of alkoxide or phenoxide converts ylids (CLXVIII) into phosphine oxides.[11]

$$\underset{\underset{Cl}{|}}{R_2P{=}CR_2'} \xrightarrow{RONa} \underset{\underset{RO}{|}}{R_2P{=}CR_2'} \xrightarrow[-R_2O]{RONa} \left[\underset{\underset{O}{||}}{R_2P{-}\bar{C}R_2'}\right]Na^+ \xrightarrow{H^+} \underset{\underset{O}{||}}{R_2PCHR_2'},$$

(CLXVIII)

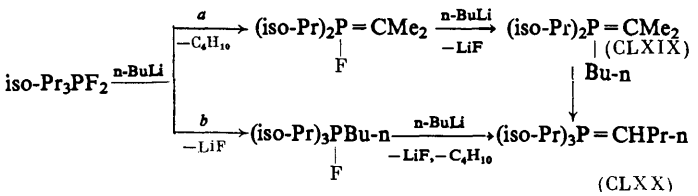
R' = SO_2Ph.

The hydrolysis of *P*-halogenated ylids proceeds extremely readily and even on interaction with moist air or the calculated amount of water they are, as a rule, converted in quantitative yield into the corresponding phosphine oxides. The hydrolysis reaction is

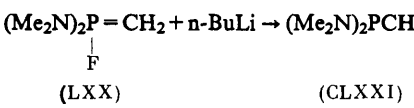
frequently used to prove the structure of *P*-halogenated ylids.[11,61,65,67,96,122]

There is no known convincing example of the replacement of fluorine by an alkyl group when interacting *P*-fluoroylids with lithium alkyls. It has been reported[123] that difluorotriisopropylphosphorane reacts with butyllithium with the formation of butylidenetriisopropylphosphorane (CLXX). It has been proposed that the reaction proceeds by route *a*, i.e. through the formation of *P*-fluoroylid, exchanging the fluorine atom for butyl, and subsequent rearrangement of the resulting ylid (CLXIX). However it is certain that there was no *P*-fluoroylid as intermediate. Consequently it may be suggested that the reaction proceeds by route *b* (Scheme 9).

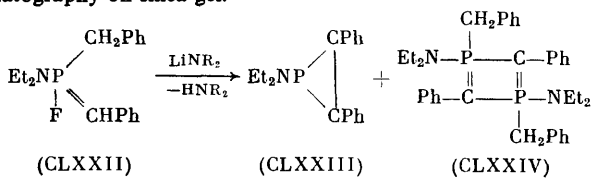
Scheme 9



Furthermore on reacting *P*-fluoroylids directly with lithium alkyls replacement of fluorine by the alkyl group does not occur. For example, the reaction of *P*-fluoroylid (LXX) with butyllithium gives a compound of trivalent phosphorus (CLXXI) only.[80]



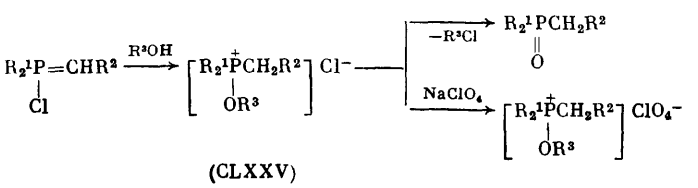
No product of nucleophilic replacement of fluorine was observed on reaction of *P*-fluoroylid (CLLXXII) with lithium amide. Only a mixture of diphenylphosphirane (CLXXIII) and diphosphetane (CLXXIV) was isolated which was separated by preparative chromatography on silica gel.[12]



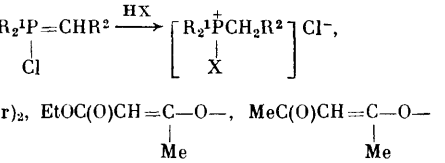
R = $SiMe_3$.

b) Addition reactions

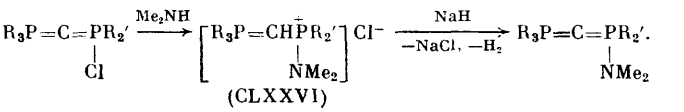
P-Chloroylids add alcohols in ether or pentane below 0 °C, being quantitatively converted into unstable alkoxyphosphonium salts (CLXXV), difficult to achieve by other routes. Salts (CLXXV) were isolated as colourless crystalline substances or viscous liquids insoluble in nonpolar solvents. On heating, alkoxyphosphonium salts (CLXXV) were converted into phosphine oxides, and on reaction with aqueous sodium perchlorate solution gave stable alkoxyphosphonium perchlorates.[58,124]



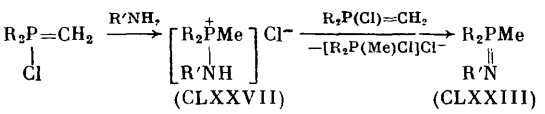
Phosphonium salts differing in structure were obtained on reacting *P*-chloroylids with hydrogen halides, hydrazoic acid, ketoenols and CH-acids. Yield of phosphonium salts were very high in all cases so the given reaction may serve as a preparative method.[33,34,124]



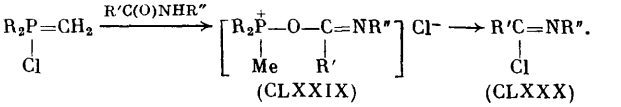
P-Chloroylids add alkyl- and dialkylamines with the formation of aminophosphonium salts. Phosphonium salts [of type (CLXXVI)] containing a dialkylaminogroup may be converted into *P*-substituted phosphorus ylids by the action of butyllithium or sodium hydride.[9,43,84,125]



Phosphonium salts (CLXXVII), resulting on interaction of *P*-chloroylids with primary alkylamines or aniline, are dehydrochlorinated by an excess of the initial *P*-chloroylid, being converted into iminophosphoranes (CLXXVIII). The reaction of *P*-chloroylids with amides of sulphonic and phosphoric acids also leads to the formation of iminophosphoranes (CLXXVIII).[125]



The reaction of *P*-chloroylids with carboxylic acid amides proceeds through the formation of an *O*-phosphorylated intermediate (CLXXIX) as a result of which imidoyl chlorides (CLXXX) are formed. Compounds (CLXXX) having substitutents R′ = Ph_2CH or R″ = H are readily dehydrochlorinated by the initial *P*-chloroylids to ketenimines or nitriles. In this case *P*-chloroylids show themselves to be dehydrating agents.[125]



* * *

Such are the main achievements in the chemistry of phosphorus *P*-halogenated ylids. It may be concluded from the material considered that the accessibility, convenient means of preparation and the ability to take part in various conversions, justify the attention which is paid to *P*-halogenated ylids and guarantee further progress in this region of the chemistry of organophosphorus compounds.

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Translated from *Uspekhi Khimii* 60 835–851 (1991) U.D.C. 541(64+183.12)

The properties of solutions and complex formation reactions of amphoteric polyelectrolytes

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ABSTRACT. The review presents the experimental results of studies on the physicochemical and complex-forming properties of synthetic polyampholytes in dilute solution. The similarity of the behaviour of polyampholytes at the isoelectric point and polyelectrolyte complexes is demonstrated. Questions concerning the complex formation reactions of polyampholytes with inorganic and organic ions, polyelectrolytes, and proteins are discussed. The role of competing interactions in the formation of intramolecular and intermolecular polycomplexes is considered.

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I. Introduction

Polyampholytes belong to the class of polyelectrolytes containing acid and basic functional groups in the macromolecule.[1–8] They can include chains with strongly and weakly acidic or strongly and weakly basic groups in various combinations.[9–12] Depending on the type of distribution of the acidic and basic units in the chain, polyampholytes can have a statistical, alternating, graft, and block structure.

The interest in the study of polyampholytes is determined primarily by the fact that they include the most important natural polymers—proteins and nucleic acids.[13] Biopolymers have a specific structure, function, and properties, which are fully realised only in a living organism.[14] Nevertheless a series of individual properties of natural polymers can be modelled with the aid of their synthetic analogues.[15]

The question of the association of polyelectrolytes with high-molecular-weight and low-molecular-weight substances of different nature constitutes the basis of processes occurring in the organism such as replication of the DNA strands, denaturation of biopolymers, protein–lipid interactions, enzyme catalysis, etc. By virtue of the high content of ionogenic groups in the chain, polyampholytes have found extensive practical application as flocculants, complexones, polymeric catalysts, agents prolonging the action of medicinal preparations, semipermeable membranes, artificial vaccines, etc.[16–20]

In the present review, an attempt is made to analyse the experimental data accumulated in recent years in order to discover the prospects for the development and the possible applications of this interesting class of macromolecular compounds.

II. Characteristic features of the behaviour of synthetic polyampholytes in solution

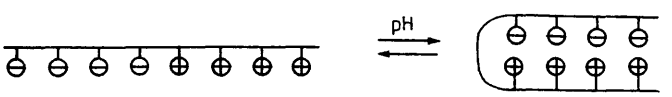
The behaviour of polyampholytes is determined both by the nature of their functional groups and by the features due to their macromolecular nature. Depending on the pH of the medium, they behave as polymeric acids or as polymeric bases and therefore exhibit the properties of homopolyelectrolytes. The pH at which the charge of the macromolecule is zero corresponds to the isoelectric point (IEP) of the polyampholyte.

It is assumed that in the vicinity of the IEP an appreciable proportion of the acid and basic units condense into a compact globule, displacing the solvent.[21] Hydrogen bonds and hydrophobic interactions can participate together with intra-ionic contacts in the stabilisation of such compact species.[22] The compactness of the macromolecules at the IEP can depend on the contributions of the above interactions.

The state of the polyampholyte species at the IEP is described satisfactorily by the "fringed globule" model, which has been analysed theoretically in detail by Lifshits et al.[23] As predicted previously by the theory,[24] the structural organisation of the globule presupposes the presence of two phase regions—a dense core from which almost the entire solvent has been displaced and fluctuating loop-shaped sections of the molecule present in the solvent and forming the fringe round the globule. This feature makes it possible to regard polyampholytes as convenient objects for the study of the phenomenon of collapse[25,26] and of the phase state of polymer molecules.[27]

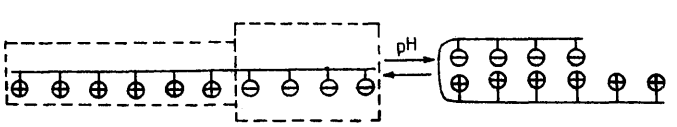
Information about the hydrodynamic and conformational properties of a series of amphoteric polyelectrolytes, soluble in the vicinity of the IEP, has been published.[28–37] The following features of the behaviour of synthetic polyampholytes of the IEP have been noted: (1) the "antipolyelectrolyte" effect, i.e. the increase in intrinsic viscosity with increase in the ionic strength of the solution; (2) the absence of intermolecular associated species (this is indicated by the similar average hydrodynamic molecular weights M_{η} calculated at different pH, including pH_{IEP}); (3) the anomalous dependence of the intrinsic viscosity on the molecular weight (in the Mark–Kuhn–Houwink equation, $a < 0.5$).

Polyampholytes with a block structure of the chains have a series of distinctive features, compared with the statistical and alternating analogues, due to the combination in the chain of long acidic and basic sequences. One of these features is the possibility of the formation of intramolecular polyionic complexes in the vicinity of the IEP. It has been shown for a diblock copolymer of sodium polystyrenesulphonate and poly-2-vinylpyridine[38] that the conformation of the macromolecules changes as a function of the degree of ionisation of the vinylpyridine blocks in the following manner: in the uncharged state ($\beta = 0$), they have a "segregated" structure with a core made up of vinylpyridine blocks maintained in water by the polystyrenesulphonate block; for low values of β, the structure consists of a coil "frozen" by rare ionic cross-links; for $\beta = 0.86$ (IEP), the macromolecules have the compact structure of a polyelectrolyte complex (PEC) stabilised by the cooperative interactions of the acidic and basic blocks. Polyelectrolyte complexes were also formed at the IEP by block copolymers based on poly-1-methyl-4-vinylpyridinium methochloride and polymethacrylic acid (P1M4VP-PMAA).[38] For example a broad region of insolubility (ΔpH ~3.5) in water is characteristic of P1M4VP-PMAA with an equimolar composition, the region becoming appreciably narrower and ultimately vanishing completely with increase in the ionic strength of the solution (Fig. 1). The precipitation of P1M4VP-PMAA in the vicinity of the IEP is evidently associated with the formation of an intramolecular stoichiometric PEC (S-PEC) as a result of the coooperative interaction of the acidic and basic blocks.



The dissolution of P1M4VP-PMMAA at a high ionic strength is caused by the decomposition of the S-PEC species as a result of the shielding of the oppositely charged units of the block polyampholyte by low-molecular-weight ions.

Block polyampholytes containing an excess of the acidic or basic block can be fully classified as intramolecular non-stoichiometric PEC (N-PEC). The relatively long cationic or anionic blocks can play the role of the lyophilising polyelectrolyte (LPE) in this instance, while the role of the blocking polyelectrolytes (BPE) is assumed by short acidic or basic blocks.



Such N-PEC species are maintained in solution and their precipitation is prevented by the hydrophilic fringe, consisting of unreacted cationic or anionic blocks. Calculation of the degree of conversion† in the N-PEC formation reaction showed that the process has a cooperative character.[39]

†The degree of conversion θ is the fraction of the intramolecular or intermolecular salt bonds formed relative to their maximum possible number.

III. Association of polyampholytes with transition metal ions, dyes, and surfactants

The study of the polyampholyte–metal complex formation processes is of interest from the standpoint of bioorganic chemistry.[40,41] A quantitative characteristic of the strength of the binding of metal ions to macromolecular ligands is the formation constant or the so-called formation function proposed by Bjerrum.[42]

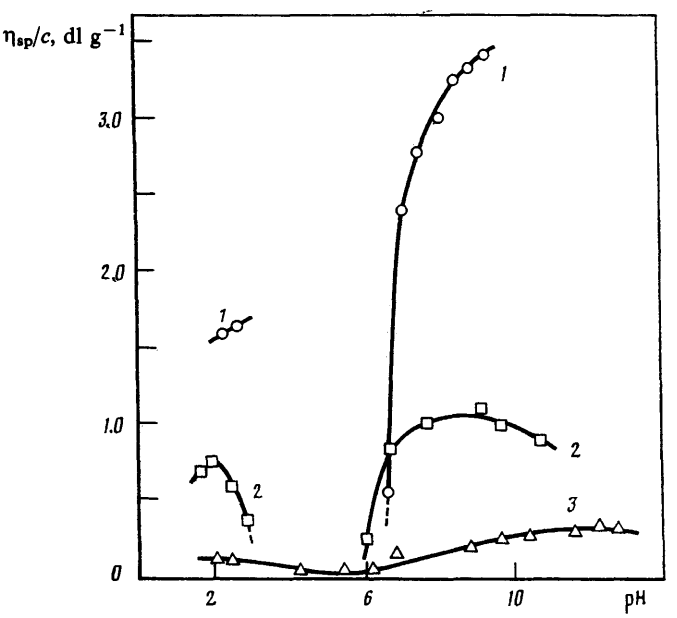
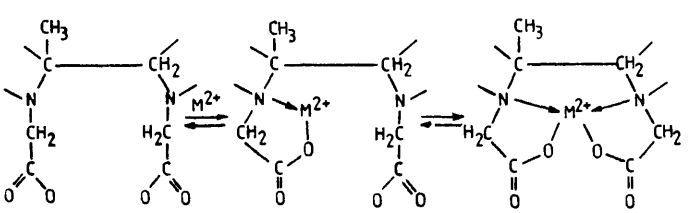


Figure 1. Dependence of the intrinsic viscosity of solutions of the block polyampholyte based on poly-1-methyl-4-vinylpyridinium methochloride and polymethacrylic acid (45:55 mol.%) on the pH in water (curve *1*) and in the presence of 0.01 M (curve *2*) and 0.3 M KCl (curve *3*); c_{BPA} = 0.045 g dl^{-1}.

Multidentate polyampholytes have been synthesised[43] and their chelating properties have been investigated. The polyampholytes react with metal ions in two stages:



As a consequence of the formation of five-membered rings, the polyampholyte–metal complexes have high stability constants. The stability of the chelate compounds varies in the sequence Zn^{2+} > Ni^{2+} > Cd^{2+} > Co^{2+} > Pb^{2+} > Fe^{2+} > Ca^{2+} > Mg^{2+}. It

identical with the stability series of the complexes of the same metals with EDTA.[44]

Depending on the pH of the medium, amphoteric polyelectrolytes are capable of forming several types of complexes with participation of carboxy- or amino-groups and also complexes of a mixed type.[8] The binding of Ca^{2+}, Mg^{2+}, Co^{2+}, Cu^{2+}, and Zn^{2+} ions by polyampholytes based on *N,N*-dimethylaminoethyl methacrylate and methacrylic acid (DMAEM-MAA) has been investigated by the potentiometric method.[45] The Mg^{2+} ion formed a stable complex at pH > 9.7, while Co^{2+} was bound to DMAEM-MAA in the range 7.5 < pH < 9.5. The formation of Cu^{2+} and Zn^{2+} complexes was observed in the region of pH 5.8 and 7.4 respectively. The Ca^{2+} ion showed no complex-forming capacity at any pH.

On the basis of theoretical studies and the intermolecular cross-linking of macromolecules, Plate et al.[46] were able to predict the principal characteristics of the complex formation reaction between macromolecules and metal ions in relation to the interaction of poly-N^{ε}-methacryloyl-*L*-lysine (PML) with copper(II) ions. Comparison of potentiometric titration, UV spectroscopic, and equilibrium dialysis data shows that at pH > 4.5 copper ions are bound to two lysine residues of PML. Two monomeric units of one macromolecule are involved predominantly in the process. Such a process is an example of an intramolecular cross-linking reaction.

In order to identify the structure of the copper complexes of aminocarboxypolyampholytes, the EPR spectra of the latter were compared[47] with those of copper–glycine and copper–alanine complexes. It was shown that the complexes formed in the amino-acid solutions at pH > 3 are analogous to the complexes in aminocarboxy-resins. Depending on the pH of the medium, copper ions are coordinated predominantly to carboxy-groups or carboxy- and amino-groups of the polyampholytes. The fraction of the structure of each type is determined by the pH of the solution.

Analysis of the EPR spectral lines for the 2-methyl-5-vinyl-pyridine-acrylic acid/copper(II) (2M5VP-AA/Cu^{2+}) complex revealed two types of spectra differing by the parameters $g_{\perp}$, $g_{\parallel}$, and $A_{\parallel}$.[48,49] In an acid medium, the signal characteristic of the type "A" structure with the parameters $g_{\perp} = 2.058$, $g_{\parallel} = 2.334$, and $A_{\parallel} = 136 \times 10^{-4}$ cm^{-1} predominates in the spectrum. On passing to the neutral region, the intensity of this line gradually falls and is replaced by an increase in the intensity of the EPR signal of a complex of another type (type "B") with the parameters $g_{\perp} = 2.035$, $g_{\parallel} = 2.298$, and $A_{\parallel} = 157 \times 10^{-4}$ cm^{-1}. Bearing in mind the similarity of the parameters of the "A" spectrum to those of the spectrum of the copper complex with polyacrylic acid and copper acetate, one may conclude that in an acid medium the carboxy-groups of the acrylic acid units are predominantly coordinated around the copper ions. The dependence of the average coordination number $\bar{n}$ on the pH of the medium shows that the formation of the complex ML_2 is completed at pH < 6.0. The higher value of $A_{\parallel}$ and the lower value of $g_{\perp}$ for the EPR signal in the spectrum of the "B" complex show that the coordination environment of copper includes, apart from two carboxy-groups, two pyridine units. These results permit the conclusion that a complex with $\bar{n} = 2$ and $\lg\beta = 13.5$ is formed at pH < 6.0, while a complex with $\bar{n} = 4$ and $\lg\beta = 21$ is formed in the range 6.0 < pH < 10.0.

A similar rearrangement of the coordination sphere of copper ions has been observed also for ternary polymer–metal complexes (TPMC), which have been examined in detail.[50–52] In particular, it was noted that two types of structures (A and B), differing in the structure of the coordination sphere of the central ion, are characteristic of the products of the interaction of polyacrylic acid (PAA), linear polyethyleneimine (PEI), and copper(II) ions. At high pH, the amino-groups of PEI are not protonated and the complex $Cu(PEI)_2^{2+}$ with a type A structure is mainly formed. As the pH is reduced, the nitrogen atoms of the PEI ligand are protonated and the fraction of the type A structure begins to diminish with the simultaneous increase in the fraction of the type B structure, in which one of the two amino-groups in the coordination sphere is replaced by two carboxylate ions of PAA: $(CuPEI)(PAA)_2$. Thus in this case too the number and type of functional groups of the polyampholytes in the coordination sphere of the metal ion are determined by the pH of the medium.

In the course of the study of the complex-forming properties of synthetic polyampholytes, we observed that polyampholytes based on piperidinol derivatives[53,54] are capable of binding metal ions at certain pH values and of liberating them strictly at the IEP. The principle of the action of polyampholytes at the IEP is apparently that, after the attainment of pH_{IEP}, the cooperative interaction forces between the acidic and basic groups become more effective, which leads to the "expulsion" of the previously bound metal ions from the bulk of the coil of the macromolecule. If the IEP of the polyampholyte is located in the alkaline region, then transition metal ions are precipitated while the polyampholyte remains in solution and can be regenerated and used anew. In this sense, the behaviour of polyampholytes at the IEP resembles that of TPMC.[50–52] For example, at certain pH values the nitrogen–metal coordinate bonds and carboxylate–metal ionic bonds in the polyethyleneimine–metal–polyacrylic acid system are replaced by cooperative polycation–polyanion salt contacts.[55] In contrast to the ampholyte, the PEC is then precipitated, while the metal ions remain in solution.

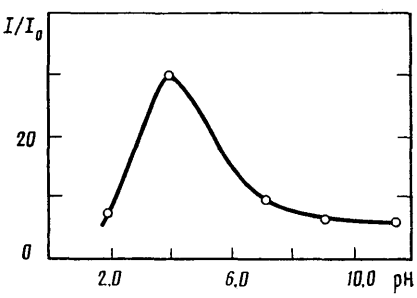


Figure 2. Dependence of the relative fluorescence intensity of 1-anilinonaphthalene-8-sulphonic acid on the pH in the presence of the 2,5-dimethyl-4-vinylethynyl-4-piperidinol–acrylic acid copolymer (DMVEP:AA = 45.2:54.8 mol.%); [DMVEP-AA]:[ANS] = 100:1; [ANS] = 5 × 10^{-5} M.[57]

The available literature data concern in the main the association of polymeric acids, polymeric bases, and non-ionic polymers with dyes and surfactants.[56] On the other hand the data obtained in studies of the interaction of synthetic polyampholytes with dyes and surfactants are virtually lacking. The results of the investigation of the dependence of the intensity of the fluorescence of 1-anilino-naphthalene-8-sulphonic acid (ANS) (I/I_0) in the presence of the polyampholyte over a wide pH range are presented in Fig. 2.[57] The

greatest increase in the intensity of the fluorescence of the dye is observed at pH 3–3.5, i.e. in the region of the intense ionisation of the basic groups of the polyampholyte. The sharp decrease of I/I_0 from 30 to 4 in the vicinity of the IEP of the polyampholyte (pH_{IEP} = 7.0) indicates the decomposition of the polyampholyte–ANS complex and the appearance of free dye molecules. The dye is liberated similarly after the addition of polyacrylic acid to the polydiallyldimethylammonium chloride–ANS system, as a consequence of the competing effect of the second macromolecular component.[58]

The mechanism of the "expulsion" of ANS at the IEP of the polyampholyte is apparently similar to the mechanism of the expulsion of the metal from the polyampholyte–metal system examined above.

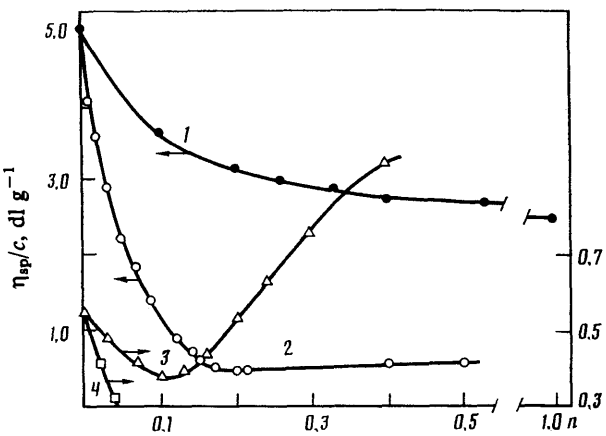


Figure 3. Dependence of the intrinsic viscosity of solutions of polyampholytes based on 1,2,5-trimethyl-4-vinylethynyl-4-piperidinol and acyrlic acid (TMVEP : AA = 40 : 60 mol.%) (curves *1* and *2*) as well as styrene and *N,N*-dimethylaminopropylmonoamide of maleic acid (S : DMAPMAMA = 50 : 50) (curves *3* and *4*) on the [surfactant] / [polyampholyte] = *n* molar ratio; [TMVEP-AA] = [S-DMAPMAMA] = 1 × 10^{-2} M.[59–61]

Synthetic polyampholytes have the ability to bind cooperatively anionic and cationic surfactants undergoing at the same time appreciable conformational changes.[59–62] The binding of anionic and cationic detergents by polyampholytes takes place mainly via electrostatic interaction, while the compact polymeric complex species is stabilised by the hydrophobic interactions of the long alkyl components of the surfactant and is maintained in solution and its precipitation is prevented by the hydrophilic components of the copolymers which have not been involved in the complex.[59–62] Fig. 3 illustrates the influence of sodium dodecyl sulphate (DDS) and cetyltrimethylammonium chloride (CTMA) on the hydrodynamic dimensions of the molecules of polyampholytes. The decrease in the intrinsic viscosity η_{sp}/c in the presence of surfactant is evidently associated with the formation of ampholyte–surfactant polymeric complexes. The results of the calculation of the degree of conversion in the formation reaction of the polyampholyte–surfactant complexes shows that the polymeric complexes are formed within a narrow pH range, which indicates the cooperative nature of the process.

In contrast to a statistical polyampholyte, the styrene–maleic acid, *N,N*-dimethylaminopropylmonoamide copolymer (S–MADMAPMA), with a regular structure, contains, together with hydrophilic groups, also styrene units (50 mol.%), which can intensify the hydrophobic interactions between the non-polar units of the copolymer and the hydrocarbon components of the surfactant. This feature of S–MADMAPMA is clearly manifested in relation to CTMA and DDS. The addition of even an insignificant amount of CTMA induces a sharp decrease in viscosity as far as the formation of an insoluble deposit. This is caused by the marked conversion of the macromolecules into a hydrophobic form, which leads to the formation of globular polymeric complex species. On titration of the same copolymer with DDS, the viscosity of the system passes through a minimum. This form of the viscometric curve can be accounted for by the fact that initially the detergent molecules are bound electrostatically by the polyampholyte which results in the formation of an intramolecular micelle-like structure, giving rise to a more coiled conformation of the polymer coils. Subsequently additional adsorption of surfactant molecules on the polymer chains takes place, which leads to charge transfer in the macromolecules and to the swelling of the polyelectrolyte.

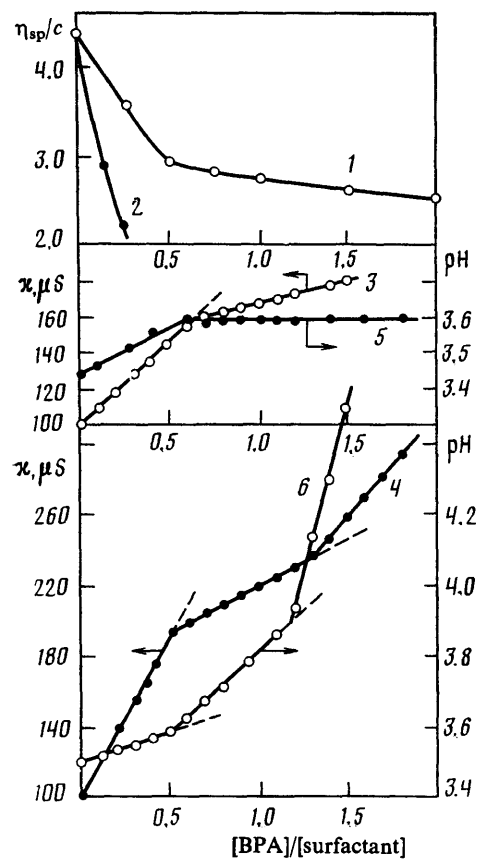
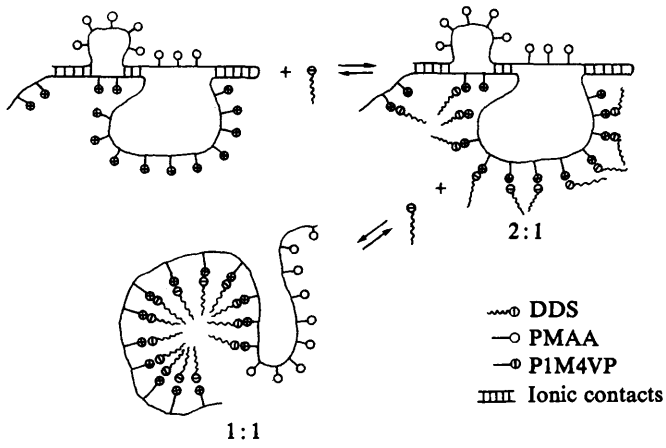


Figure 4. Viscometric (curves *1* and *2*), conductimetric (curves *3* and *4*), and potentiometric (curves *5* and 6) titration curves for a block polyampholyte based on poly-1-methyl-4-vinylpyridinium methochloride and polymethacrylic acid (64 : 36) the [BPA] / [surfactant] molar ratio: *1*, *3*, and *5*, [BPA]–[CTMA]; *2*, *4*, and *6*, [BPA]–[DDS]; [surfactant] = 5 × 10^{-2} M.

On potentiometric and conductimetric titration of an aqueous solution of a block polyampholyte (BPA) with a DDS solution, the formation of complexes with the ratios [BPA]:[DDS] = 2:1 and 1:1 was observed (Fig. 4). Initially only half of all the vinylpyridinium units enter into the reaction. On further addition of the ionic surfactant, the composition of the complex approaches the equimolar composition, which indicates the binding of an additional amount of DDS. It was shown previously by the luminescence quenching method[63] that micellar surfactants containing sulphogroups can compete with polymeric acids in polymeric complex formation reactions with linear synthetic polymeric cations. Consequently the mechanism of the interaction of BPA and DDS can be considered within the framework of competing reactions which occur in N-PEC/surfactant systems.[63] The formation of a 2:1 polymeric complex can be accounted for by the interaction of DDS with longer and shorter sections of the cationic block which do not enter into the formation reaction of the intramolecular N-PEC. The formation of the stoichiometric 1:1 polymeric complex is apparently due to the breakdown of the cooperative ionic contact between the acid and basic blocks ($COO^- - \overset{+}{N}\!\!\swarrow$) and their replacement by cooperative ionic contacts ($SO_3^- - \overset{+}{N}\!\!\swarrow$). Taking into account these considerations, the competing reaction of the anionic surfactant and BA can be represented schematically in the following way:



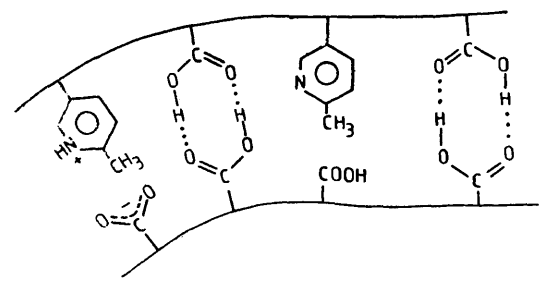
However, after the addition of a cationic surfactant, namely CTMA, to a solution of BPA, only an inflection corresponding to the 2:1 composition of the polymeric complex is observed on the potentiometric, conductimetric, and viscometric titration curves. This can be explained by the fact that the ionic contact with participation of the cationic surfactant cannot compete with the cooperative ionic contacts between the acidic and basic blocks, while the surfactant reacts only with the PMAA "loops" which constitute the "fringe" (see the scheme above). Thus the behaviour of the anionic surfactant–BPA system can be described satisfactorily on the basis of data obtained for the DDS–N-PEC system.[63]

It is of interest to trace the influence of organic additives on the behaviour of associating polyampholyte–surfactant systems.[59–62] In the case of the polyampholyte–DDS polymeric complex, a sharp increase in viscosity within a narrow range of variation of the solvent composition (in the range from 60 to 80 vol.% of methanol) was observed on the curve relating the intrinsic viscosity to the composition of the methanol–water solvent. In the remaining regions (above 80 and below 60 vol.% of methanol), the viscosity changes only slightly as the methanol content in the mixture is varied. These results can be interpreted in the following way. In pure water, the polymeric complex species acquire a compact structure stabilised by hydrophobic interactions. It persists up to a methanol content in the mixture of 60 vol.%. Further increase in the fraction of the alcohol induces a sharp increase in viscosity, which indicates the cooperative uncoiling of the compact structure as a consequence of the solvation of the hydrophobic components of the polymeric complex by methanol and of the hydrophilic components by water. In the latter case, we are dealing with an inverted micelle, which is formed as a result of the "precipitation" of the hydrophilic components of the copolymer by methanol. Thus the transition from one compact structure to another takes place via a stage involving rearrangement of the structure of the polymeric complex.

IV. Interpolyelectrolyte reactions with participation of synthetic polyampholytes

Considerable experimental data have accumulated hitherto on complex formation between synthetic polyelectrolytes. There have been surveys in a number of communications.[64–71] However interpolymer reactions with participation of synthetic polyampholytes have been studied very inadequately. Synthetic polyampholytes have the ability to bind cooperatively to both anionic (or cationic) and amphoteric macromolecules. Earlier Morawetz and Hughes[72] investigated the association of human serum albumin with the TMAEM–MAA copolymer. Kabanov et al.[73] investigated by potentiometric titration and turbidimetric methods the reactions between amphoteric 2M5VP-AA copolymers of different composition and PAA (5,6-ionene). The maximum turbidity of the system is observed in the pH range where the components are linked by the maximum possible, under the given conditions, number of ionic contacts and hydrogen bonds.

The stoichiometry of the 2M5VP-AA/PAA complex is independent of the composition of the copolymer and is 1:1. In contrast to the polyampholyte–polymeric acid system, 5,6-ionene forms a weak complex with the polyampholyte. According to the authors,[73] this is due to the impossibility of the formation in the polyampholyte–ionene system of a single cooperative sequence of ionic and hydrogen bonds between the interacting chains. The proposed structure of the polyampholyte–PAA polymeric complex can be represented as follows:



Interpolyelectrolyte reactions with participation of a sulpho-derivative of chitosan—a polyampholyte containing amino- and sulpho-groups in the chain—have been examined.[74] Fig. 5 presents curves for the turbidimetric titration of a solution of 2,5-ionene bromide with a solution of chitosan sulphate at pH 2.5 and 11.5. Evidently the compositions of the polyelectrolyte complex in the acid and alkaline regions differ significantly. In the acid region, only half of the OSO_3^- groups of chitosan sulphate ($Z' = 2$) participate in the formation of the polyelectrolyte complex. The remaining groups are incorporated in zwitter-ionic pairs with the amino-groups of a neighbouring glucoside ring. In an alkaline medium, the polyelectrolyte complex has the equimolar composition ($Z' = 1$), i.e. virtually all the sulpho-groups participate in the formation of the polyelectrolyte complex. In other words, as the pH of the medium is varied, there is competition between the formation of the zwitter-ions and the formation of the polyelectrolyte complex. The examples quoted above show that, by alternating the state of ionisation of the acidic and basic groups of polyampholytes, it is possible to vary within broad limits the composition and hence the structure and properties of the polyelectrolyte complex.

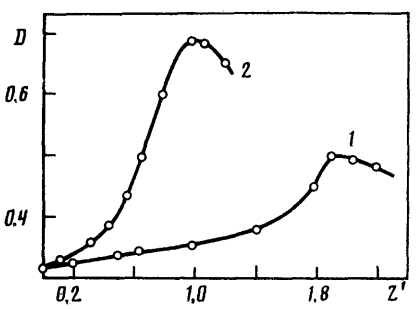


Figure 5. Curves for the turbidimetric titration of 2,5-ionene bromide with chitosan sulphate at pH 2.5 (curve *1*) and 11.5 (curve *2*); [2,5-ionene] = 5×10^{-4} M.[74]

The formation reaction of the polyelectrolyte complexes between synthetic polyampholytes (PAM) and polyacrylic acid was investigated previously[75] and the composition of the polymeric complexes was determined. The influence of the order of mixing of the polyelectrolyte components, the ionic strength of the solution, temperature, and the addition of an organic solvent on the composition and stability of the polyelectrolyte complexes was demonstrated.

The influence of the pH of the medium on the complex formation reaction between the equimolar 2,5-dimethyl-4-vinylethynyl-4-piperidinol–acrylic acid (DMVEP–AA) polyampholyte and PAA, polydiallyldimethylammonium chloride (PDADMAC), and human serum albumin (HSA) has been investigated.[76–78]

When aqueous solutions of polyelectrolyte components are mixed, the solution pH changes appreciably and this is accompanied by the appearance of turbidity in the system, which indicates the occurrence of the polyelectrolyte complex formation reaction. Fig. 6 illustrates the variation of the intrinsic viscosity of the polyelectrolytes and the polyelectrolyte complex as a function of the pH of the medium. The polyelectrolyte complex consisting of a polyampholyte and PAA is precipitated in the pH range from 3.0 to 5.5. The onset of the segregation of the reaction product as a separate phase corresponds to the onset of the ionisation of the amino-groups of the polyampholyte and to the partly ionised state of PAA. The dissolution of the polyelectrolyte complex in the strongly acid medium is apparently associated with its decomposition as a consequence of the suppression of the ionisation of the carboxy-groups of PAA and the formation of an ionic atmosphere around the positively charged nitrogen atoms caused by the excess inorganic acid. The precipitation of the polyelectrolyte complex consisting of a polyampholyte and polydiallyldimethylammonium chloride takes place at pH $\geqslant$ 8.2, i.e. with increase in the degree of ionisation of the carboxy-groups of the polyampholyte.

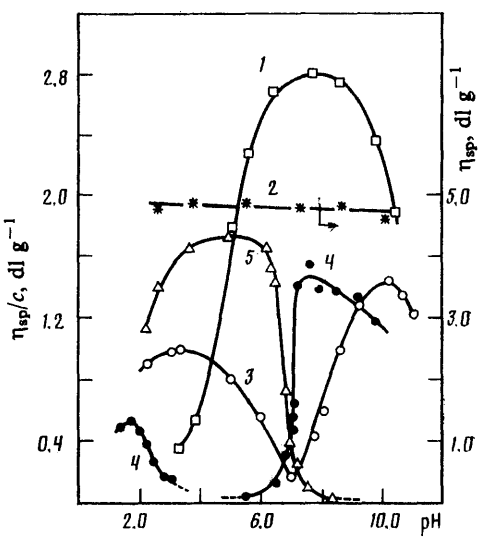


Figure 6. The influence of the pH of the solution on the intrinsic viscosity of polyacrylic acid (PAA) (curve *1*), polydiallyldimethylammonium chloride (PDADMAC) (curve *2*), the 2,5-dimethyl-4-vinylethynyl-4-piperidinol–acrylic acid copolymer (DMVEP : AA = 45.2 : 54.8) (curve *3*), and the polyelectrolyte complexes [DMVEP-AA] : [PAA] = 3 : 1 (curve *4*) and [DMVEP-AA] : [PDADMAC] = 3 : 1 (curve *5*); [DMVEP-AA] = 2.5×10^{-2} M.[77]

After the addition of human serum albumin to the polyampholyte, the quantity η_{sp}/c for the polyampholyte solution gradually diminishes, reaching a limiting value at $m_{HSA} : m_{PAM} = 3 : 2$. However, despite the appearance of a strong opalescence, phase separation does not take place in the system. The most favourable region of the interaction of the polyampholyte and human serum albumin corresponds to the pH range between their isoelectric points, since at these pH values the polyampholyte and human serum albumin macromolecules become positively and negatively charged respectively. The formation of a polyelectrolyte complex between the polyampholyte and human serum albumin apparently takes place as a result of the "adhesion" of more or less long sections of the polyampholyte chain to the surface of the

negatively charged protein globule.[79] It has been noted[80] that, on mixing aqueous solutions of natural polyampholytes—β-lipoprotein and γ-globulin—the formation of the polyelectrolyte complex is also observed. As in the interaction of a polyampholyte and human serum albumin, here the maximum degree of salt formation between the β-lipoprotein and γ-globulin takes place in the pH range between their isoelectric points.

There are literature data showing that the complexes of carbochain linear polyampholytes with proteins exhibit reduced immunogenic properties.[20] It has been found that the stability of the complexes formed depends on the composition of the 2-methyl-5-vinylpyridine–acrylic acid copolymer. According to the authors, hydrogen bonding and hydrophobic interactions play a decisive role in the formation of the polyampholyte–protein complex. However, against their background there is also a possibility of the formation of salt bonds by virtue of the induced ionisation of the corresponding ionogenic groups.

Thus the results obtained fully confirm the conclusion that[73] synthetic polyampholytes are capable of cooperative binding to both anionogenic or cationogenic and amphoteric molecules, differing significantly from homopolymers by the width of the spectrum of cooperative interactions.

Attention should be drawn to one of the characteristic features of the polyampholyte–polyelectrolyte complex, namely the sharp increase in viscosity occurring at the isoelectric point of the polyampholyte (pH_{IEP} 7.0) (Fig. 6). This phenomenon, which we called the "expulsion effect", occurs following a change in the pH of the medium induced by the coil–globule conformational transition in the polyampholytes. The process mechanism is apparently as follows.

Since the structure of the polyampholyte–polyelectrolyte complex consists of a double-stranded pair sequences formed by a single cooperative system of ionic and hydrogen bonds and also of defects of the loop ("fringe") type, it follows that, as the isoelectric point is approached, the cooperative interactions between the acidic and basic units of the polyampholyte, leading to the formation of intramolecular polyelectrolyte complexes (IAPEC), ultimately cause the decomposition of the polymeric polyampholyte–polyelectrolyte complex into individual components. The main driving force of the polyelectrolyte decomposition process at the isoelectric point of the polyampholyte is evidently the decrease in the Gibbs free energy as a consequence of the increase in the entropy of the system.

In order to demonstrate the cooperative nature of the decomposition of the polyelectrolyte complex species, sedimentation measurements were made. Fig. 7 illustrates the sedimentation diagrams for the 2,5-dimethyl-4-vinylethynylpiperidinol–acrylic acid (DMVEP-AA) polyampholyte, PAA, and the polyelectrolyte complex at different pH. At pH 6.1 and 6.9, a single peak with S = 4.75 and 4.18 Svedberg units can be seen on the sedimentogram. This shows that under these conditions the sedimenting particles are those of the polymeric complex. However, at pH $\geqslant$ pH_{IEP} (pH_{IEP} 7.0) two peaks appear on the sedimentogram with sedimentation coefficients of 1.9 ("slow" peak) and 5.6 Svedberg units ("fast" peak). Under identical conditions, the individual components have S = 1.06 (PAA) and 3.53 Svedberg units (DMVEP-AA). The appearance of the slowly and rapidly sedimenting particles within a fairly narrow pH range (ΔpH = 0.2) can be attributed to the cooperative decomposition of the polyelectrolyte complex species. However, in the presence of a low-molecular-weight salt, the cooperative nature of the decomposition is less marked. This is associated with the fact that the low-molecular-weight electrolyte leads to the shielding of the charges on the macromolecule and the loosening of the compact polyampholyte particles at the isoelectric point.

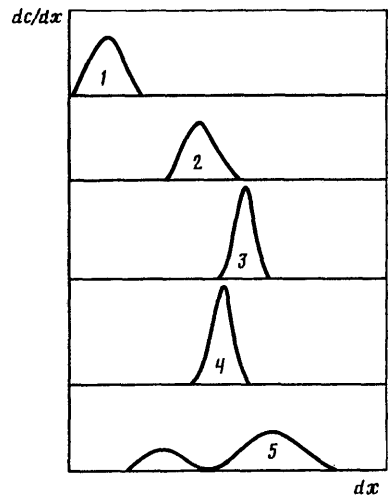


Figure 7. Sedimentograms for PAA (curve *1*), DMVEP-AA (curve *2*), and the [DMVEP-AA]:[PAA] = 3:1 polymeric complex (curves *3*–*5*) at different pH of the solution. Rate of rotation of the rotor 40,000 rev min^{-1}, T = 298 K, I = 0.005, τ = 60 min; pH: *1*, and *2*, 7.2; *3*, 6.1; *4*, 6.9; *5*, 7.1.

Polyampholytes with a block chain structure are capable of binding macromolecules with a more pronounced cooperative behaviour, in contrast to statistical and alternating polyampholytes.[39] The interpolymer complexes formed under these conditions can be stabilised by both ionic and hydrogen bonds. The compositions of the complexes, found from conductimetric, potentiometric, and viscometric titration curves, correspond to BPA:PAA = 1:1, where PAA may also be polybenzyltrimethylvinylammonium chloride (PBTMVAC), polyallyldimethylammonium chloride (PADMAC), or polyvinylpyrrolidinone (PVPD), and BPA:PEG = 2:1 (Fig. 8).

Calculation of the degree of conversion θ in the polyelectrolyte formation reaction between the block polyampholyte and an anionic (cationic) polyelectrolyte shows that the process is cooperative (Fig. 9, curves *1* and *2*). It is also noteworthy that the block polyampholyte is capable of forming a ternary polyelectrolyte complex by becoming "loaded" with cationic and anionic polyelectrolytes. However, the cooperative nature of such a reaction is less marked than that of the reaction quoted above, which is associated with the conversion of the macromolecules of the initial polyelectrolyte complexes into a compact form (Fig. 9, curve *3*). At the isoelectric point of the block polyampholyte, there is also a possibility of the existence of cooperative ionic contacts between the acid and basic blocks, leading to the formation of intramacromolecular polyelectrolyte complexes (Fig. 9, curve *4*). This justifies the assumption that, as the isoelectric point of the block polyampholyte is approached, the alternative possibilities of intramacromolecular and intermacromolecular

complex formation reactions may arise. If the first reaction is more cooperative than the second, then one cannot rule out the possibility of the decomposition of the interpolyelectrolyte complex and the formation of an intramolecular polyelectrolyte with subsequent liberation of the sorbed polyelectrolyte.

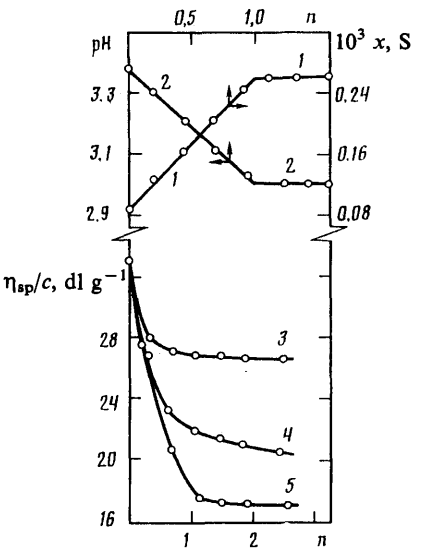


Figure 8. Variation of the electrical conductivity (curve *1*), pH (curve *2*), and intrinsic viscosity (curves *3*–*5*) with the molar ratio of the components *n*; *n*: *1*, and *2*, [BPA]/[PAA]; *3*, [BPA]/[PEG]; *4*, [BPA]/[PADMAC]; *5*, [BPA]/[PVPD].[39]

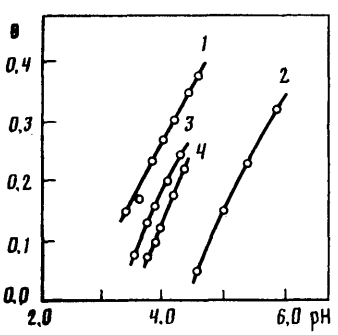


Figure 9. The profile of the dependence of θ on the pH for the BPA–PAA (curve *1*), BPA–PADMAC (curve *2*), and (BPA-PADMAC)–PAA (curve *3*) systems. Curve *4* corresponds to the formation of an intramolecular polyelectrolyte complex.[39]

The cooperative decomposition of the polyelectrolyte complex species at the isoelectric points of polyampholytes resembles the macromolecular substitution reaction, which is one of the important properties of interpolyelectrolyte complexes. In the case of interpolyelectrolyte complexes, the substitution process takes place as a result of the interaction of two complementary macromolecules with subsequent liberation of the third. In the case of polyampholytes, this reaction occurs within the limits of one macromolecule as a result of the formation of a single cooperative system consisting of intrachain ionic and hydrogen bonds and also hydrophobic contacts.

Thus the stability of the polymeric complexes formed from different polyampholyte–polyelectrolyte, polyampholyte–metal ions, and polyampholyte–dye pairs is apparently determined by the competing intramolecular and intermolecular complex formation reactions.

V. Conclusion

On the basis of the detailed study of the mechanism of the binding of metal ions by synthetic polyampholytes, the structures of the complexes, and the regions corresponding to their formation and decomposition, a new procedure has been proposed for the extraction of noble metal ions from dilute solutions.[54] It is based on the "expulsion effect" whose essential feature consists in the ability of synthetic polyampholytes to sorb transition metal ions and to liberate them in the vicinity of the isoelectric point.

A polyampholyte network with a controllable permeability to water and human serum albumin molecules has been synthesised.[53] As can be seen from Fig. 10, the maximum permeation of water molecules through the cross-linked polyampholyte is attained at the isoelectric point. It has been established that the maximum desorption (up to 96%) of the human serum albumin molecules takes place under these conditions. The mechanism of this process apparently consists in the alteration of the pore sizes in the polyampholyte network as a result of the electrostatic interaction of the acidic and basic units, leading to a change in the conformation of the macromolecules.

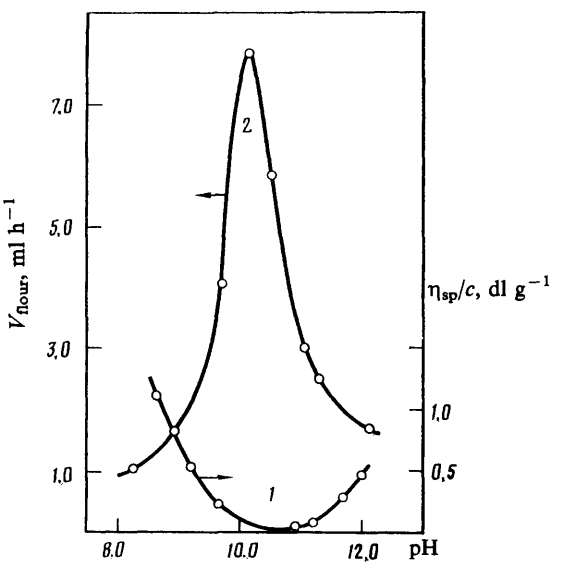


Figure 10. Variation of the intrinsic viscosity (curve *1*) and the permeability to water molecules (curve *2*) for linear (curve *1*) and cross-linked (curve *2*) polyampholytes based on DMVEP-AA with the pH of the solution.[53]

We may point to certain promising ways of using the "expulsion" effect. These are in the first place the creation of a pH-sensitive container which is capable of transporting specific immobilised substances (proteins, enzymes, antibiotics, and medicinal drugs) to the affected regions of the organism and also of "pH-muscles". The idea of creating pH-controlled containers is due to Frenkel'.[81] Let us suppose that a polyampholyte–medicinal drug associated species has been produced. The pH_{IEP} of the polyampholyte is "tuned" to a large section of the given body. So long as the polymeric polyampholyte–drug complex has not reached its "target" the medicinal drug should remain in the bound state. As soon as it reaches the affected region of the organism, whose pH is equal to pH_{IEP}, the drug begins to be released from the bulk of the macromolecular coil of the polyampholyte.

Microscopic conformational transitions are known to lead to macroscopic changes in the dimensions of solid polymers, which permits their use as converters of chemical energy into mechanical energy.[82] Bearing in mind that the polyampholyte–polyelectrolyte polymeric complex is formed cooperatively or decomposes within a very narrow pH range (for example, in the case of the system presented in Fig. 6 the range is 0.1–0.2 pH units), one may expect the creation of pH-muscles or pH-sensors.

We shall consider further the possibilty of creating self-regulating enzyme systems with the aid of polyampholyte–enzyme associated species or conjugates. The main principles governing the creation of a new generation of reversibly soluble immobilised enzymes with the aid of conjugates formed by enzymes with N-PEC have been described in detail.[67,68] On the basis of these principles, one can assume that the active centres of the enzyme bound to the polyampholyte can be "switched off" at the isoelectric point as a result of the formation of dense compact structures and can be "switched on" in the acid or alkaline reigons, i.e. when the chains are uncoiled to the maximum extent. If, for example, the pH of the medium changes as a result of the enzymic reaction, then, after the attainment of pH_{IEP}, the reaction should stop spontaneously.

The idea of using ampholytes with a block structure in matrix synthesis is also attractive. The mechanism of matrix polymerisation on a block polyampholyte chain should not differ fundamentally from the synthesis of polymers on polymeric acid or polymeric base matrices. However, when the reaction is carried out on a block polyampholyte, one may expect the following advantages: (1) the possibility of carrying out matrix polymerisation on individual blocks of the acid or base; (2) an increase in the degree of conversion in the reaction and the formation of water-soluble products maintained in solution and protected against precipitation by the hydrophilic "fringe"; (3) the possibility of separating the polymerisation products from the matrix at the isoelectric point of the block polyampholyte, after which the cyclic process is carried out.

In our view, the above examples and predictions by no means exhaust the theoretical and practical importance of the new property of polyampholytes at the isoelectric point. Further research on these lines is necessary.

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Translated from *Usepkhi Khimii* 60 852–880 (1991) U.D.C. 547.298.1:547.554

Synthesis and reactivity of *N*-substituted aminoamides, antiarrhythmic and local anaesthetic activity

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ABSTRACT. Preparative methods, reactivity and biological action of *N*-substituted aminoamides of the monoacylated diamine type RCONH–CH(–)–(CH$_2$)$_n$N< are considered and systematised. An interconnection has been shown between structure, reactivity and the pharmacological activity of aminoamides.

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I. Introduction

The interest in aminoamides, organic compounds containing an amino and an amide group, is explained by the wide spectrum of their biological action. Aminoamides display various pharmacological activities and from them several medicinal preparations such as novocainamid, trimecaine, xycaine, flecainide, morphocycline, etc. have been produced in the USSR. A special place is occupied by compounds displaying antiarrhythmic activity, since disturbances of heart rhythm are the most widespread cardiovascular illnesses.

However in contrast to the amides of aminoacids which have been studied in detail, aminoamides of the monoacylated diamine type have received little investigation.

There are no literature reviews on the chemistry and biological action of *N*-substituted aminoamides. However information on individual compounds has been given in reviews.[1–3]

The increase observed in recent years in the number of publications on the development of synthetic methods, on the study of properties and especially on areas for their practical application, has caused a need for correlation and separate consideration of the accumulated information in this new trend in synthetic organic chemistry.

The methods for obtaining, the reactivity and the biological action of *N*-substituted aminoamides of the monoacylated diamine type RCONH–CH(–)–(CH$_2$)$_n$N< are discussed and systematised in the present review. An interconnection has been shown between structure, reactivity and the pharmacological activity of the aminoamides. Literature data published up to and including 1989 are discussed.

II. Methods of synthesis of *N*-substituted aminoamides

All the methods of synthesising aminoamides used at the present time may be provisionally divided into three types and will be considered in turn in this section.

1. Synthesis of aminoamides by introducing an amide group into an amine molecule

The most widespread means of obtaining aminoamides by the first type of method is the acylation of diamines.

$$R_2N(CH_2)_nNH_2 \xrightarrow{R^1COX} R_2N(CH_2)_nNHCOR^1.$$

Acylating agents used include carboxylic acids,[4–8] acid chlorides[9–12] and anhydrides,[13] and esters.[14–18]

Reactions are carried out in benzene, ether, chloroform or without solvent.

A series of aminoamides $RC_6H_4CONH(CH_2)_2NR^1R^2$ (I) has been obtained by acylation of the appropriate diamines with substituted benzoic acids in benzene or toluene in the presence of boron trifluoride and a strong organic base.[19] The yields of aminoamides were from 28 to 100%.

Diethylaminoethylbenzamide was synthesised in 81.8% yield by prolonged stirring of a mixture of the acid and amine in benzene over anhydrous magnesium sulphate.[20]

$$C_6H_5COOH + H_2N(CH_2)_2N(C_2H_5)_2 \xrightarrow[MgSO_4]{BF_3-(C_2H_5)_2O} C_6H_5CONH(CH_2)_2N(C_2H_5)_2.$$

Diamines have been acylated with substituted salicylic acids in dimethylformamide in the presence of ethyl chloroformate and triethylamine at room temperature.[21]

When using carboxylic acids of high molecular weight the reaction is carried out with heating and under pressure.[22]

Carboxylic acid chlorides are most frequently used as acylating agents. Reactions are carried out both in aqueous alkaline medium by the Schotten-Baumann method and in anhydrous organic solvents.

An intermediate aminoamide in the synthesis of novocainamid is obtained by the Schotten-Baumann method,[23] sodium hydroxide is used as the hydrogen chloride acceptor.

A series of arylbenzamides[24] and amides of 2-thiophencarboxylic acid[25] has been obtained in the presence of alkali metal carbonates.

Acylation in organic solvents is frequently carried out in the presence of strong organic bases.[26–29]

However aminoamides contain a strongly basic centre (a tertiary amino group, as a rule) in the molecule and obviously this may serve as an acceptor of hydrogen chloride when obtaining them by the acylation of diamines. In this case the preparation of the hydrochlorides of these compounds in one stage has proved possible.

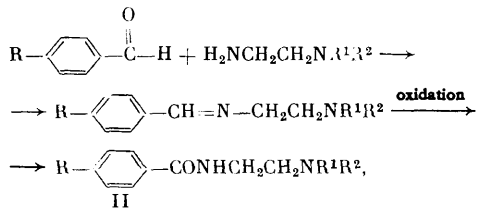
$$H_2N(CH_2)_nNR_2 + ArCOCl \longrightarrow ArCONH{-}(CH_2)_n{-}NR_2\cdot HCl.$$

The hydrochloride of *N*-(2-diethylaminoethyl)-*p*-nitrobenzamide was obtained from 2-diethylaminoethylamine and *p*-nitrobenzoyl chloride.[24] Aminoamides have also been obtained as hydrochlorides in dry chloroform[30] and dry ether.[31]

The acylation of diamines by the action of acetonitrile and water in the presence of sulphur or a catalyst generating sulphur in the reaction has been described.[32]

$$NH_2{-}(CH_2)_n{-}NR_2 + CH_3CN + H_2O \xrightarrow{S} CH_3CONH(CH_2)_nNR_2.$$

The condensation of a diamine with an aromatic aldehyde has been used for the synthesis of aminoamides (II).[33] The target aminoamide was obtained by the hydrogen peroxide oxidation of the aminoimine formed in the first stage of the reaction.



$R = NO_2$, $NR^1R^2 = N$⟨⟩; $R = CH_3O$, $NR^1R^2 = N(C_2H_5)_2$;

$R = NO_2$, $NR^1R^2 = N(C_2H_5)_2$.

The most widespread methods of synthesising diamines are reduction reactions.

The reduction of amino compounds containing a nitro group is carried out with metals in the presence of mineral acid or by catalytic hydrogenation.

$$R_2N(CH_2)_nNO_2 \xrightarrow{M,\ H^{\oplus}} R_2N(CH_2)_nNH_2.$$

The manufacture of paramion, liothyronine, ethmozine, novocainamid, etc. may serve as examples of the industrial application of this method.[34,35]

The reduction of nitriles of aminoacids is carried out with hydrogen in alcoholic-ammonia solution over a rhodium catalyst.[35]

The reductive amination of aminocarbonyl compounds is carried out either catalytically or with formic acid in the presence of ammonia and the amines.

Reductive amination over a platinum catalyst or Raney nickel proceeds usually under mild conditions, but yields differ appreciably.[36] The limitation of this method is the presence in the carbonyl compound or amine molecule of readily reducible groups, such as NO_2 or a double bond. Reductive amination by the Leuchardt reaction proceeds under fairly drastic conditions. Ammonium formate, formamide, and mixtures of them are used as aminating agents.[36] Best results are obtained in this reaction using a mixture of formamide with ammonium formate, occasionally with the addition of 90% formic acid.[37] The reducing action of formamide is enhanced in acidic media, better use is made of the ammonia formed in the reaction and the probability of side reactions occurring is reduced.[38]

$$RCO(CH_2)_nNR_2^1 + 2HCOONH_4 \longrightarrow RC(NHCHO)(CH_2)_nNR_2^1 + 2H_2O$$

$$+ NH_3 + CO_2 \longrightarrow RCH(NH_2)(CH_2)_nNR_2^1.$$

Diamines may be obtained from dibasic alcohols, dihalogen derivatives or halo-amines by a substitution reaction.[35]

Hydrolysis of urethanes or aminoamides is most frequently used.[35]

$$R_2N(CH_2)_nNHCOR^1 \longrightarrow R_2N(CH_2)_nNH_2.$$

In addition diamines are obtained by the interaction of aminoketones with hydroxylamine with subsequent reduction of the resulting amino-oxime.[39]

$$RCO(CH_2)_nNR_2^1 \xrightarrow{HONH_2} HON{=}C(R){-}(CH_2)_nNR_2^1 \xrightarrow{[H]} R{-}CH(NH_2){-}(CH_2)_nNR_2^1.$$

The synthesis of diamines has been described from ketonitriles through oximes by reduction with lithium aluminium hydride in absolute ether.[40]

$$RCO{-}(C)_n{-}CN \longrightarrow R{-}C(HO{-}N){-}(C)_n{-}CN \longrightarrow R{-}CH(NH_2){-}(C)_nNH_2.$$

Aminoamides may also be obtained by the action of primary or secondary amides on an amino-containing compound.[41] The similar reaction with amides proceeds with great difficulty and at increased temperature 170–180 °C, but on the other hand, with urea it proceeds readily and in high yield.[42]

$$RCONH_2 + X(CH_2)_nNR_2^1 \longrightarrow RCONH(CH_2)_nNR_2^1,$$

$X = OH$, Cl.

The addition reaction of acid amides to *N*-vinylamines leading to the formation of aminoamides is known.[43]

$$RCONH_2 + CH_2{=}CH{-}NR_2^1 \longrightarrow RCONHCH_2CH_2NR_2^1.$$

One of the most promising methods of obtaining branched aminoamides is the reaction of aminoalcohols with nitriles in the presence of strong mineral acid (Wieland-Ritter reaction),[44–46] which is widely used in the synthesis of various *N*-substituted amides and nitrogen-containing heterocycles.[47–48]

In addition to 100%[49] and fuming[50–52] sulphuric acid the following may be used as catalysts in the Ritter reaction: 85–96% sulphuric acid,[53–54] phosphoric acid,[55] benzene-sulphonic acid,[56] dichloroacetic acid,[57] toluene-*p*-sulphonic acid,[57] cyclohexane-sulphonic acid,[58] 90% formic acid,[58] 20% solution of sulphuric acid in glacial acetic acid,[59] 10% aqueous solution of hydrogen fluoride,[60] a mixture of concentrated sulphuric and formic acids,[61] and a mixture of sulphuric and phosphoric acids.[62]

The nature of the catalyst proves to have an appreciable influence on the temperature at which reaction occurs. When using sulphuric acid heating of the reaction mixture at 40–80 °C is required,[59,63,64]

but use of formic acid requires a boiling reaction mixture.[58] Depending on the nature of the reacting components the synthesis may be conducted at both low temperature (0 °C) and on heating to 90–175 °C under pressure.[66]

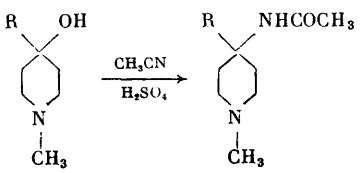
Acetic acid and dibutyl ether are frequently used as solvents in the Wieland-Ritter reaction.[63] The yield of amide is significantly reduced when using formic acid, dioxan, carbon tetrachloride and hexane, and in methyl and ethyl alcohols the reaction does not go at all (Table 1).[67]

Table 1. Influence of solvent on the yield of acrylic acid *N*-t-butylamide.

Solvent	Reaction time, h	Yield of amide, %
Acetic acid	16	98.4
Dibutyl ether	15	86.0
p-Dioxan	24	78.0
Methanol or ethanol	24	0

Ritter and co-workers and also other investigators have described the reaction of olefins and alcohols with various nitriles. Apart from aliphatic[60,66] and aromatic nitriles[45,57] nitriles of dibasic acids such as maleic, adipic, malonic, terephthalic and other acids are widely used in the Ritter reaction.[61] It should be noted that this reaction has been used in a very limited manner until recently for obtaining aminoamides.

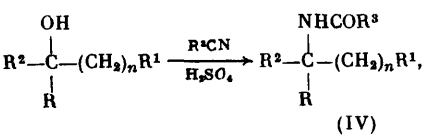
There are definite data in the literature only on the preparation of aminoamides from 1-phenyl-3-piperidino-propanol,[68] diphenyl-(2-piperidylethyl)carbinol[69] and other heterocyclic aminoamides (III).[70]



(III)

R = CH_3, C_2H_5, C_4H_9.

A series of studies has been carried out on the preparation of aminoamides (IV) with various lengths of the methylene chain between the functional groups and with various substituents on nitrogen and in the main chain.[71–77]



(IV)

R = H, CH_3, C_2H_5, C_4H_9, R^1 = $NHCH_3$, NHC_2H_5, NHC_3H_7, NHC_4H_9, NH–⬡, $NHCH_2C_6H_5$, $N(CH_3)_2$, $N(C_2H_5)_2$, N⬡, N⬡O;

R^3 = CH_3, C_2H_5, C_4H_9, C_6H_5; R^3 = H, CH_3, $CH{=}CH_2$, C_6H_5, $CH_2C_6H_5$, $OCH_2C_6H_5$, $C_6H_4R^4$, n = 1–8.

Optimum conditions have been established for carrying out the reaction and it has been shown that in parallel with the main reaction product, viz. the *N*-substituted aminoamide, several side products are formed such as the unsubstituted amide and unsaturated compounds. The structure of the alcohol and especially the character of the susbtituents on the carbonyl carbon atom have a significant influence on the composition of the resulting reaction products. The reaction occurs fairly smoothly with secondary aminoalcohols with 50–70% main product and 15–20% olefin. However replacement of R = H with R = C_2H_5 leads to an increase in the side reaction. Diphenylcarbinols are converted into unsaturated compounds in yields of 70–80%. The influence of the length of the hydrocarbon chain of the aminoalcohol on the yield of the reaction proved to be much weaker (Table 2).[71–73]

The behaviour of nitriles in the Ritter reaction varies depending on their structure. Thus hydrocyanic acid, acetonitrile and benzyl cyanide give amides with both tertiary and secondary alcohols, but benzonitrile and phenoxyacetonitrile react only with secondary aminoalcohols and unsaturated compounds are formed in the remaining cases (Table 3).[74–77]

Table 2. Dependence of yield (as %) of aminoamides (IV) on structure of the initial aminoalcohol (R^2 = C_6H_5, R^3 = CH_3).

R	R^1 $N(CH_3)_2$			$N(C_2H_5)_2$		NC_5H_{10}	NC_4H_8O
	n 1	2	3	1	2	2	2
H	73	67	49	60	63	59	52
C_2H_5	26	25	25	43	29	23	22

Table 3. Dependence of yield (as %) of aminoamides (IV) on the nature of the nitrile [R = $N(CH_3)_2$, R^2 = C_6H_5; n = 2].

R	R^3				
	H	CH_3	C_6H_5	$CH_2C_6H_5$	$CH_2OC_6H_5$
H	52	67	42	42	22
C_2H_5	62	25	0	51	0

The aminoalcohols used in the Wieland-Ritter reaction may be synthesised by various methods.[78–79]

The most widespread means of synthesising aminoalcohols is the interaction of aminoketones and aminoaldehydes with Grignard reagents or by reduction. Variation of these reactants leads to the preparation of primary, secondary and tertiary alcohols. Reduction of aminoketones and aminoaldehydes is effected by catalytic means (platinum and palladium are usually used as catalysts). Reactions are carried out as a rule in alcohol or in aqueous alcohol solution,

mostly at room temperature and atmospheric pressure. The reduction products, viz. primary and secondary aminoalcohols, are formed in good yield. Hydrogenation in the presence of a nickel catalyst is used relatively rarely, since in this case increased pressure and high temperature are necessary.[78]

Lithium aluminium hydride and sodium borohydride are also used as reducing agents.[79] The present method enables reduction of aminoketones without preliminary purification which is accompanied by partial decomposition of the latter.

2. Synthesis of aminoamides by amination of amide-containing compounds

The most widespread example of this approach to the synthesis of aminoamides is the amination of amidoalcohols[80] which is carried out in aqueous solution at 100 °C or in glacial acetic acid at 75 °C.

$$R{-}CONH{-}\underset{|}{\overset{|}{(C)_n}}{-}OH + R_2^1NH \longrightarrow RCONH{-}\underset{|}{\overset{|}{(C)_n}}{-}NR_2^1.$$

It has been established[80] that monoamides are formed by this scheme only when using secondary amides. With primary amines the reaction does not stop at the stage of forming a monoaminoamide but goes further giving bis-aminoamides.

$$RCONHCH_2OH + H_2NCH_3 \longrightarrow (RCONHCH_2)_2NCH_3,$$
$$R = C_6H_5,\ C_6H_5CH_2,\ C_6H_5C_3H_6.$$

Acylketimines[81] and *N*-α-haloalkylamides[82] are also subject to amination.

$$RCON{=}CAr_2 \xrightarrow{R_2^1NH} RCONHC(NR_2^1)Ar_2,$$
$$RCONHCHXR^1 + R_2^2NH \longrightarrow RCONHCH(NR_2^2)R^1.$$

A method has been described for obtaining aminoamides from aminonitriles[83] by acylation of the latter and subsequent reduction over Raney nickel.

$$Ar{-}\underset{|}{\overset{|}{CH}}{-}NH_2 \xrightarrow{RCOCl} Ar{-}\underset{|}{\overset{|}{CH}}{-}NHCOR \xrightarrow[Ni]{[H]} Ar{-}\underset{|}{\overset{|}{CH}}{-}NHCOR.$$
$$\quad\ CN \qquad\qquad\qquad CN \qquad\qquad\qquad\quad CH_2NH_2$$

3. Synthesis of aminoamides by the aminomethylation of acid amides

The most widely used method of synthesising aminomethylamides (V) is by condensation of primary amides with formaldehyde and amines.

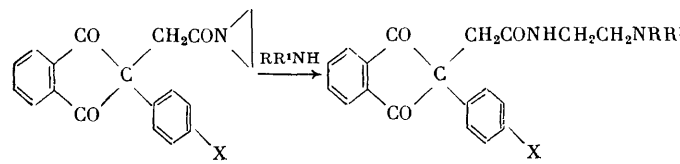
$$RCONH_2 + CH_2O + NHR_2^1 \longrightarrow \underset{(V)}{RCONHCH_2NR_2^1}.$$

Condensation is carried out by the usual conditions for the Mannich reaction. It was established that the yield of aminoamide depends to a significant degree on the acidity of the amides and the basicity of the reacting amine.[82] The yield of aminoamide fell from 53% to 0 with an increase in pK_a of the corresponding amide from 1.25 for dichloroacetic acid amide to 4.27 for *m*-toluic acid amide. Such weak bases as aniline (pK_a 4.58), methylaniline (pK_a 4.85) and *o*-toluidine (pK_a 4.39) did not react. The yield of aminoamide reached 50% when using *N*-t-butylamine.

In addition to formaldehyde aromatic aldehydes may be used in the condensation. In this case aliphatic-aromatic aminomethylamines are obtained.

$$Ar{-}CONH_2 + Ar^1CHO + HNC_5H_{10} \longrightarrow ArCONHCH(Ar^1)NC_5H_{10}.$$

A method has been described for the synthesis of aminoamides through acid *N*-ethylenimides.[84] The *N*-ethylenimides having electron-accepting substituents on the nitrogen atom (so-called 'activated' *N*-ethylenimides) readily break the aziridine ring on reaction with amines.[85]



It follows from an analysis of the data mentioned above that the majority of methods of obtaining aminoamides are not universal. This is linked either with limitations peculiar to one or other synthetic method or to the availability of starting materials. Thus aminoamides with branched carbon atoms at the amide group but with a short methylene chain between the functional groups are synthesised by the aminomethylation of acid amides. Branched aminoamides with the most varied methylene chain length are obtined by amination of amide-containing compounds, but here there is a limitation linked with the use of secondary amines only. Aminoamides with a tertiary carbon atom at the amide group are obtained by the acylation of diamines. However in this case the main synthetic complexities are linked with the obtaining of unsymmetrically substituted *N*-t-alkyldiamines.

Of the existing methods the most promising is the Wieland-Ritter reaction for the synthesis of aminoamides with a branched carbon atom on the amide group and any length of methylene chain between the amide and amine groups.

III. Reactivity of aminoamides

The most important feature of the structure of *N*-substituted aminoamides is their bifunctionality which undoubtedly shows up in all the properties of these compounds whether it be salt formation,[10,86] oxidation by peroxides at the amino group[7] or reduction[87] and hydrolysis of the amide group.[88] However there is special interest in those properties of aminoamides in which this influence is clearly shown and may be determined quantitatively. It seemed expedient to consider these in more detail.

It is known that all the properties of amino-containing compounds are determined primarily by their basicity. This depends on the electron density at the nitrogen atom, its steric accessibility and is extremely sensitive even to a small change in structure. Undoubtedly the basicity of aminoamides $RCONH{-}\underset{|}{\overset{|}{C}}{-}(CH_2)_nN\diagup\diagdown$ (VI) depends on the presence of the amide group, the character of the environment of the amino group and on the removability of the polar amide group.

In the general case several factors may influence the basicity of the resulting aminoamide on introducing an amide group into an amine molecule:

a) displacement of electron density to the amide group along the carbon chain (inductive effect, independent of steric obtacles and conformation) and the direct mutual interaction of the amino and amide groups through space (polar effect);

b) formation of an intramolecular hydrogen bond binding the unshared electron pair of the nitrogen atom;

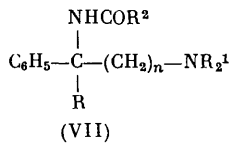
c) increase in the steric obstacles for conversion of the trigonal nitrogen atom into tetrahedral and in the steric difficulties of solvation;

d) formation of a hydrogen bond in the ammonium ion thereby stabilising it;

e) increase in the solvation of molecules due to the appearance of new polar groups.

Factors (a–c) must cause a reduction in the basicity of aminoamides in comparison with simple amines and factors (d–e) an increase. The overall result is determined by their relationship. Data of several studies[89–93] indicate a reduction in the basicity of aminoamides in comparison with the simple amines which indicates the predominant influence of factors (a–c).

Analysis of the data on the basicity of *N*-substituted aminoamides

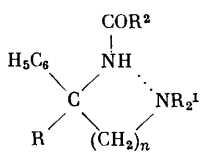


(VII)

in ethanol using correlation equations[92,94] enabled determination of the relationship of effects (a–c).

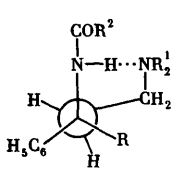
A good correlation was observed[94] between the pK_a values of aminoamides with the inductive constants σ for the influence of substituents.[95] This indicates that in amphoteric strongly solvating solvents aminoamides are in a free, open conformation and all the factors, except the inductive, are of little significance. The influence of the amide group (as for other substituents) is transmitted mainly along the chain of σ-bonds.

In aprotic non-solvating solvents (nitrobenzene, carbon tetrachloride, etc.) aminoamides exist in a folded cyclic conformation with a contiguous disposition of functional groups, stabilised by a hydrogen bond.[96–98]



Quantitative assessment of the stability of such a bond[97] showed that the latter is proportional to the number of CH_2 groups between the amine and amide groups, i.e. on transition from a 5- to a 6- or 7-membered ring the stability of the hydrogen bond was increased. This phenomenon is explained by the change in N–H...N angle, approaching 180° in a 7-membered ring which corresponds to maximum bond strength.

The introduction of a bulky substituent into the α-position to the amide group (R = C_2H_5) leads to strengthening of the hydrogen bond as a result of repulsion between R and $CH_2NR'_2$ and maximum approach of the NH and $CH_2NR'_2$ groups.

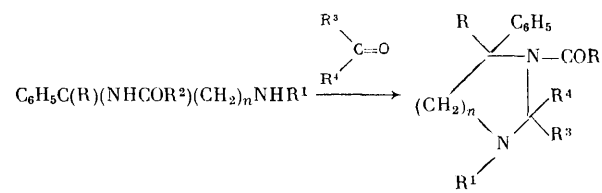


Due to the presence of two polar groups, an amide and an amine, in the aminoamide molecule they are able to form complexes differing in constitution and structure with metals.[99–100]

The complex-forming ability of *N*-lauroylethylenediamine with transition metals has been studied,[101] as has the ability of *N*-picolinoylethylenediamine to form complexes with copper.[102] It was shown with the aid of potentiometric titration and absorption spectra that in similar compounds the metal is bound both with the amide and with the amino group. Most probably the amide group is bound through nitrogen as a result of deprotonation and partially through the carbonyl oxygen.

Investigations have been carried out on the complex-forming ability of several aliphatic-aromatic aminoamides (IV) with Cu, Co and Ni.[103] An analysis of the data obtained was conducted with the aid of correlation equations and enabled an assessment of the contributions of both polar groups to the ability of aminoamides to form complexes with these metals. It was concluded that aminoamides form chelate complexes with transition metals, i.e. both functional groups participate in this process. Furthermore, from the data obtained it proved to be possible to select compounds from the whole series with a high complex-forming ability for use as extractants of non-ferrous metals.[103]

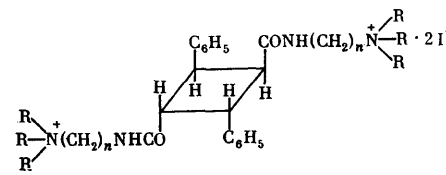
Due to the presence of the amide and amine groups the *N*-substituted aminoamides are capable of cyclisation with aldehydes and ketones with the formation of imidazolidines and hexahydropyrimidines.[104,105]



IV. Biological action of aminoamides

Aminoamides display various physiological activities. Among them substances are known which possess cholinolytic[106] and spasmolytic,[107] hypotensive,[108] antifibrillating[109] and curare-like[110] effects.

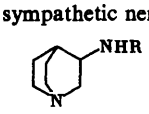
Investigations have shown that on transition from amides of monocarboxylic to dicarboxylic acids the curare-like action of compounds is increased.[110] The nature of the dicarboxylic acid plays an important role. Thus in difference to bis-aminoamides of dibasic alkylcarboxylic acids,[10] bis-aminoamides of α-truxilic acid of the type



possess significantly more marked curare-like activity.[111]

It is possible to name aminoamides which are antibiotics (morphocycline),[112] display insecticidal[112] and bactericidal[113,114] properties and also fungicidal[12] and antiviral[115] effects.

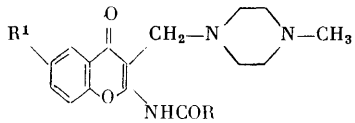
Study of 3-hydroxy- and 3-aminoquinuclidines (VIII)[116] showed that they show a ganglion-blocking action on the parasympathetic and sympathetic nervous systems.



(VIII)

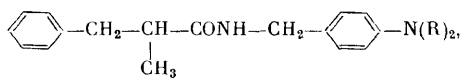
R=COC_6H_5; $COC_6H_4NH_2$.

Derivatives of 2-acylaminochromones[117] show a stimulating action but display high toxicity.



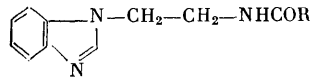
$R = OC_2H_5$, $R^1 = H$; $R = CHCl_2$, $R^1 = H$; $R = CCl_3$, $R^1 = H$; $R = C_6H_5$, $R^1 = H$; $R = OC_2H_5$, $R^1 = Cl$.

Aminoamides of β-phenylisobutyric acid have been synthesised in the search for new neurotropic agents.[118] In physiological action they proved to be antagonists of amphetamine and significantly potentiated the hypnotic effect caused by chloral hydrate and sodium amobarbital. The duration of amobarbital hypnosis was increased along the series $CH_3 \rightarrow C_2H_5 \rightarrow n\text{-}C_3H_7$.

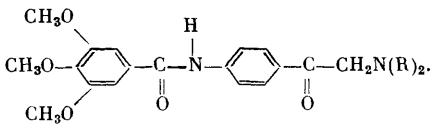


$R = CH_3$; C_2H_5; $n\text{-}C_3H_7$.

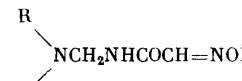
Several acyl derivatives of 1-(2-aminoethyl)benzimidazoles possess weak sedative and antiserotonin activity.[119]



The α-amino derivatives of 4-(3,4,5-trimethoxybenzoylamino)-acetophenone are stimulants and depressants of the central nervous system.[120]

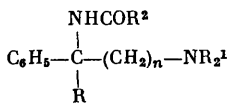


Amides of oximinoacetic acid are active reactivators of cholinesterase.[121] In many cases they are more active than their methiodides.



$R = R^1 = CH_3$; $R = R^1 = H$; $R = H$; $R^1 = CH_3$; $R = R^1 = C_2H_5$; $RR^1N = (CH_2)_4N$; $(CH_2)_5N$.

Introduction of a second quaternary ammonium group strengthens the reactivating properties to cholinesterase. Amides are more stable than esters in aqueous media and show a therapeutic action on contamination of animals by organophosphorus compounds (fosfakol). Compounds with a tertiary amino group are capable of penetrating the blood-brain barrier and show a pharmacological action on the central nervous system. In addition certain aliphatic-aromatic aminoamides display anticholinesterase properties.

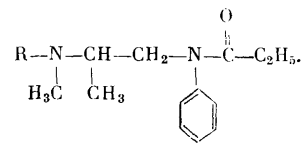


$R = H$, C_2H_5; $R^1 = CH_3$, C_2H_5, C_3H_7, C_4H_9; $R^2 = CH_3$, $CH_2C_6H_5$, C_6H_5; $n = 1$ to 8.

It was shown[122] that these compounds are reversible inhibitors of cholinesterase and their activity depends to a significant extent on the bifunctionality, the character of the amide and amine groups, the branching of the main chain and the distance between the functional groups.

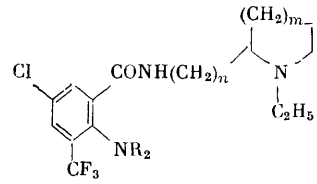
Analgesic activity became apparent when investigating a series of amides of benzilic, diarylglycollic and substituted benzoic acids. It was established that the anaesthetising action depends on the character of the radicals on the tertiary nitrogen atom and on the number of methylene groups between the nitrogen atoms. Enhancement occurs on introducing a methyl group into the amide.[123]

The analgesic activity of compounds (IX) depends on their configuration.[124] It was shown that the (+) (*S*)-isomer was more active than the (–) (*R*)- and (±)-isomers. This indicates that analgesics of the methadone type vary in the form of their bonding with receptors.



(IX)

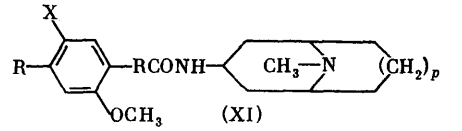
Antitubercular[125] and antibacterial[126] properties have also been described for some aminoamides. Some compounds of this class of chemical susbtances are applied in stomatological practice for the prevention of deposits on teeth.[7] There are several reports on the use of aminoamides as preparations with a wide spectrum of biological action. Thus benzamides (X) are used as antiemetic and antiulcer preparations and also as anticonvulsants and neuroleptics.[127]



(X)

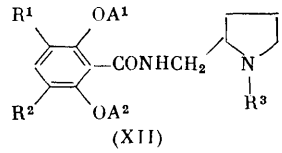
$n = 1.2$; $m = 1.2$.

It has been pointed out that azabicycloalkylbenzamides (XI) may find use in the treatment of arrhythmia, migraine, neuralgia, disturbances of bowel motility, and as antiemetic agents.[128]



$R = NH_2$, acylamino; X = Cl, Br, alkylthio; $p = 0-1$.

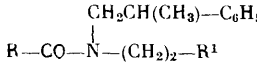
Benzamides (XII) possess psychotropic action and may be considered as potential drugs for psychiatric practice and also as antiemetic agents.[129,130]



(XII)

R^1, $R^- = H$, halogen; $R^3 = A^1 =$ lower alkyl; $A^2 = (C_1-C_6)$ acyl.

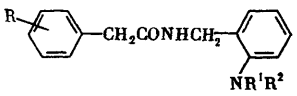
Compounds (XIII) proved to be depressants and analeptics.



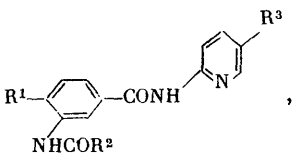
(XIII)

R = CH_3, *p*- and *o*-$CH_3OC_6H_4$; 3,4,5-$(CH_3O)_3C_6H_3$; R^1 = 2- or 4-pyridyl, 2- or 4-alkylated 2-pyridyl.

Diaklylaminoethylanilides[131] synthesised in the search for antihypertensive preparations proved to be active in the treatment of arrhythmia, migraine, hypertonia and glaucoma. Monoalkylated amides of phenylacetic acid[131,132] reduce blood sugar content and may find use in the treatment of diabetes.

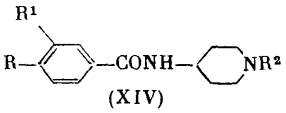


Aminoamides containing a pyridine ring may find use in stomatology.[133]



where R^1 = H, CH_3, OCH_3; R^2 = branched or unbranched C_2-C_8 alkyl, substituted or unsubstituted phenyl; R^3 = H, C_1-C_4 alkyl in various positions.

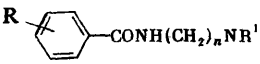
Benzamidopiperidines (XIV) display local anaesthetic and analgesic activity, they are used as antiemetic preparations, tranquilisers, and also in the treatment of diseases of the gastrointestinal tract.[6]



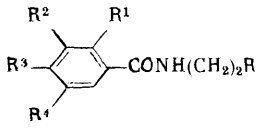
(XIV)

R = H, OCH_3, $NHCOCF_3$, $NHCOCH_2Cl$, R^1 = Cl, H, SO_2NH_2, CH_3SO_2NH, OCH_3; R^2 = H, *p*-$FC_6H_4CO(CH_2)_3$, CH_2CH_3.

Substituted anthranilamides are used as analgesics, antiulcer and antiinflammatory agents.[134]



N-Substituted benzamide derivatives (XV) possess a combination of analgesic, spasmolytic and antiemetic activity.[135]



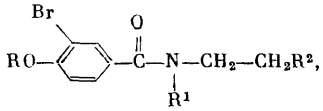
(XV)

R = $N(C_2H_5)_2$, $R^3 = NO_2$, $R^1 = R^2 = R^4 = H$; R = $N(C_2H_5)_2$, R^1 = Cl, $R^2 = R^3 = R^4 = H$; R = $N(C_2H_5)_2$, $R^1 = R^4 = H$, $R^2 = R^3 = CH_3O$; R = NC_5H_{10}, $R^1 = R^2 = R^4 = H$, $R^3 = NO_2$.

The local anaesthetic activity of aminoamides has been studied widely.[136–139] Amides of heterocyclic acids have been studied in most detail,[140,141] to which group the known anaesthetic Sovcaine (dibucaine, cinchocaine) belongs. The activity of these compounds as a rule is increased on introducing a bulky alkyl group into the aminoamide molecule.[141] It is necessary to record that amides of 3-alkoxycinchoninic acid, unlike 2-alkoxy derivatives, do not display anaesthetic activity,[140] which probably indicates the influence of the geometry of the molecule on the physiological properties of the amides.

Alkyl and alkoxy groups aid the development of the pharmacological activity indicated not only in the series of Sovcaine analogues but also among amides of substituted benzoic acids previously considered to have little promise for practical application as drugs.[141] However di- and trimethylbenzamides proved to be effective.[142] The anaesthetic activity of *o*-alkoxy-, especially *o*-butoxy-,[138–143] and also *o*-benzoyloxybenzamides[144] is close to the activity of xylocaine. Compounds containing substituents in the *para*-position are usually less active but some of them are used in medicine because of their low toxicity.[145]

The use of aminoamides with a tertiary nitrogen atom in the amide group (XVI) has been described.[146,147]



(XVI)

R = CH_3, R^1 = H, $R^2 = N(C_2H_5)_2$; R = CH_3, $R^1 = CH_3$, $R^2 = N(C_2H_5)_2$;

R = CH_3, R^1 = H, $R^2 = NC_5H_{10}$, R = CH_3, $R^1 = CH_3$, $R^2 = NC_5H_{10}$;

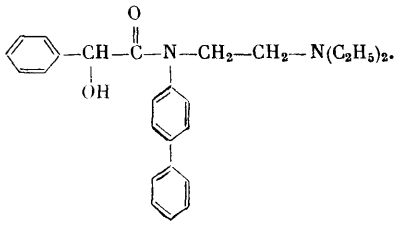
R = C_2H_5, R^1 = H, $R^2 = NC_4H_8O$;

R = C_2H_5, R^1 = iso-C_3H_7, $R^2 = NC_4H_8O$.

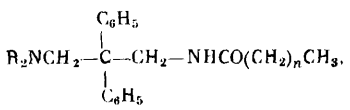
It was established that such compounds display enhanced pharmacological activity compared with compounds with a secondary nitrogen atom. In particular an increase in local anaesthetic and analgesic action was observed for aminoamides with an alkylated nitrogen atom in the amide group (XVI) (R^1 = CH_3, iso-C_3H_7) in comparison with compounds (XVI) (R^1 = H), in which the nitrogen atom is secondary.[146]

This tendency was more marked in aminoamides with *p*-butyloxy- and *p*-amyloxy- than with *p*-methoxy- and *p*-ethoxy-substituents in the phenyl ring. However the toxicity of compounds was not reduced by this.[146]

Arylation of the amide group also increases anaesthetic activity. It is asserted that the following compound is a strong anaesthetic.[147]

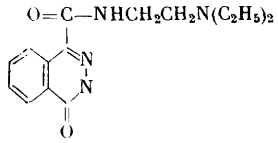


The local anaesthetic activity of γ-dimethylaminodiphenylpropylamides of acetic, propionic and butyric acids has been described.[148]

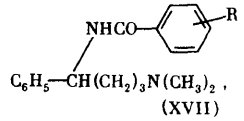


n = 0, 1, 2.

Aminoamides of 4-phthalazone-1-carboxylic acid possess high local anaesthetic activity at low toxicity.[149]



Dimethylaminobutylamides of substituted benzoic acids (XVII) proved to be extremely effective.[150]

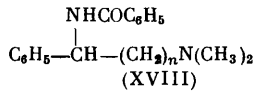


(XVII)

R = H, *p*-CH_3, *m*-NO_2, *p*-Cl, *p*-NH_2.

It was established that the local anaesthetic action of amides depends on the character of the substituent in the benzene ring. Compounds with R = *p*-CH_3 and *m*-NO_2 proved to be most effective and long-acting substances with low toxicity.

An important factor influencing the local anaesthetic activity of aminoamides is the distance between the amide and amino groups. The influence of the number of methylene groups between the nitrogen atoms on conduction, infiltration and terminal anaesthesia of benzamides (XVIII) has been investigated.[151]

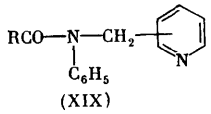


(XVIII)

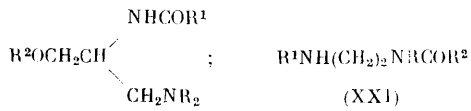
$n = 1$—6.

It was shown that there were maxima of local anaesthetic activity at n = 3, 4 and 6.

Among other active aminoamides it is possible to mention 4-alkoxyphthalimides,[152] 3,3-diphenylacrylamides,[153] amides (XIX),[154] (XX)[155] and *N*,*N*-disubstituted monoacylated ethylenediamines (XXI).[156]

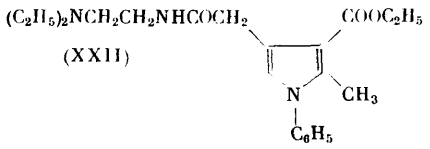


(XIX)



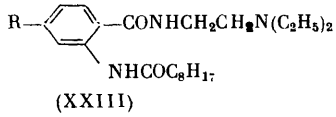
(XX) (XXI)

Preparation (XXII) is of interest, containing in its structure an aminoamide and an aminoacid ester, causing rapid, stable and extended anaesthesia.[157]



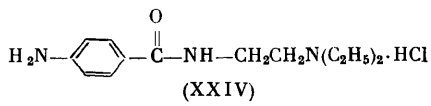
(XXII)

Diamide (XXIII) exceeds novocaine in local anaesthetic activity 200-fold.[158]



(XXIII)

Among other biologically active aminoamides it is possible to mention novocainamid (XXIV) (the β-diethylaminoethylamide of *p*-aminobenzoic acid).[112] It is close to novocaine in chemical structure. Novocainamid also has a similarity to novocaine in pharmacological properties and displays local anaesthetic activity.

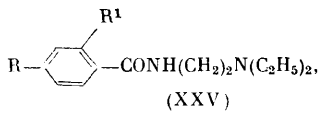


(XXIV)

However the most distinctive feature of (XXIV) is its ability to reduce the excitability of the myocardium and to retard the transmission of a nervous impulse in heart muscle and also to suppress the formation of impulses in ectopic foci of excitation. It is significantly more active than novocaine in this respect. The increased stability of novocainamid *in vivo* is explained by its slow breakdown to novocaine by blood plasma enzymes. It is also less toxic than novocaine. Novocainamid is used in various disorders of cardiac rhythm, viz. the paroxysmal form of ciliary arrhythmia, paroxysmal tachycardia, extrasystolia and other forms of rhythm disturbance. It is used for the prevention and treatment of disorders of cardiac rhythm in operations on the heart, large vessels and lungs.[112]

The (XXIV) molecule has been modified with the aim of increasing activity and reducing toxicity. All parts of the molecule have been changed, viz. the aromatic ring and its substituents, the length and branching of the hydrocarbon chain and the substituents on the nitrogen atom.

Replacement of the amino group in novocainamide (XXIV) by chlorine or an ethoxy group leads to loss of antiarrhythmic activity.



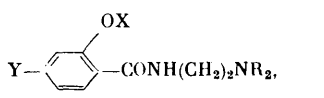
(XXV)

R = NH_2, OC_2H_5, Cl, $NHCOCH_3$; R^1 = Cl, H

Compounds (XXV) (R = NH_2, OC_2H_5, R^1 = Cl) possess an antiemetic action but the *ortho*-chloro derivative (XXV) (R = NH_2, R^1 = Cl) is active,[26,159] and also displays local anaesthetic activity more than 4 times greater than the activity of novocainamid (XXIV).[27] *N*-Acylated novocainamid (XXV) (R = $NHCOCH_3$, R^1 = H) is an active metabolite of novocainamid[160] and interrupts arrhythmia caused by aconitine.

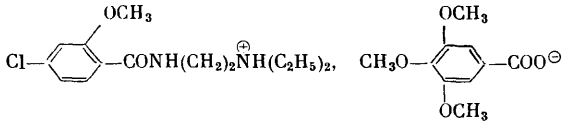
On replacing the NH group in the (XXIV) molecule by a nitro or hydroxy group the antiarrhythmic activity is reduced.[28] The introduction of a methoxy group into the phenyl ring significantly increases the antiarrhythmic effect. 3,4,5-Trimethoxy-*N*-(2-diethylaminoethyl)benzamide is 4 times more active than novocainamid.[29]

Derivatives of salicylamide are active antiarrhythmics.

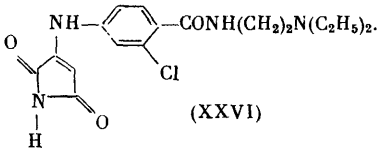


X = H, alkyl; Y = H, Cl, Br; R = alkyl.

The most active of these compounds is the 3,4,5-trimethoxybenzoate salt of 4-chloro-2-methoxy-*N*-(2-diethylaminoethyl)benzamide.[161].

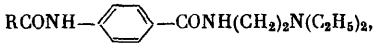


Compound (XXVI), in which nitrogen is alkylated by substitution with a dehydropyrrolidinedione, is also more active than novocainamid.[162]



(XXVI)

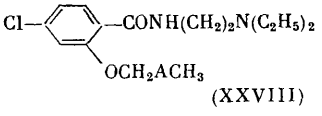
Several derivatives (XXVII) were obtained by acylation at nitrogen. Of this series the acyl derivative with R = CH_2CH_3 shows the greatest activity in calcium chloride arrhythmia.[163]



(XXVII)

R = $ClCH_2$, Cl_2CH, CH_2CH_3, $C(CH_3)_3$, $CH(CH_3)_2$, $CH_2CH_2CH_3$.

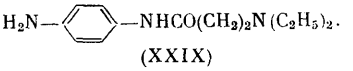
Novocainamid derivatives (XXVIII) are used for stopping vomiting caused by chemotherapeutic preparations.[164]



(XXVIII)

A = CHOH, C = NOH, C = $NOCH_3$.

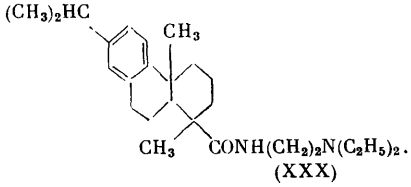
ortho-Methylation significantly increases antiarrhythmic activity.[165] Inversion of the amide group (XXIX) leads to loss of activity.[165]



(XXIX)

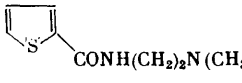
Replacement of the phenyl ring in the novocainamid molecule leads to the preparation of new compounds with various biological activities.

Compound (XXX) displays activity in strophanthin arrhythmia.[166]



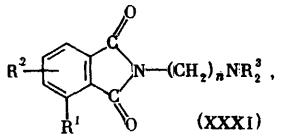
(XXX)

The thiophen analogue of novocainamide shows analgesic and spasmolytic activity.[25]



Analogues of novocainamid are known in which the benzene ring is replaced by another aromatic ring, such as quinoline.[167]

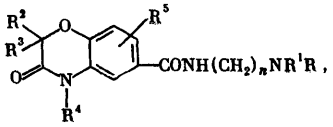
Phthalimides (XXXI) also display antiarrhythmic activity.[168,169] The most active is the compound with $n = 4$, $R^3 = C_2H_5$.



(XXXI)

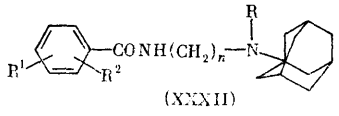
R^1 = H, *o*-alkyl; R^2 = *o*-, *p*-, *m*-NHR^4.

Amides of 1,4-benzoxazinecarboxylic acid, which are novocainamid derivatives, display marked antiarrhythmic properties.[170]



where NRR^1 = piperidino, morpholino, 4-*m*-tolyl-1-piperazine.

N-(Adamantylaminoalkyl)benzamides (XXXII) prevent ventricular fibrillation caused by chloroform.[30] They are less toxic than procainamide.

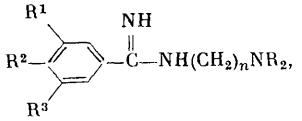


(XXXII)

R = H, C_2H_5; $n = 2, 3$; R^1 = H, Cl, CH_3; R^2 = NH_2, NO_2.

Compound (XXXII) (R = C_2H_5, R^1 = H, R^2 = *p*-NH_2, n = 2) proved to be the most active. The influence of the surroundings of the tertiary nitrogen atom on the antiarrhythmic activity of compounds has also been investigated.[171] Replacement of ethyl groups by another radical (isopropyl) significantly reduces activity, while replacement of one ethyl by an aromatic group significantly increases it.

Compounds (XXXIII) contain a benzimido group.

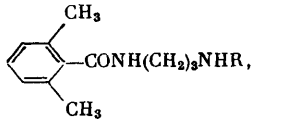


(XXXIII)

n = 2, 4; R = CH_3, C_2H_5 or NR_2 = 2-pyrrolidine; R^1 = H, CF_3, OCH_3; R^2 = H, CH_3, F, NO_2, NH_2, R^3 = H, OCH_3.

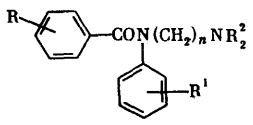
Of 28 *N*-substituted benzimidines synthesised 15 possess antirrhythmic activity, 4 compounds surpass novocainamid in activity and duration of action, display low toxicity and a weak cardiodepressant action.[172–174]

Aminoalkylpropylamides of 2,6-dimethylbenzoic acid interrupt tachycardia in dogs.[175]



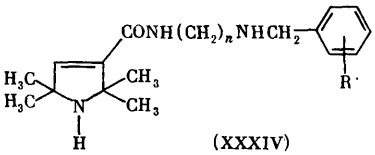
R = C_2H_5, $CH(CH_3)_2$, C_6H_5—CH—$(CH_3)CH_2$.

Benzamides substituted at nitrogen display antiarrhythmic activity.[176]



$n = 2, 3$; R = 3, 4, 5(OCH_3)$_3$, 2, 4,-(OCH_3)$_2$, 2-Cl;
R^1 = H, 2(4)-CH_3, 2(4)-C_2H_5;
NR_2^2 = morpholino, pyrrolidino, piperidino.

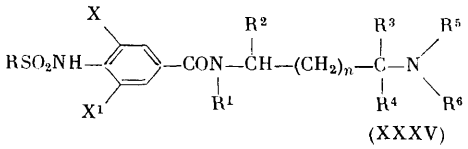
The antiarrhythmic activity of amides of tetramethylpyrrolidinecarboxylic acid (XXXIV) has been described.[177]



(XXXIV)

m = 2, 3; R = H, 4-Cl, 4-CF_3, 2-OCH_3, 2-OH, 4-OC_6H_5, 4-$OCH_2C_6H_5$ etc.

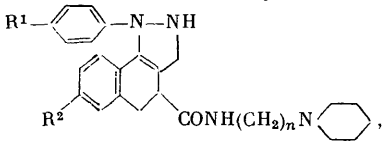
Some of them surpass quinidine in therapeutic index (aconitine arrhythmia model). Aminoamide (XXXIV) (n = 3 and R = $OCH_2CH{=}CH_2$) is 6.3 times more active than quinidine.[177] Substituted sulphonamidobenzamides (XXXV) display antiarrhythmic activity similar to that of novocainamid.[178,179]



(XXXV)

where X and X^1 = H, halogen; R^1, R^2, R^3, R^4 = alkyl, cycloalkyl, alkenyl; R = alkyl, cycloalkyl, benzyl, alkoxyl. Derivatives of (XXXV) containing a methanesulphonylamino group showed antiarrhythmic action of the cordarone type (class III antiarrhythmic preparations).[180] There is an indication of an increase in the duration of action of preparations (XXXV) in comparison with compounds containing an RSO_2 group (prolongation effect).[178]

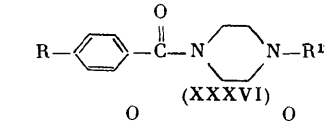
Aminoamides of 4,5-dihydrobenz[d]indazole-3-carboxylic acids are able to retard the ventricular tachycardia induced by aconitine.



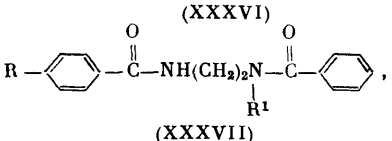
R^1 = H, CH_3O, F, Cl; R^2 = H, Cl, $(CH_3)_2N$, CH_3O; n = 2, 3.

A large group of aminoamides comprises compounds in which the tertiary nitrogen atom is linked with the amide function through a cyclic system.

Cyclic analogues of novocainamid (XXXVI) and diacyl derivatives of ethylenediamine (XXXVII) have been investigated.[181]



(XXXVI)

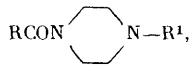


(XXXVII)

R = H, NH_2, NO_2, Cl, OCH_3; R^1 = C_2–C_5 alkyl.

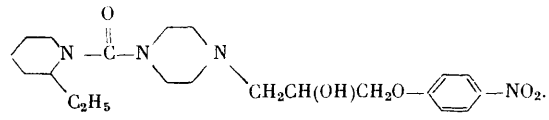
Replacement of the tertiary amino group in the novocainamid molecule by an amido group (XXXVII) leads to loss of antiarrhythmic action as does replacement of the amide and amino nitrogens by piperazine (XXXVI) R = NH_2, R^1 = C_2H_5. Derivatives (XXXVII) with R ≠ NO_2 display depressant activity. The action, like that of novocainamid, is displayed by compounds containing a chlorine atom (XXXVI) R = Cl.

Certain derivatives of piperazine display activity against the arrhythmia induced by adrenaline.[182]

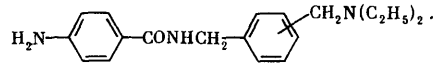


where R = 2-piperidinoethyl, $(C_6H_5)_2N$, 3,4,5-$(CH_3O)_3C_6H_2$. R^1 = phenoxy, piperidino, naphthoxy, 4-CH_3-piperidino, 2-hydroxypropyl, 3,4,5-$(CH_3O)_3C_6H_2CO$.

The most active compound is

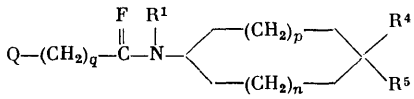


Cyclic analogues of novocainamid (XXXVIII) proved to be weakly active as antiarrhythmics, however *meta*- and *para*-derivatives are 45 and 37 times more active than novocainamid in local anaesthetic action.[183]



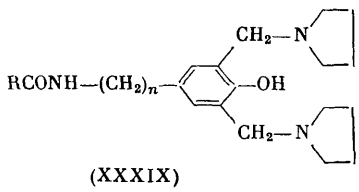
(XXXVIII)

Aminoamides containing saturated rings joining the amide and amino nitrogen atoms in the hydrocarbon chain may be potential antiarrhythmics.[184]



q = 0–4, p = n = (0–9); Q = 1-, 2-naphthyl, C_6H_3XY; R^1 = H, (C_1–C_3) alkyl; R^2 = H, (C_1–C_3) alkyl, branched alkyl; R^3 = alkyl, cycloalkyl; R^4 = H, OH, OCH_3, OC_2H_5, SH; R^5 = H, OH, (C_1–C_3) alkoxy; E = O or S; X = Y = halogen, C≡N, C_6H_5.

Substituted phenols (XXXIX) disclose antiarrhythmic activity and show action on the parasympathetic nervous system.[185]

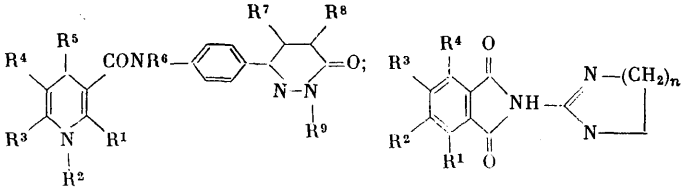


(XXXIX)

R = substituted phenyl or thienyl; n = 0 or 1.

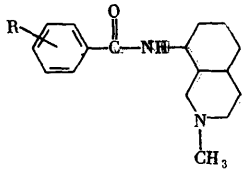
A correlation between antiarrhythmic activity and action on the nervous system was observed for this class of compounds.

Substituted amides of dihydropyridinecarboxylic acids (XL)[186] and phthalimides (XLI)[187] show antiarrhythmic activity in animal experiments.



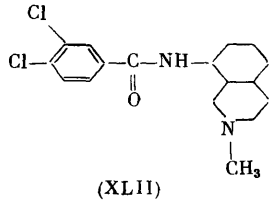
(XL) (XLI)

Certain derivatives of 5-, 6-, and 8-substituted 2-methyldecahydroquinolines surpass quinidine in anti-arrhythmic activity and therapeutic index.[188,189,167]



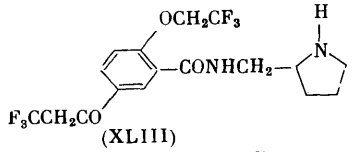
R=H, 4-Cl, 3,4-Cl_2, 4-OCH_3, 3,4-$(OCH_3)_2$, 3,4,6-$(OCH_3)_3$.

The most active compound is *cis*-(XLII), which is more than 2 times as active as quinidine, *trans*-(XLII) surpassed quinidine by almost 4 times in therapeutic index.

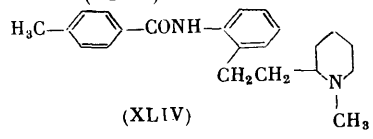


(XLII)

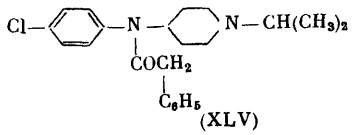
Study of cyclic analogues of novocainamid led to the design of new drugs for the treatment of disturbances of cardiac rhythm, viz. flecainide (XLIII),[190] encainide (XLIV) and lorcainide (XLV).[191]



(XLIII)

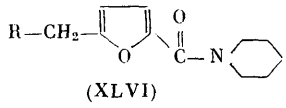


(XLIV)



(XLV)

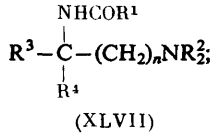
Antiarrhythmic activity is possessed by preparations from the *N*-aryl-8-pyrrolidizinalkanamide[192] and 2-ethoxycarbonylaminophenothiazine[193] series. The synthesis of aminoamides of the furanoic acid series (XLVI) has been reported.[194] Investigations of coronary vasodilator activity showed that the citrates and hydrochlorides of these compounds increase the rate of coronary blood flow by 87–120%.[194]



(XLVI)

R = NC_5H_{10}, HN— etc.

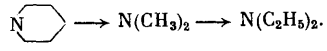
Quite recently a communication[195] appeared on the synthesis and study of the antiarrhythmic and anaesthetic activity of aliphatic-aromatic aminoamide (XLVII) which are analogues of novocainamid with secondary and tertiary carbon atoms on the amide group and various lengths of carbon chain.



(XLVII)

R^1 = H, CH_3, $CH=CH_2$, C_6H_5, $CH_2C_6H_5$, $CH_2OC_6H_5$, RC_6H_4; cycloalkyl, adamantyl; NR_2^2 = $N(CH_3)_2$, $N(C_2H_5)_2$, piperidino, morpholine, $N(C_3H_7)_2$, $N(C_4H_9)_2$, R^3 = alkyl, C_6H_5, $C_6H_4R^5$; R^4 = H, alkyl; n = 1 to 8.

It was shown that removal of the amino or amide group led to loss of activity. Local anaesthetic and antiarrhythmic effects depend on the character of the amino group (NR_2^2) group and fell in the series



Maximum activity was detected for amides of substituted benzoic, adamantanecarboxylic and cyclohexanecarboxylic acids, and minimum for amides of acetic acid. Amides of phenylacetic and phenoxyacetic acids occupy an intermediate position. The introduction of substituents into the benzene ring (R) leads in the general case to a reduction in antiarrhythmic action and toxicity, but local anaesthetic activity depends on the nature of this susbtituent. Donor substituents reduce the activity and acceptor substituents enhance it, halogens increase the local anaesthetic action.

Substitution in the benzene ring of the main chain (R^5) leads to an increase in antiarrhythmic and local anaesthetic action along the series H→CH_3→Br→Cl. The determining influence on the pharmacological action of aminoamides (XLVII) proved to be multiple. All forms of activity have several maxima at various values of *n*.

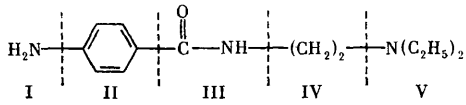
It follows from the data presented that aminoamides differing in chemical structure to a significant degree display antiarrhythmic activity.

Modification of the novocainamid molecule, as the first antiarrhythmic of the monoacylated diamine type of aminoamide, led to the design of a large number of compounds, among which are substances displaying high antiarrhythmic activity.

The multiplicity of chemical structures and the differences in methods of determining antiarrhythmic activity do not permit an unequivocal analysis of the influence of structure on activity. Quantitative data on activity and toxicity are frequently absent.

However it is possible to draw certain conclusions on the dependence of antiarrhythmic activity on the chemical structure of compounds.

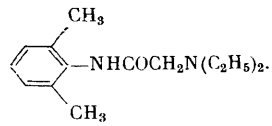
It is possible to divide the novocainamid into five portions which are subject to modification.



I. Acylation of the NH_2 group by fatty acid derivatives leads to an increase in antiarrhythmic activity.[28,160,163] Alkylation also enhances it.[162] Sulphonation of the amino group prolongs the antiarrhythmic action of a preparation.[178] Replacment of the NH_2 group by chlorine or by an ethoxy group leads to loss of antiarrhythmic action.

II. Introduction of various substituents into the *ortho*-position of the benzene ring (Cl, *O*-alkyl, alkyl) increases activity.[27,161,165] The introduction of methoxy groups into the benzene ring increases activity significantly. However in a series of quinoline analogues of novocainamid chlorine substituted derivatives were more active than methoxy compounds.[167,180–189] Replacement of the benzene ring by non-benzenoid systems does not make a significant contribution to antiarrhythmic properties, although *ortho* substitution frequently leads to an increase of activity.[25,166,169,170,177]

III. Inversion of the amide group transforms monoacylated diamines into the aminoacid series. Simple inversion in the novocainamid molecule leads as a rule to a reduction in anti-arrhythmic effect.[165] However the known effective anti-arrhythmic lidocaine (XLVIII) is dimethylaminoacetylxylidine and a large number of its derivatives display antiarrhythmic activity.[3,167]



(XLVIII)

Replacement of the amide group by imido and sulphonamide groups leads to the appearance of new classes of potential anti-arrhythmics.[172–174,184] Arylation of the amide nitrogen in the novocainamid molecule also shows a positive influence on the antiarrhythmic properties of compounds.[176]

IV. An increase in the hydrocarbon chain leads to an increase in the activity of substances,[168,169] although several maxima in activity were observed at various chain lengths.[195] Antiarrhythmic action of compounds increases by several orders of magnitude in comparison with that of novocainamid. The introduction of alkyl[178,179] and aryl radicals[195] into the hydrocarbon chain has a positive influence on activity. Inclusion of nitrogen atoms in one saturated ring leads to loss of antiarrhythmic activity.[181] The inclusion of saturated rings in the hydrocarbon chain between the amino and amide groups may prove to be promising.[184,187–191]

V. The presence of an amino group in the amide molecule is very important for antiarrhythmic activity.[195] It may be secondary in character.[175,177,190] However the majority of the antiarrhythmics of the monoacylated diamine series contain a tertiary amino group in the form of a dialkylamino group, alkylarylamino groups or saturated cyclic amines. In several cases it was shown that cyclic saturated amines increase antiarrhythmic action,[119] replacement of one of the alkyl groups by an aromatic group is also useful.[171]

At the present time there is no conclusive hypothesis on the link between the structure of chemical compounds and their biological activity. It is evident that every change in the conformation of a molecule is accompanied by changes in physiochemical properties and influences its ability to be absorbed, to pass through a membrane to interact with cellular enzymes and receptors.

It has been reported[167,188,189] that among aminoamide derivatives of quinoline which are antiarrhythmically active the *trans*-isomer is as a rule more active.

There are data on the resolution of racemic aminoamides into optical antipodes.[124,184,195,196] Results of pharmacological testing show that the (+) (*S*)-isomer of propionic acid dialkylamino-ethylamide was more active in analgesic activity than the (–) (*R*)- and (±)-isomers.[124]

The preparation flecainide shows approximately the same antiarrhythmic activity for both enantiomers and the racemate.[196] A higher antiarrhythmic and local anaesthetic activity was noted for the (+) (*R*)-isomer than for the (–) (*S*)- and (±)-isomers in a series of dialkylaminopentylamides.[195] The enantiomers also differed in toxicity.

Conclusions have been drawn on the influence of basicity[190] and lipophilicity[197] on the antiarrhythmic properties of aminoamides. The more basic and the better soluble in lipids a substance is then the higher the antiarrhythmic activity it displays.

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Several publications on the synthesis,[199,200] biological action[200] and study of the interconnection of structure and biological activity[201] of aminoamides have appeared since the manuscript was prepared for printing.

In spite of the large number of publications devoted to the search for promising antiarrhythmics and of the significant quantity of antiarrhythmic preparations used in therapy, the search for new active compounds is as pressing as ever.[3] There is a need for long-acting drugs with low toxicity. There is a requirement for preparations to treat post-infarct disturbances. One of the most rational approaches in the search for promising new compounds is the investigation of the dependence of activity on structure in chemical series among representatives of which active anti-arrhythmics have been detected.[198]

The available data on practically useful properties of *N*-substituted aminoamides and the interesting chemical and physicochemical properties discovered separate them into a discrete class of organic compounds which is of interest not only for chemistry but also for other regions of science and technology.

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Translated from *Uspekhi Khimii* **60** 881–910 (1991) U.D.C. 543.253.577.087.4:546/7

Amperometric sensors based on immobilised enzymes

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ABSTRACT. The state, problems, and prospects of the development of one of the new fields of analytical chemistry—"reagent-free" analytical methods—are described and surveyed using as an example enzyme-based amperometric sensors. Questions associated with the design of biosensors and the characteristics of their functioning under various conditions are examined. The applied aspects of the use of enzyme electrodes of this type in various fields of science and the national economy are noted.

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I. Introduction

One of the most important problems in analytical chemistry is the creation of sensitive and selective methods which would make it possible to analyse biological objects. In connection with ecological problems, the task has become of still more urgent interest. The use for these purposes of enzymes—preparations or biological materials containing them—which can be called new generation analytical reagents, proved to be attractive and promising.

Enzymes as biological catalysts exhibit a very high catalytic activity combined with a high specificity. These factors combined with the mild conditions under which enzyme reactions take place, the possibility of recording the useful signal, and also the advances achieved in the field concerned with the creation of stabilised enzyme preparations via immobilisation[1–6] have ensured the development of a new aspect of analytical chemistry—"reagent-free" analytical methods based on the use of biochemical sensors (biosensors).[7]

A biochemical sensor usually consists of some kind of physicochemical detector-sensor (electrochemical, solid-state, opticoelectronic, enthalpimetric, etc.) and a layer of immobilised enzyme fixed on its surface or near it. Many biosensors contain a semipermeable membrane.[7–9] The principle governing their activity is based on the diffusion of the substrate into a thin layer of biocatalyst, in which the enzyme reaction takes place, and on the determination of any component of the enzyme reaction (product or substrate) by some kind of sensor. If electrochemical sensors are used (ion-, gas-, and molecule-selective electrodes, etc.), then, depending on the measured quantity (current or potential), the biosensors (their initial name was "enzyme electrodes") are divided into potentiometric and amperometric.[10] The potentiometric biosensors exhibit a linear dependence of the potential on the logarithm of the concentration of the substance determined, while in the amperometric sensors the analytical signal is the current of the electrochemical reaction, which depends on the concentration of the compound to be determined.[10,11] Differences are observed in the range of the component concentrations determined and in the response time.

Since the first mention of enzyme electrodes in 1967 by Updike and Hicks,[12] the interest in this field of bioelectroanalytical chemistry has continuously grown. The number of publications has increased every year. Symposia and conferences devoted to electrochemical biosensors and related questions are held annually, i.e. the world interest in this problem is extremely high. This is in fact not surprising because enzyme electrodes make it possible to solve successfully a whole series of complex problems in the analysis of enzyme substrates, activators, and inhibitors; they are extremely promising in biochemical analysis, medicine, and pharmacology.[13,14] Furthermore, effective electroanalytical analysers have already been created on the basis of enzyme electrodes which combine the specificity of biocatalysts with the high sensitivity of electrochemical apparatus.[15]

This review is devoted to one of the types of biosensors with amperometric signal indication and covers the literature from 1977 up to the present time. A systematic account of earlier data has been given elsewhere.[7,8,10,11,16] It may be of interest to mention them in connection with the establishment of the field of electroanalytical chemistry and bioelectrocatalysis.[17] A whole series of subsequent reviews were devoted to the description of a large number of enzyme systems and a wide variety of amperometric sensors based on them.[18,19] Most attention has been devoted to the theoretical description and properties of various types of enzyme electrodes[18–24] and their components,[21] questions of the kinetics of enzyme reactions,[25–27] and the conditions under which electrodes operate (*in vivo* and *ex vivo*).[28,29] From year to year, the number of new enzyme electrodes has increased and the range of their applications has expanded.[30] However, despite the wide variety of enzyme sensors, there exist unique methodological approaches to their design and unique requirements as regards the function of the electrodes and also the methods for monitoring the stability and reproducibility of the readings.[31]

Modern enzyme electrodes make it possible to determine with a high sensitivity and selectivity many organic and inorganic substances which are enzyme substrates, inhibitors, and activators, i.e. direct and indirect participants in enzyme reactions. The sensitivity of many biosensors reaches in some cases several picomoles per litre.[30]

Reviews[32,33] as well as proceedings of symposia and conferences[13,34–39] have been devoted to problems of the practical application of enzyme electrodes in clinical research, microbiology, immunology, other branches of medicine, as well as ecology and agriculture. The undoubted economic gain in the application of

enzyme systems in analysis[37,40] and good prospects for the use of biosensors *in vivo* and *in vitro*[38,41] have been noted.

Despite the sudden rise in the interest shown by various investigators in this field of knowledge, which has been reflected in the publications mentioned above, one should note that the bibliography in the reviews, which appeared relatively quickly, reflects the "specific" interest of the authors and is as a rule not repeated, so that each review constitutes a supplement to the others.

II. Amperometric sensors based on various enzyme systems

Analysis of the literature on problems associated with the preparation of biosensors makes it possible to distinguish four main stages in the preparation of any enzyme electrode:[16] the choice of enzyme as a reactant; the preparation of the enzyme; the immobilisation of the enzyme; the construction of the enzyme electrode itself.

It is also necessary to note that the choice of the method of recording the useful signal, i.e. the choice of a particular (in the given instance electrochemical) sensor, is important in the preparation of the electrode. It is possible to make electrodes of three types: type A—dialysis membrane electrode; type B—with physical deposition of the enzyme on the surface; type C—with direct immobilisation of the enzyme on the membrane.[16]

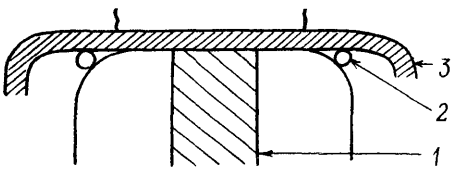


Figure 1. Schematic diagram of an enzyme glucose electrode prepared on the basis of a membrane oxygen sensor:[8] *1*, cathode; *2*, reference electrode; *3*, semipermeable Teflon membrane; 4, enzyme gel layer.

The first biosensor was a type A enzyme electrode for the determination of glucose, which was constructed on the basis of the Clark cell (electrode) where glucose oxidase was retained in the form of a thin layer between two dialysis membranes.[7,8] Subsequently the glucose oxidase solution was replaced by glucose oxidase immobilised in a polyacrylamide gel. The design of one of the first biosensors is illustrated in Fig. 1.[8] At the present time the enzyme electrode is represented by a two-membrane model (Fig. 2),[42] which makes it possible to obtain by theoretical analysis complete and approximate equations characterising the stationary behaviour of monoenzyme electrodes over the entire substrate concentration range. It is possible to estimate the influence of various factors, such as the diffusion layer and the ratio of the thickness of the enzyme-containing layer and of the outer membrane, on the working characteristics of the sensors.

It has also been suggested that the enzyme preparation be fixed on the surface of the stirrer or on the surface of an easily replaced stationary component placed within the enzyme reactor, which improves, according to the authors,[43] a number of analytical characteristics of such designs.

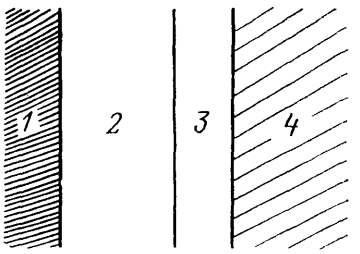


Figure 2. General schematic arrangement of the enzyme electrode:[42] *1*, indicator electrode (planar); *2*, layer of immobilised enzyme; *3*, outer membrane; *4*, substrate solution being analysed.

The operation of enzyme electrodes is based on the direct electron transfer between the active centre of the immobilised enzyme and the surface of the electrochemical sensor, which is frequently modified in some way. However, electron transfer can be effected also with the aid of special mediators.

The principal requirements which must be met by the mediators can be formulated as follows:[44,45] the stage in which the mediator interacts with the active centre of the enzyme must be rapid, i.e. the mediator must in essence behave as an enzyme substrate; the oxidation-reduction potential of the mediator must be low and must be independent of the pH; the mediator must be oxidised (or reduced) electrochemically at the electrode made from the given material under conditions close to reversibility; the electron transferring agent must be stable (its reduced form must not be oxidised, for example, by atmospheric oxygen).

Low-molecular-weight compounds characterised by a high mobility of the electrochemical equilibrium are most often employed as mediators. These are dyes, quinone type compounds, hexacyanoferrates-(II) and -(III), and conducting organic salts, i.e. molecules and ions which exist in solution in two forms corresponding to different oxidation states of one of their constituent elements.[21,25,26] Thus the choice of mediator constitutes a special problem.

1. Biosensors for the determination of glucose

It is noteworthy that the greatest number of various biosensors and the corresponding analytical devices have been created at the present time for the determination of glucose. This is associated with the need to monitor the sugar content in biological liquids not only for the diagnosis but also for the therapy of a whole series of diseases. Soviet designs for the industrial production of such analysers are already available.[9]

All the enzyme electrodes for glucose with amperometric indication, which employ the ability of glucose to be oxidised [Eqn. (1)], are constructed on the basis of Clark oxygen electrodes, peroxide electrodes, or certain other detectors.[46]

Electrodes made of platinum, gold, silver, or rhodium are used as indicator electrodes in Clark oxygen cells and its modifications. The electrode component is as a rule separated from the object analysed and the solution by a thin polymer film which is impermeable to both high- and low-molecular-weight compounds but is permeable to oxygen (Fig. 1).

The principle of the operation of such an electrode is simple: the enzyme catalyses the removal of oxygen from the solution at a rate which depends on the glucose content and this is indicated by the oxygen electrode:

$$\text{glucose} + O_2 + H_2O \xrightarrow{GO} \text{gluconic acid} + H_2O_2; \quad (1)$$

GO = glucose oxidase.

The principal advantage of oxygen sensors is the simplicity of their preparation, high stability, selectivity, and reproducibility of the readings, and a fairly high sensitivity.

The oxidation of hydrogen peroxide [Eqn. (2)] usually follows reaction (1), which can be detected by appropriate electrodes corresponding to hydrogen peroxide:

$$H_2O_2 \longrightarrow O_2 + 2H^+ + 2e\ . \quad (2)$$

Such sensors are made from various materials (platinum, gold, and nickel, graphite). A distinct diffusion current makes it possible to use reaction (2) for the quantitative determination of glucose (at a platinum electrode, this reaction is observed at 0.6–0.7 V relative to s.c.e.†). Analysers for hydrogen peroxide are distinguished by a short reponse time in the range 45–60 s (120 s for a continous flow-type blood analyser), but their selectivity is lower because at the H_2O_2 oxidation potentials a number of organic compounds, which may be present in the specimen, also undergo electrochemical reactions.

Apart from glucose analysers with an oxygen electrode and with a hydrogen peroxide electrode, devices have been developed in which the enzymic oxidation of glucose is effected not by oxygen but by another oxidant, for example potassium hexacyanoferrate(III):

$$CH_2OH(CHOH)_4CHO + H_2O + [Fe(CN)_6]^{3-} \longrightarrow$$

$$\longrightarrow CH_2OH(CHOH)_4COOH + [Fe(CN)_6]^{4-}. \quad (3)$$

The hexacyanoferrate(II) formed as a result of reaction (3) is oxidised at a platinum electrode:

$$[Fe(CN)_6]^{4-} \longrightarrow [Fe(CN)_6]^{3-} + e. \quad (4)$$

Reaction (4) takes place at a potential of −0.5 V relative to a silver,silver chloride reference electrode, which serves simultaneously as an auxiliary electrode.[46]

The hydrolysis of glucose takes place also with participation of quinone. The hydroquinone formed is usually detected by a platinum electrode. This principle is used in a glucose sensor with glucose oxidase (GO) immobilised on cellophane.[15] Enzyme electrodes for glucose, based on similar principles and developed previously, have been described in detail.[7,8,10,11] The use of various carbonaceous materials as the electrochemical sensor proper in similar devices has been described by Razumas et al.[21] A whole series of studies in this field have been described by Sorochinskii and Kurganov.[30]

The characteristics of various enzyme sensors, including those for the determination of glucose, are compiled in Table 1.

An enzyme electrode has been developed for the determination of glucose with the aid of which one can follow the variation of the H_2O_2 concentration in the molybdenum(VI)-catalysed reaction with iodide ions:

$$H_2O_2 + 2H^+ + 2I^- \xrightarrow{Mo(VI)} I_2 + 2H_2O. \quad (5)$$

By varying the rate of rotation of a disc electrode with a ring, on which glucose oxidase has been immobilised, one can determine the rate of mass transfer of the substrate and the rate of the catalytic reaction. The life of such an electrode is about 6 days.[47] The advantages of using rotating electrodes of the "disc with a ring" type in amperometric sensors have also been discussed by Guilbault.[20]

In the development of glucose sensors, glucose oxidase was immobilised in three ways: (1) by covalent grafting by means of a bifunctional reagent (glutaraldehyde) on a modified silica carrier Silochrome S-50; (2) with the aid of a synthetic water-soluble acrolein–vinylpyridine copolymer; (3) by oxidising the carbon components of the enzyme. The carrier with the immobilised enzyme was placed on the bottom of the cell under a porous nylon filter. With the aid of this type of enzyme sensor, it is possible to carry out in the course of two weeks more than 200 determinations of standard glucose solutions relative to a single calibration graph. The electrode response time is 10–15 s. The immobilised glucose oxidase preparation, obtained by oxidising the hydrocarbon components of the enzyme, was stored for more than two months at room temperature without loss of activity.[50] The relative standard deviation of a single determination (s_r) was about 0.03 in the substrate concentration range 0.18–0.10 g ml^{-1} and 0.13 for a substrate concentration of 0.005 mg ml^{-1}.[50] In order to increase the rate of electron transfer, various mediators are used, as mentioned above, in many biosensors. Thus a selective enzyme electrode has been proposed for the determination of glucose, the mechanism of the response of which is based on the selective oxidation of glucose to gluconic acid by $[Fe(CN)_6]^{3-}$ in the presence of glucose oxidase.[52] The $[Fe(CN)_6]^{4-}$ formed is reoxidised to $[Fe(CN)_6]^{3-}$ on the surface of the indicator enzyme electrode consisting of an aluminium rod whose end-face is coated with a graphite-containing material. A layer of gel with immobilised glucose oxidase, covered by a cellophane membrane, is deposited on the graphite. In the interval between measurements, the electrode was stored at 4 °C in phosphate buffer containing $K_3[Fe(CN)_6]$. The standard deviation s_r was 0.03–0.06 for the glucose concentration range 5×10^{-6}–5×10^{-5} M and was less than 0.03 for higher substrate concentrations.

The response time depends on the glucose concentration and amounts to 2–4 min for low concentrations. The operation of the electrode is stable for at least 3 weeks and the electrode has been used for determining glucose in blood serum and in urine relative to a calibration graph which was plotted daily. The presence of other enzymes, including catalase, does not interfere with the determination.

An enzyme electrode has been described for the determination of glucose in blood and plasma, where ferrocene and its derivatives, oxidised to ferrocenium ions, are used as the mediator between the immobilised glucose oxidase and the graphite electrode.[53] Flavin-adenine dinucleotide has been used for the same purpose.[54]

† Saturated calomel electrode (Ed. of Translation).

Table 1. Analytical possibilities of amperometric enzyme sensors.

Compound determined	Enzyme	Method of immobilisation	Amperometric detector	Range of concentrations determined	Refs.
Glucose	Glucose oxidase	Cross-linking by glutaraldehyde to the surface of the carbon paste containing added amines	Rotating disc electrode with a ring	—	[47]
	"	Cross-linking with albumin	Platinum H_2O_2 electrode	0.05 – 10 mM	[48]
	"	Entrainment in the electrode layer	Two platinum hexacyanoferrate electrodes	6.9 – 27.8 mM	[49]
	"	(a) Covalent grafting by glutaraldehyde on Silochrome S-50; (b) with the aid of a synthetic acrolein – vinylpyridine copolymer; (c) oxidation of hydrocarbon components of enzyme	Clark oxygen electrode	$3.10^{-5} – 1.10^{-3}$ M	[50]
	"	Covalent grafting to polyamide networks	Membrane O_2 electrode	0.1 – 7.0 mM	[51]
	"	Entrainment in the gel in the near-electrode layer	Aluminium rod with a graphite end face on which a layer of gel has been deposited, mediator – $K_3[Fe(CN)_6]$	$5.10^{-6} – 2.10^{-3}$ M	[52]
	"	Covalent grafting to graphite modified by 1-cyclohexyl-3-(2-morpholinoethyl)-carbodiimide *p*-methyltoluene-sulphonate	Graphite electrode, mediator – ferrocene	1 – 30 mM	[53]
	"	Entrainment in near-electrode layer	Platinum disc covered by a semi-permeable membrane	0.01 – 7.00 mM	[54]
	"	Covalent grafting to collagen films	Platinum H_2O_2 electrode	$10^{-6} – 10^{-3}$ M	[55]
	"	Film with immobilised glucose oxidate	Cathode – silver, anode – platinum	0.8 mg ml^{-1}	[58]
	"	Electropolymerisation of pyrrole in the presence of the enzyme	Platinum or carbon glass electrode	$10^{-4} – 10^{-2}$ M	[57]
	"	Incorporation in a poly-*N*-methylpyrrole film	Platinum disc electrode	0.22 M	[58]
	"	Covalent grafting to a carbon glass electrode via the borate groups of 3-aminophenylboronic acid	Carbon glass electrode modified by 3-aminiphenylboronic acid	—	[59]
	"	Adsorption of glucose oxidase on a modified graphite electrode	Graphite electrode modified by the ionic sputtering of palladium and gold	$3.10^{-6} – 4.10^{-3}$ M	[60]
	"	Homogeneous membrane	Membrane O_2 electrode	1.0 – 5.0 M	[61]
	"	Glucose oxidase modified by the introduction of ferrocene derivatives	—	—	[28]
	"	Incorporation in a semipermeable membrane	Carbon paste electrode modified by *p*-benzoquinone	—	[62]
	"	Incorporation in a semipermeable membrane together with *p*-benzo-quinone	Gold electrode and platinum mesh electrode	—	[63]
	"	Attachment of *p*-benzoquinone-activated glucose oxidase to a cellulose acetate membrane with covalently bound bovine albumin	Platinum electrode	—	[64]
	"	Covalent binding to ferrocene-carboxylic acids	Carbon glass electrode	—	[65]
Uric acid	Uricase	Covalent binding to glutaraldehyde	Platinum electrode with a thin layer of immobilised enzyme	0.02 – 0.08% in serum, 0.25 – 0.75% in urine	[66]
	"	Covalent grafting to porous glass with the aid of glutaraldehyde	Platinum H_2O_2 electrode	2 – 8 mg/100 ml of serum	[67]

Table 1 (contd.).

Compound determined	Enzyme	Method of immobilisation	Amperometric detector	Range of concentrations determined	Refs.
Aromatic amines	Peroxidase	(a) Adsorption; (b) adsorption followed by treatment with glutaraldehyde	Epoxidised carbon glass electrode in a Teflon shell	0.1–3 μM	[68]
Cholesterol	Cholesterol oxidase	Incorporation in a collagen membrane	Membrane O_2 electrode	0–0.2 mM	[69]
	"	Entrainment in a 2-hydroxymethyl methacrylate gel treated with glutaraldehyde	Platinum O_2 electrode	0.4–12 mM	[70]
Ethanol	Alcohol oxidase	Entrainment in near-electrode layer under a nylon film	Platinum disc H_2O_2 electrode	10 mg in 100 g of the substance to be determined	[46]
Lactate ion (lactic acid)	Lactate monoxidase	In a gelatine gel	Clark-type O_2 probe	10^{-5}–6.10^{-4} M	[71]
	Cytochrome b_2	Cross-linking with albumin	Platinum hexacyanoferrate electrode	1.2 mM	[48]
	"	Adsorption on a current conducting matrix	Organic metals	2 mM	[72]
Galactose	Galactose oxidase	Cross-linking with albumin	Electrochemical H_2O_2 sensor	0–27.8 mM	[73]
Phenol	Polyphenol oxidase	Cross-linking with albumin	Membrane O_2 electrode	0–0.08 mM	[74]
Oxalate ion	Oxalate oxidase	Grafting to polyamide membrane	Platinum H_2O_2 electrode	10^{-7}–10^{-4} M	[75]
Pyruvate ion	Pyruvate oxidase	Immobilisation on nylon	Platinum H_2O_2 electrode, O_2 electrode	10^{-3} mM	[76]
Salicylate ion	Salicylate hydroxylase	Chemical immobilisation on the electrode surface	O_2 sensor	10^{-5}–2.10^{-3} M	[77]
Sucrose	Invertase	Adsorption and entrainment in the polymer matrix of poly(vinyl alcohol)	Pyrographite electrode	—	[78]
Acetylcholine, choline	Acetylcholinesterase, cholinesterase	Immobilisation on a nylon mesh in the near-electrode layer	Amperometric H_2O_2 sensor	1–10 μM	[79]
Butylrylthiocholine iodide (BTCI)	Cholinesterase	Incorporation in a polyacrylamide gel with the aid glutaraldehyde	Stationary amalgamated silver electrode	0.05–0.85 mg ml^{-1}	[80]
BTCI and CE inhibitors	Cholinesterase	Covalent grafting to nitrocellulose with the aid of glutaraldehyde	Stationary amalgamated silver electrode	10^{-3}–10^{-6} M 10^{-3}–$n\times10^{-11}$ M	[81] [82]
Indoxyl acetate	"	In a geletine gel on a cellulose hydrate membrane	Carbon glass rotating disc electrode	1.5×10^{-3} M -5.0×10^{-3} M	[83]
Hypoxanthine, xanthine, purine	Xanthine oxidase	Adsorption on the electrode	Conducting organic tetrathiofulvalene$^+$/tetracyanoquinodimethane$^-$ organic salts	10^{-5}–6×10^{-4} M	[84]
NADH	Glucose dehydrogenase	Adsorption on the electrode	*N*-methylphenazene$^+$/tetracyanoquinodimethane$^-$ conducting organic salts	—	[84]
α-Ascorbic acid	Ascorbic oxidase	Plate (5×5×2 mm) made of cucumber (pumpkin) skin	Clark oxygen electrode	—	[85]
Dopamine, dopaminequinone	Polyphenol oxidase	Tissue of banana fruit	Carbon paste electrode	1.3×10^{-6}– 9×10^{-5} M	[86]
Glycerophosphate	α,α-Glycerophosphate oxidase	Cross-linking with the surface of a Teflon membrane with the aid of serum albumin and glutaraldehyde	Clark oxygen electrode	—	[87]
Choline-containing lipids	Choline oxidase	Physical immobilisation—incorporation in a cellulose triacetate membrane	"	3.3×10^{-5}– 8.6×10^{-5} M	[88]
Maltose, glucose	Glucoamylase, glucose oxidase	Covalent grafting to collagen films	Platinum anode, H_2O_2 electrode	5×10^{-8} M (after two months, 2.5×10^{-7} M)	[55]
Cholesterol	Cholesterol oxidase, cholesterol hydrolase	Entrainment in a 2-hydroxymethacrylate gel treated with glutaraldehyde	Platinum oxygen electrode	4×10^{-4}– 12×10^{-3} M	[70]

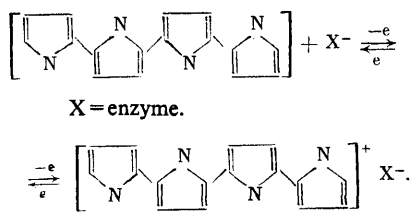
Table 1 (contd.).

Compound determined	Enzyme	Method of immobilisation	Amperometric detector	Range of concentrations determined	Refs.
Aromatic amides	Peroxidase, glucose oxidase	Covalent grafting of glutaraldehyde to the electrode surface	Carbon glass electrode	4.7×10^{-5} M	[68]
Glucose	Glucose oxidase, catalase	Entrainment in a homogeneous membrane in the near-electrode layer	Membrane oxygen electrode	1×10^{-3} M	[61]
Ethanol	Alcohol oxidase, peroxidase	Membrane in the near-electrode layer	Carbon glass electrode	—	[89]
Uric acid	Uricase, peroxidase	Covalent grafting to albumin with glutaraldehyde on a dialysis membrane	"	$(0.5-10)\times10^{-5}$ M	[90]
α-Lactate ions, pyruvate ions	Lactate oxidase, lactate dehydrogenase	Grafting to a Teflon membrane	Clark oxygen electrode	8×10^{-8}–8×10^{-6} M	[91]
Glucose, urea	Glucose oxidase and uricase	Covalent grafting by means of glutaraldehyde to graphite	Graphite electrode	$0-7\times10^{-6}$ M	[92]

Collagen films, on which the enzyme is immobilised, are subjected to preliminary activation by the acyl-azide method.[55] A platinum electrode is coated by a collagen membrane with immobilised glucose oxidase and is dried for periods ranging from 2 days to 2 weeks before measurements. Between measurements, the electrode is stored in air, since dehydration entails a denser coating of the platinum electrode by the membrane which facilitates the diffusion of H_2O_2 to the electrode. After inserting the electrode in the solution, the membrane remains tightly attached to the electrode. The resulting electrode is stable for a month or 160 days when the glucose content is measured. The response time before drying was somewhat more than 10 min, while after drying for 2 days it improved by 35% and was only 4–8 min.

In order to eliminate the interfering effect of ascorbic and uric acids, bilirubin, and aminoacids in the analysis of biological liquids for glucose, a cellulose acetate diaphragm permeable only to low-molecular-weight compounds with a small molecular size is introduced into the enzyme electrode between the membrane with the immobilised glucose oxidase and the platinum anode.[56] The standard deviation s_r in the determination of 0.20 mg ml^{-1} glucose was 2–3% (the number of determinations was 20).

One of the promising ways of obtaining enzyme electrodes involves the immobilisation of the enzyme in polymer coatings directly on the surface of the electrochemical sensor itself. The monomers, from which the polymer can be produced, are polymerised and the polymer macromolecules are cross-linked in the layer near the electrode. This new interesting method of immobilising glucose oxidase via electrochemical polymerisation has been described by Umana and Waller[57] and Bartlett and Whitaker.[58] For example, glucose oxidase is entrained by a polypyrrole film growing on the electrode surface.[57] This immobilisation procedure has a number of advantages. Polypyrrole, which is a conducting organic material, and the product of the enzymic reaction with glucose are in the immediate vicinity of the conducting material. The H_2O_2 concentration is also monitored from its reaction with the iodide anion (I^-), which is followed by the electrochemical reduction of iodine at a potential $\leqslant$0.2 V relative to the saturated calomel electrode:



X = enzyme. (6)

The electrode obtained is stable for 7 days. The preparation of immobilised glucose oxidase in a poly-*N*-methylpyrrole film for the preparative electrochemical oxidation of *N*-methylpyrrole on a platinum disc in the presence of 0.1 M $(C_2H_5)_4NBH_4$ supporting electrolyte in an aqueous phosphate buffer (pH 7.2) containing 1 μg ml^{-1} of glucose oxidase has been described.[53] It was shown that the H_2O_2 formed is oxidised on the rear surface of the platinum and not on the polymer film. The electrode response is observed at 0.95 V (relative to the saturated calomel electrode).

Direct electron transfer also takes place between glucose oxidase and the surface of a carbon glass electrode modified with 3-aminophenylboronic acid.[59]

An interesting electrode has been proposed by Jonsson and Gorton.[60] They noted that the partial removal of oxygen from the solution analysed lowers the electrode response, but the oxygen contained in the enzyme layer on the graphite electrode is sufficient to maintain the linearity of the calibration plot in the determination of glucose at concentrations $\leqslant$1 mM. The apparent rate constant for the Michaelis–Menten enzyme reaction is ~50 mmol. The stability of the response of the electrode obtained depends on the pH, the potential applied to the electrode, and the frequency at which samples are introduced.

A stable and fairly rapid response of the enzyme electrode is usually observed when only the glucose concentration is varied.[61] The same workers established that the response time can be reduced by diminishing the thickness of the membrane in the layer near the

electrode and by increasing the catalytic constant for the immobilised enzyme. In order to optimise the electrode response, variations in the thickness of the membrane and in the diffusion coefficient have been examined. Yet another model of the enzyme electrode for glucose has been proposed.[28] In this model, the electron-transferring agent is incorporated in the structure of glucose oxidase. Thus a modified glucose oxidase was obtained with the aid of ferrocene and its derivatives and was then deposited on the electrode. Glucose was oxidised even in the absence of oxygen directly on the electrode.

p-Benzoquinone, already mentioned, was used as the mediator.[62] It is introduced into the bulk of a carbon paste electrode whose surface is covered by a semipermeable membrane with the immobilised glucose oxidase. A similar procedure has been used also for other enzymes (gluconate dehydrogenase, ethanol dehydrogenase).

The possibility of using gold electrodes coated by a film of glucose oxidase with *p*-benzoquinone and of platinum mesh electrodes coated by a glucose oxidase film and covered by an oxygen-permeable membrane has been demonstrated.[63] One of the latest varieties of the glucose electrode has been described by Steruberg et al.[64] (Fig. 3). The immobilisation procedure proposed by the authors makes it possible to obtain membranes with a high surface activity, which are stable for a month and longer. Electrochemical monitoring and monitoring with the aid of radioactive labels demonstrated only a slight inactivation of the enzyme on immobilisation.

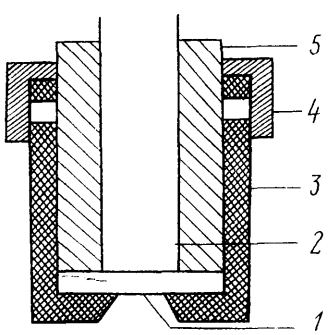


Figure 3. Schematic diagram of a rotating membrane glucose electrode:[64] *1*, membrane containing the immobilised enzyme; 2, platinum electrode (axis of rotating electrode); *3*, membrane holder; *4*, threaded lock ring; *5*, electrode shell.

The covalent binding of glucose oxidase to ferrocenecarboxylic acids has also been proposed.[65] The catalytic constant is a maximum when glucose oxidase is modified with ferroceneacetic acid.

The measurement of the response of a platinum electrode coated by a layer of immobilised glucose oxidase as a function of time and substrate concentration demonstrated a satisfactory correspondence between theoretical ideas and experiment.[93] The variation of the concentration profiles in the mathematical model of a multilayer enzyme sensor also agrees satisfactorily with the experimental findings for a commercial sensor for the determination of glucose.[94] These calculated concentration profiles describe the operation of the sensor more satisfactorily than the single-layer model.

2. The use of various enzymic reactions in biosensors

The glucose electrodes constitute the largest group of amperometric enzyme sensors. Other enzymes and enzymic reactions have so far been used much more rarely for such purposes (Table 1).

For example, uric acid is determined with the aid of enzyme sensors based on immobilised uricase:[66,67]

$$\text{uric acid} + O_2 + H_2O_2 \xrightarrow{\text{uricase}} \text{allantoin} + CO_2 + H_2O_2. \qquad (7)$$

A decrease in the amount of dissolved oxygen during the oxidation of the substrate has been detected at −0.6 V (relative to the saturated calomel electrode) by a platinum electrode with a thin layer of immobilised enzyme.[66] The error of the determination does not exceed 4% in the determination of uric acid in urine and 6% in its determination in blood serum. When the electrode is used several times per week, its activity diminishes by only 29% in the course of 100 days.

The use of covalent grafting of the enzyme to the porous glass of the electrode by glutaraldehyde has been described.[67] Such an electrode proved to be very stable during operation (~10 months), which permitted its employment under flow conditions.

The operation of electrodes with peroxidase is based on the oxidation of the hexacyanoferrate(II) ion by hydrogen peroxide catalysed by immobilised peroxidase:

$$H_2O_2 + 2[Fe(CN)_6]^{4-} + 2H^+ \xrightarrow{\text{peroxidase}} 2H_2O + 2[Fe(CN)_6]^{3-}. \qquad (8)$$

The hexacyanoferrate(III) ion formed is reduced at a carbon glass electrode at 0 V (relative to the silver,silver chloride electrode).[68] In the presence of aromatic compounds, which activate the peroxidase oxidation of hexacyanoferrate(II), the rate of the enzymic reaction and the cathodic current increase, which makes it possible to carry out the determination of, for example, a series of aromatic amines.[68] The range of the measured concentrations varies as a function of the type or substrate. The lower limits of the measurable concentrations of *o*-dianisidine and benzidine are 0.055 and 0.065 μmol, while for the remaining compounds investigated the limit is higher. The coefficient of the sensitivity of the above enzyme electrodes varies from 0.215 to 0.0022 μA μmol^{-1} on passing from *o*-dianisidine to 1,2-diaminobenzene. For electrodes of the second type (Table 1), this coefficient is higher, as a result of which the lower limit of the measurable contents of aromatic amines is appreciably reduced.

Cholesterol is one of the physiologically important components of blood. Under the influence of cholesterol oxidase, cholesterol is oxidised:

$$\text{cholesterol} + O_2 \xrightarrow{\text{cholesterol oxidase}} \text{cholest-4-en-3-one} + H_2O_2. \qquad (9)$$

A series of enzyme electrodes have also been developed for its determination.[46,69,70] The readings are based on the H_2O_2 reduction current at a platinum oxygen electrode on the surface of which a gel with the immobilised enzyme is deposited.[70] The gel is retained by two membranes: the inner membrane made of cellulose acetate and the outer membrane made of silk. The electrode response time is 0.5 min in the flow regime and 2 min in the static regime. The standard deviations s_r are 0.027 and 0.045 in each regime respectively.

Enzyme electrodes have been developed for the determination of ethanol in blood.[46] Alcohol oxidase is immobilised on the surface of a platinum disc electrode. At a potential of −0.6 V, the loss of oxygen, which is proportional to the ethanol content, is measured:

$$RCH_2OH + O_2 \xrightarrow{\text{alcohol oxidase}} RCHO + H_2O_2. \quad (10)$$

Alcohol dehydrogenase is used for the same purposes,[46] nicotinamide-adenine dinucleotide (NADH) and flavin mononucleotide (FMN) participating in the enzyme reaction and the chemical reactions associated with it. Reduced FMN is oxidised at a platinum anode, generating a current proportional to the ethanol concentration in the test solution. The enzyme–electrode processes occurring in the amperometric sensors based on membranes with immobilised lactate dehydrogenase are similar to the processes observed in the determination of ethanol with participation of FMN, but are used to determine lactic acid.[46]

The lactate sensor makes it possible to avoid the use of NADH and FMN. The following enzyme reaction takes place in it:

$$CH_3CHOHCOO^- + 2[Fe(CN)_6]^{3-} \xrightarrow{\text{lactate dehydrogenase}} CH_3COCOO^- + 2[Fe(CN)_6]^{4-} + 2H^+. \quad (11)$$

The choice of the optimum parameters, especially the thickness of the membrane, makes it possible to determine the amount of lactate in blood in 1 min without preliminary preparation. Apart from the platinum electrode, gold or carbon working electrodes can be used.[46]

An automatic analyser with an enzyme sensor has been described for the determination of the concentration of lactate ions and the measurement of the activity of lactate dehydrogenase.[71] The enzyme sensor consists of the so called oxygen probe of the type of the Clark electrode on which is fixed a layer of gelatin where lactate monoxidase is immobilised. The standard deviation s_r is less than 0.01. The enzyme sensor operates stably for 55 days. After the addition of NADH and pyruvate ions to the sample, it is possible to carry out in succession a determination of the lactate ions and the estimation of the activity of lactate dehydrogenase, for which the calibration plot is linear in the range 2.7–54.0 units of biological activity per litre.

Apart from lactate dehydrogenase, the enzyme cytochrome b_2, which catalyses electron transfer to mediators, i.e. $[Fe(CN)_6]^{3-}$, can also be used for the determination of lactic acid in such analyses.[48,72]

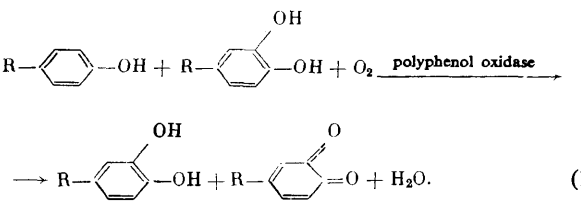
Certain improvements to enzyme electrodes have been proposed.[95] The essential feature consists in the fact that ionic compounds (C_{10}–C_{30} carboxylic acids, etc.) or non-ionic compounds [4,4′-bipyridyl, 1,2-bis-(4-pyridyl)ethylene, etc.] are introduced into the electrically conducting support made from powdered graphite, pyrographite, and metals. Functional groups for the orientation and fixation of electroactive enzymes such as cytochrome b_2, cofactors, or other biocatalysts are then formed on the surfaces of such electrodes. The surfaces of the carbon-containing supports can be coated by functional oxygen-containing groups by simple chemical oxidation. The advantage of the proposed "functionalised" electrodes consists particularly in the fact that the biocatalysts are in direct contact with the support, i.e. with the electrode itself. The oxidation or reduction of organic substrates therefore takes place under the influence of enzymes without the additional introduction of oxidants, reductants, or mediators into the solution. Such electrodes can be used not only for electroanalytical purposes but also for specific electroorganic synthesis. Enzyme electrodes are also employed for the determination of aminoacids.[8,46] Here the membrane with the covalently immobilised amino-oxidase catalyses the reaction

$$RCHNH_2COOH + O_2 + H_2O \xrightarrow{\text{amino-oxidose}} RCOCOOH + NH_3 + H_2O_2. \quad (12)$$

The enzyme exhibits group specificity and catalyses the oxidation of all the *L*-aminoacids present in the liquids analysed.

For the determination of galactose[73] and phenols,[74] enzyme electrodes have been developed whose operation is based on the reactions

$$\text{galactose} + O_2 \xrightarrow{\text{galacto-oxidase}} \text{galactosoaldehyde} + H_2O_2, \quad (13)$$



(14)

A simple and rapid method for the determination of oxalate ions in food products with a minimum of auxiliary operations has been developed. It is based on the use of a new voltammetric enzyme sensor.[75] Oxalate oxidase is immobilised on a commercial polyamide membrane. The response time of the sensor ranges from 20 to 60 s depending on the concentration of $C_2O_4^{2-}$ ions. The analytical signal is stable for almost 150 days.

A sensor, whose operation is based on the oxidation of pyruvate by dissolved atmospheric oxygen in the presence of HPO_4^{2-} ions with formation of H_2O_2, is used in clinical analysis for the determination of pyruvate ions. The process is monitored with the aid of an oxygen or H_2O_2 electrode.[76]

An enzyme electrode for the determination of salicylates in blood serum has been developed on the basis of salicylate hydroxylase immobilised on the surface of an oxygen electrode. In the determination, the enzyme sensor is immersed in a solution of a mixture of phosphate buffer with Complexon III (pH 6.75). Next the coenzyme β-NADH is added, after 5–10 min the substrate is introduced, and after 1–6 min the current is measured as a function of the salicylate concentration with the aid of the enzyme electrode[77] (s_r = 0.013–0.106).

Invertase is an enzyme which cleaves sucrose catalytically into *D*-glucose and *D*-fructose. It was immobilised by being incorporated in polymeric coatings at the instant of their formation directly on the surface of the electrode.[78] Polymeric coatings on pyrographite and aluminium electrodes can be obtained by cathodic polarisation in solution in poly(vinyl alcohol) containing boric acid.

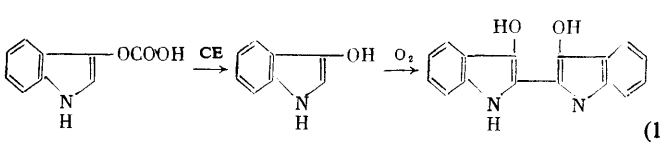
Selective biosensors based on immobilised cholinesterase (CE) and the determination of acetylcholine and choline in a 0.1–1 ml sample have been described.[79] The response time is about 1–2 min. The possibility of the simultaneous determination of these compounds in a single sample with the aid of two sensors under both stationary conditions and in a flow system has been demonstrated.

An enzyme electrode has also been proposed for the determination of the concentration of thiocholine esters.[80] The authors used, as the cholinesterase substrate, butyrylthiocholine iodide, which hydrolyses in the presence of cholinesterase:

$$C_3H_7COSCH_2{-}CH_2{-}\overset{+}{N}(CH_3)_3I + H_2O \xrightarrow{CE} C_3H_7COOH + HSCH_2{-}\overset{+}{N}(CH_3)_3I. \quad (15)$$

The determination is based on the electrochemical activity of the hydrolysis product—a thiol. the volume of the solution analysed is 4–5 ml. The error of the determination does not exceed 9%. With the aid of this electrode, it is possible to determine also other thiocholine esters as well as cholinesterase inhibitors, for example, phosphorus-containing pesticides, which is extremely important for the solution of the problem of monitoring the environment. Various procedures for the immobilisation of cholinesterase have been assessed: incorporation in a polyacrylamide gel accompanied by treatment with glutaraldehyde and adsorption on carriers—silica gel, activated charcoal, and various films.[80] The advantages and disadvantages of this procedure as regards use in enzyme sensors have been indicated. An improved model of such a sensor makes it possible to determine phosphorus-containing pesticides and certain physiologically active substances down to very low concentrations of the order of $n \times 10^{-11}$–$n \times 10^{-12}$ M.[81,82]

A number of synthetic compounds, including indoxyl acetate, are also hydrolysed in the presence of cholinesterase. Indoxyl, the product of the hydrolysis of indoxyl acetate, dimerises in the presence of atmospheric oxygen in an alkaline medium (pH 7.5–8.0). The rate of oxidation of indoxyl acetate has been studied with the aid of a carbon glass rotating disc electrode with immobilised cholinesterase:[83]



(16)

Enzyme sensors with conducting organic salts, functioning as the electrode material, have been developed. The possibility of determining hypoxanthine, xanthine, and purine in blood plasma with the aid of xanthine oxidase immobilised on the tetrathiofulvalene$^+$/tetracyanoquinodimethane$^-$ electrode has been demonstrated. The response and stability of the sensor are influenced by temperature, pH, and traces of oxygen. Glucose dehydrogenase, immobilised on the *N*-methylphenazine$^+$/tetracyanoquinodimethane$^-$ electrode, is used to determine NADH.[84]

Various enzyme-containing plant materials, rather than preparations of the enzymes themselves have recently come to be used increasingly in the development of the enzyme electrodes. Plant tissues in biosensors function as sources of catalytic enzyme activity. For example, an enzyme sensor consisting of a Clark electrode and a plate comprising a cucumber or pumpkin skin, which serve as sources of ascorbic oxidase, has been devised for the amperometric determination of α-ascorbic acid.[85] The determinations are carried out in a buffer solution (pH 6.0) with 0.5 mM EDTA. The enzyme activity is sufficient to ensure 50–80 determinations. The plates can be stored, without loss of activity, in 50% glycerol for a year. Phenols, acids, and vitamins B do not interfere with the determination. Ascorbic acid has been determined with the aid of this electrode in juices and pharmaceutical preparations with $s_r = 0.03$.

A similar principle has been used in another study.[86] The tissue of the banana fruit is introduced into a carbon paste electrode and dopamine is determined. The response time of this biosensor is not more than 12 s. The catalytic reaction current increases with increase in the content of the plant tissue in the paste. The optimum content of the tissue is 5.5%. Catechol and hydroquinone interfere with the determination.

Among the latest designs of amperometric sensors based on the Clark electrode, mention may be made of sensor systems for glycerophosphate and choline-containing lipids.[87,88]

New attempts have been made to improve the components of the enzyme oxygen electrode. A film permeable to H_2O_2 and impermeable to substrates has been proposed for this purpose. It is made from polyamides, polyurethane, cellulose acetate, and other polymers or copolymers.[96] Enzymes whose reaction with substrates proceeds with formation of H_2O_2 are immobilised on the porous surface of such films. They include, for example, glucose oxidase, uricase, xanthine oxidase, *D*- and *L*-aminoacid oxidases, as well as enzymes producing substrates for enzymic reactions with liberation of H_2O_2, for example, lipase, mutarotase, and phosphorylase. The smooth side of the film is applied to the surface of a silver anode (other metals are also employed). Such films are very strong, are satisfactorily joined to the electrode, and ensure an effective contact between the enzyme and the substrate, selective permeability, and a high accuracy of the measurements.

3. Polyenzyme biosensors

In those cases where the products or substrates of an enzymic reaction are electrochemically inactive, successive reactions of the substrates with the aid of several immobilised biocatalysts are used in the construction of amperometric sensors. Dienzyme reactions are most often employed. For example, the operation of electrodes sensitive to disaccharides is based on this principle.[10] Two enzymes are usually employed for the determination of lactose and maltose: glucose oxidase, which oxidises glucose via reaction (1), and β-galactosidase or maltase. The disaccharide, diffusing through the membrane, splits off glucose under the influence of the corresponding enzyme and the glucose is then oxidised by glucose oxidase to gluconic acid. The consumption of O_2, which is proportional to the content of the disaccharide in the solution analysed, is measured with an oxygen electrode:

$$\text{lactose} + H_2O \xrightarrow{\beta\text{-galactosidase}} \text{glucose} + \text{galactose}, \quad (17)$$

$$\text{maltose} + H_2O \xrightarrow{\text{maltase}} \text{glucose}. \quad (18)$$

In order to determine sucrose, it is necessary to have an additional enzyme which epimerises α-glucose—a sucrose hydrolysis product—to the β-form, which is oxidised by glucose oxidase:

$$\text{sucrose} + H_2O \xrightarrow{\text{invertase}} \alpha\text{-D-glucose} + \text{fructose} \quad (19)$$

$$\alpha\text{-D-glucose} \xrightarrow{\text{mutarotase}} \beta\text{-D-glucose}. \quad (20)$$

The rate of the non-enzymic mutarotation is high and it is therefore possible to abandon the use of mutarotase. The sensitivity of the electrode to the disaccharide is then greatly reduced.[10]

The joint immobilisation of glucoamylase and glucose oxidase is also employed for the determination of maltose:[55]

$$\text{maltose} + H_2O \xrightarrow{\text{glucoamylase}} 2\beta\text{-D-glucose}. \quad (21)$$

It has been suggested that a system comprising two immobilised enzymes, cholesterol oxidase and cholesteric ester hydrolase, be used for the determination of cholesterol esters.[70] The solution analysed is initally acted upon by cholesterol hydrolase and then cholesterol oxidase, after which the total amount of cholesterol is found.

For the determination of aromatic amines, the enzyme electrodes are prepared using glucose oxidase in order to replace the unstable substrate H_2O_2. A mixture of peroxidase and glucose oxidase in 0.02 ml of the basis buffer solution is deposited on a carbon glass electrode and treated with a 2.5% solution of glutaraldehyde (12–14 h, 4 °C). In the presence of 0.1 mM glucose and 1.0 mM potassium hexacyanoferrate(III) in the buffer solution, the parameters of these electrodes are close to those of the corresponding monoenzyme electrodes. They exhibit the highest stability, retaining 45–62% of their sensitivity for 40 days at 18–22 °C. During the functioning of these dienzyme electrodes, hydrogen peroxide is formed under the influence of glucose oxidase and hexacyanoferrate(III) is generated by the peroxidase. Under conditions where the peroxidase reaction is rate-limiting (at a glucose concentration about 0.1 mM), the activators (aromatic compounds) increase the rate of the process and the current in the system increases. At a lower glucose concentration, the glucoside reaction becomes rate-limiting and activators do not affect the electrode current. The dienzyme electrodes obtained are more convenient for practical use in view of their higher stability. They are used to determine aromatic amines, for example, *o*-dianisidine,[68] glucose,[61] ethanol,[89] uric acid,[90] and α-lactate and pyruvate ions.[91]

In order to determine ethanol, the electrolysis is carried out in a buffer solution (pH 7–8) with subsequent measurement of the reduction current.[89] Potassium hexacyanoferrate(III) at a concentration of 1.0–1.5 mM is introduced into the test solution before electrolysis to increase the selectivity of the determination. Uric acid is determined in the diagnosis of haematological diseases with the aid of an electrode based on immobilised microbial urease and peroxidase.[90] In a borate buffer solution containing 1 mM potassium hexacyanoferrate(III), the residual current does not exceed 1–2 mA when an enzyme electrode is used. After the addition of uric acid to the solution, the current increases appreciably. The dependence of the stationary current on the substrate concentration is linear up to 0.30–0.35 mM. The duration of the determination is 2–3 min.

These dienzyme electrodes exhibit a high specificity and a satisfactory reproducibility in the determination of uric acid in urine, blood, and serum. The electrodes are also very stable, retaining their initial sensitivity at the level of 50% under the conditions of daily 5 h use and on storage in buffer solution at 20–22 °C for 70 days.

The introduction of α-lactate or pyruvate ions into a phosphate buffer solution (pH 7.4) containing 10^{-3} M NADH induces an appreciable decrease of the dienzyme electrode current (ΔI = 0.5 μA), whereas in the absence of NADH in the solution ΔI < 8 mA.[91]

The mechanisms of the enzyme-catalysed reactions in the layer near the electrode are presented below:

$$O_2 + 2e \xrightarrow{\text{lactate oxidase}} H_2O_2, \quad \alpha\text{-lactate} \xrightarrow{-2e} \text{pyruvate}, \quad (22)$$

$$H^+ \xrightarrow{\text{lactate dehydrogenase}} NAD^+ + 2e, \quad \text{pyruvate} + 2e \rightarrow \alpha\text{-lactate}. \quad (23)$$

This enzyme electrode "does not distinguish" α-lactate and pyruvate ions and can be used for the quantitative determination of lactate only in those specimens where the concentration of pyruvate ions is much lower than that of lactate. The duration of the determination is 3–5 min and the electrode is stable for more than 10 days with a reproducibility of the determination of ±10%.

A dienzyme electrode with glucose oxidase and uricase, the latter being necessary to suppress the interfering influence of urea, can be employed to determine glucose and urea.[92]

An enzyme electrode with trypsin and glucose oxidase, adsorbed on the surface on a graphite electrode modified by aluminium, titanium, and zirconium oxides, has also been described.[97]

III. Flow analysers based on immobilised enzymes

The concept of monitoring, continuous *on line* and *in line* type analysis with the aid of physicochemical and biological procedures, which can ensure mathematical checks on a real time scale, has acquired very great importance in the methodology of analytical chemistry.

Studies on the development of the so called enzyme reactors or analysers with immobilised enzymes have become important for the continuous analysis of various substances to determine their content of enzyme substrates, inhibitors, and activators, for making possible the automatic monitoring of the composition of air, water, and other objects in the environment, and for the determination of components in a flow. They usually contain a fairly large amount of an enzyme immobilised on a carrier, in the form of layers or rings, which makes it possible to convert the entire substrate in the specimen into the product during the relatively short time interval when the specimen is in the reactor.

Three types of reactors, differing in form and in the disposition of the carrier, the immobilised enzyme, and the specimen, have been differentiated: a tubular reactor for gaseous specimens; a reactor filled with layers of spherical beads containing the immobilised enzymes; a tubular reactor filled with solid spherical beads made up of fibres with the immobilised enzyme.[24] Reactors for the determination of glucose and lactose with amperometric detection have been developed on the basis of such principles.

Reviews have been devoted to the study of the structure and properties of enzyme membranes for bioreactors obtained by the immobilisation of one or several enzymes on natural or synthetic carriers.[24,98] Flow enzyme reactors can be used also for the continuous recording of the kinetics of enzymic reactions.[7] Industrial specimens of enzyme reactors and the mechanisms of their functioning have been described in a review devoted to the use of immobilised enzymes in analytical chemistry.[99]

The employment of enzyme reactors and various enzyme electrodes in a version of the flow-injection analysis is extremely promising.[100] Mathematical models of the functioning of such analysers have been developed in relation to the determination of glucose with the aid of an indicator oxygen electrode consisting of a platinum disc to the surface of which two cellulose membranes were attached. Glucose oxidase in a polyurethane layer is placed between the membranes. The proposed mathematical model has been almost fully confirmed experimentally.[101] With the aid of this system, it is possible to determine glucose in almost 300 specimens (sample volume 1.5 ml) in the course of 1 h and the linear relation between the current and glucose concentration holds in the range 0.01–100 mM.

Platinum macroelectrodes and microelectrodes with glucose oxidase immobilised on a nylon mesh, placed tightly against the platinum electrode or immobilised directly on the surface of the platinum wire, have also been used.[102] The calibration plots are linear in the glucose concentration ranges $1 \times 10^{-5}-3 \times 10^{-3}$ and $1 \times 10^{-4}-2 \times 10^{-2}$ M respectively.

In order to determine glucose in the flow-injection version of analysis, use is also made of graphite electrodes, both a glass mesh electrode[103] and an electrode modified by the ionic sputtering of palladium and gold[60] (Table 1), with covalently immobilised or adsorbed glucose oxidase. The productivity of the reactor varies from 30 to 77 samples per hour with $s_r = 0.02$ as the flow rate varies from 0.5 to 2 ml min^{-1}. In the glucose concentration range 2.5–10 mM, a linear calibration graph is observed.[103] The electrode retains 30% of its initial activity for 40 days during storage at 2 °C.

There exists an example of the use of a flow-injection system based on a spherical enzyme reactor for the study of the kinetics of the mutarotation of *D*-glucose in the presence of phosphate ions and *D*-galactose.[104] Glucose, fructose, and sucrose present jointly in the given system can be determined with the aid of a series of enzyme reactors arranged in parallel and a multichannel potentiostat.[105] In the determination of glucose, a reactor with immobilised glucose oxidase was placed ahead of the corresponding reactor in order to eliminate the interfering effect of glucose. In this case, hydrogen peroxide was detected amperometrically. The interfering effect of ascorbic acid was fully eliminated by using a reactor with immobilised ascorbate oxidase. In the analysis of fructose, potassium hexacyanoferrate(II) was detected. The reproducibility of the system was 1.6–1.8%.

One of the latest devices of this type for the determination of free and total cholesterol (ChL) in blood serum is of great practical importance.[106] After the introduction of the microsample into the carrier stream containing a phosphate buffer solution, $K_4[Fe(CN)_6]$, and Triton X-100, the stream is divided into two components, one of which is passed through a column with immobilised cholesterol esterase, after which the two streams are combined and are passed through a column with immobilised cholesterol oxidase.

The amperometric detector with two polarised electrodes records two peaks: the first corresponds to the content of free cholesterol and the second corresponds to the total cholesterol in the sample ($c_L = 8 \times 10^{-7}$ and 3×10^{-6} mM respectively‡).

Apart from the flow-injection systems enumerated, there also exist a whole series of examples of the use of enzyme electrodes in a continuous regime. Thus it has been suggested that a platinum mesh electrode subjected to a preliminary treatment with 3-aminopropyltriethoxysilane and containing an immobilised mixture of enzymes—glucose oxidase and catalase or glucose oxidase and peroxidase with bovine albumin and glutaraldehyde—be used for the determination of glucose in blood serum and urine.[107] The calibration graph is linear in the range 20–800 mg $litre^{-1}$ for a sample volume of 5 μl (glucose oxidase–catalase) and 30–40 mg $litre^{-1}$ for a sample volume of 1 μl (glucose oxidase–peroxidase).

The possibility of using sensors for glucose, lactate, and urea in systems with constant sampling of blood for the continuous express monitoring *in vivo* of blood metabolites has been examined.[27,28] The aim of the authors of the above investigations was in essence to create, on the basis of such systems, sensors implanted in the patient's organs.

‡ c_L represents the lower limit of the measured concentrations.

Under flow conditions at a flow rate of 7 ml min^{-1}, an enzyme electrode with uricase immobilised on porous glass was used to determine uric acid.[67] With the aid of this device, it is possible to analyse up to 100 specimens per hour with an accuracy to within 2–4%. The enzyme then remains active for a long time and loses 70% of its initial activity only after 10 months.

Flow analysers based on alcohol, lactate, and glutamate dehydrogenases with regeneration of the NADH cofactor, capable of being used in repeated measurements, have been proposed.[108] The enzyme with immobilised NADH is retained between a platinum electrode and a semipermeable membrane. NADH is regenerated either by a direct electrochemical procedure or with the aid of the electrochemical oxidation of phenazine methosulphate. The linearity of the calibration plot is observed up to a concentration of 1.5 mM for lactate, 0.5 mM for glutamate, and 40 mM for ethanol. The enzyme flow analyser based on dehydrogenases is illustrated schematically in Fig. 4. A reactor based on immobilised cholinesterase has been used for the continuous monitoring of air and running water for the content of cholinesterase inhibitors—insecticides based on organophosphorus compounds and carbamates. Cholinesterase is immobilised by being entrained in a starch gel and is fixed on the surface of a mixed polyurethane carrier placed in the electrochemical cell (Fig. 5).[99] A theoretical description of the inhibitor analytical method using an enzyme flow system, which has recently acquired increasing importance in connection with the need to monitor an increasing number of toxic compounds, has been published.[109]

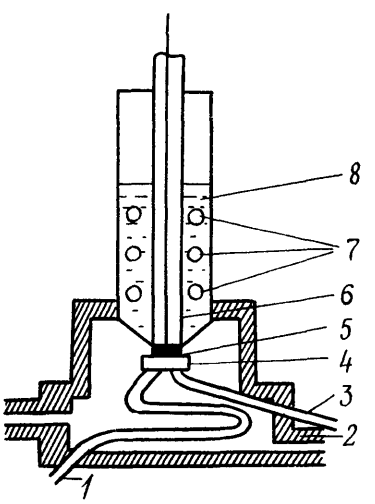


Figure 4. Schematic diagram of an enzyme flow electrode based on dehydrogenases: *1*, inlet for the flow of the test solution; *2*, heat exchanger; *3*, outlet for the products of the enzymic reaction and the stream containing the test substance; *4*, microchamber; *5*, semipermeable membrane; *6*, platinum electrode (disc); 7, auxiliary electrode; *8*, buffer solution.

One of the latest versions of the reactor for enzymic reactions has been proposed by Cerkasov and Linek.[43] The enzyme preparation is fixed on the surface of the stirrer or on the surface of a readily removable stationary component placed within the reactor.

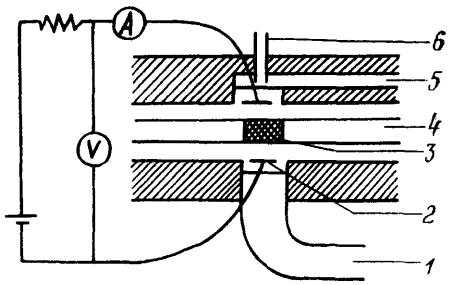


Figure 5. Schematic diagram of an electrochemical cell with an enzyme electrode based on immobilised cholinesterase: *1*, outlet for the products of the enzymic reaction; *2*, platinum electrode; *3*, immobilised cholinesterase; *4*, compartment (holder) for the immobilised cholinesterase; *5*, inlet for the stream of water or air supplied; *6*, inlet for the stream of substrate supplied.

IV. Amperometric sensors in immunoenzyme analysis

The ability of antibodies to interact highly specifically with various compounds and the ability of enzymes to accelerate chemical reactions are widely used in immunoenzymology.[7] As an alternative to radioimmunological analysis, approximately 15 years ago enzyme-markers were used in a quantitative immunological method,[110–112] which was called immunoenzyme analysis (IEA). This method is safe as regards health and the useful life of enzyme-markers is several years. It is applicable to all antigen (hapten)–antibody (AG–AB) systems and is extremely sensitive. Immunoenzyme analysis (IEA) makes it possible to detect antigens, antibodies, and other substances in biological systems at negligibly low concentrations of $10^{-14}-10^{-12}$ M.[113–118] There are two varieties of IEA: the heterogeneous solid-phase variety and the homogeneous variety. In the homogeneous IEA, the activity of the enzyme-marker changes during the immunological response. In this case, the stage involving the physical separation of the AG–AB complexes, required in the heterogeneous version, is unnecessary. With the aid of the homogeneous version of the analysis, it is possible to determine only substances with a relatively low molecular weight, for example, medicinal drugs and hormones.[113] A more clear-cut classification of IEA procedures has been given in a review.[117] It is based on the fact that, in any version of the IEA, it is possible to measure the enzyme activity of the labelled compound present either in a specific immune complex or in a complex with free binding centres which do not enter into the reaction. The majority of the immunoenzyme tests are based on spectrophotometric and fluorimetric methods for the determination of enzyme activity.[117] The use in IEA of electrochemical sensors, combining the principles of the action of analytical systems based on immobilised enzymes and immunoenzyme analytical methods, merit attention from the practical point of view. Such systems, which have been called immunoenzyme electrodes, are extremely promising because of the possibility of automating immunoenzyme methods and creating compact immunoenzyme analysers. However, one should note that the concept of "immunoenzyme electrodes" is not used quite correctly in our view. For example, the electrodes described in a number of studies[113–117] do not always contain a layer of immobilised enzyme and it would therefore be more correct to classify this procedure as immunoenzyme analysis with amperometric (voltammetric) indication of the analytical signal. Such systems usually contain an immobilised antigen or antibody.

The oxygen sensor described above was one of the first to be used in competitive solid-phase IEA.[118] A capron mesh, containing immobilised antigens against human serum albumin (anti-HSA) or insulin, was fixed on the surface of an oxygen electrode. In a solution containing HSA or insulin, the immobilised antibodies react with the antigen. If an enzyme is grafted beforehand to HSA or insulin (catalase to HSA and glucose oxidase to insulin), then an anti-HSA.HSA-E or an anti-insulin.insulin-E, where E is the enzyme, is formed on the capron mesh. When the solution contains, together with the labelled antigen molecules, also the antigen without enzymes, then mixed complexes are formed where the amount of enzyme is higher the lower the concentration of the unlabelled antigens. Under conditions where the response of the oxygen electrode depends on the enzyme concentration, the readings of the electrode are proportional to the antigen concentration in solution. The response time for such a system is 2 min. The overall duration of the determination, including the regeneration of the membrane by treatment with a glycine buffer solution, is 10 min. The antibody immobilised on the capron mesh retains its activity for several days.

It has been suggested that one should use alkaline phosphatase as the marker of the α-acid glycoprotein antigen fixed by glutaraldehyde in a competitive IEA method involving the binding of the excess antigen and the enzyme-labelled antigen to a limited number of highly specific antibodies:[119]

$$\begin{array}{lll} \mathrm{AG} & \nearrow & \mathrm{AG:AB} \\ & +2\mathrm{AB} & \\ \mathrm{AG^*} & \searrow & \mathrm{AG^*:AB} \end{array} \qquad (24)$$

The "bound" and "free" labelled antigens are separated under the conditions of heterogeneous IEA and a calibration plot of the ratio of the "bound" and "free" antigens against the antigen concentration is plotted (the standard deviation s_r = 0.03–0.05). A carbon paste electrode is used as the electrochemical sensor.

The heterogeneous version of IEA has also been applied to the determination of immunoglobulin G.[120] In this case the determination is carried out directly on the surface of the carbon glass electrode on which the antibodies had been adsorbed. The surface of the electrode then functions as the immunological solid phase and the electrochemical detector proper. The enzyme-marker is glucose oxidase with benzoquinone as the mediator. Procedures have been developed for the regeneration of the electrode surface after the determination, which is important for the automation of the IEA procedure.

The current arising in the electrochemical cell with serum as the electrolyte and a carbon glass disc working electrode, coated by the immobilised immunoglobulin or anti-immunoglobulin combined in a complex with immunoglobulin, increases following the addition of the serum containing immunoglobulin (the serum–immunoglobulin system) or anti-immunoglobulin (the serum–immunoglobulin–anti-immunoglobulin system).[121] It has been suggested that the complexes formed have a double-layer structure, which induces an increase in the current.

A flow immunoreactor with a platinum electrode and a flow rate of 0.5 ml min^{-1} has also been proposed for the determination of immunoglobulin G. In this case, the immunoglobulin was

immobilised on a carrier and the marker was glucose oxidase attached with the aid of *p*-benzoquinone. The analyser works stably for almost three months with an error in the determination of $\pm 3\%$.[122]

An amperometric immunodetector, based on the oxidation of glucose by immobilised glucose oxidase with ferrocenium ions playing the role of a mediator and an antigen marker simultaneously, has been used to determine the medicinal drug lidocaine (α-diethylamino-2,6-dimethylacetanilide), whose concentration in plasma must be carefully monitored.[123] Under the conditions of homogeneous competitive IEA, the antigen–ferrocenium ion complex then plays the role of an electron acceptor for glucose oxidase. The catalytic current arising in the enzymic oxidation of glucose diminishes after the binding of the antigen–ferrocene complex to the antibody. This inhibition is reversible when the free antigen is added. The duration of the determination does not exceed 15 min ($s_r = 0.03-0.06$).

In another case, in the study of the same immune complex (lidocaine–anti-lidocaine), glucose-6-phosphate dehydrogenase was used as the antigen marker. Its activity was determined from the rate of oxidation of NADH at a platinum electrode.[124]

An amperometric sensor of the flow type has been developed[125] for the determination of α-asparaginase. The enzyme-marker was horseradish peroxidase. Its enzyme activity was estimated with the aid of a carbon electrode and an I_3^- depolariser. The concentration c_L for α-asparaginase is in the case 1.8×10^{-10} M, which corresponds to clinically significant enzyme concentrations. The analyser was tested on a wide range of objects: immunoglobulin, α-amylase, the antibody to the HIV virus and the X virus of the potato, egg albumin, and cell suspensions.[126] The results of the determination are consistent with the results of spectrophotometric analysis. The productivity of the sensor (more than 350 tests per hour) makes it possible to use it to estimate the influence of biotechnical manufacturing processes on the environment and man.

The analytical possibilities and advantages of the flow-injection immunological analysis, which consists in injecting the substrate (10–20 μl) into a stream of liquid flowing through a microreactor with an immobilised enzyme covalently bound to the antigen (antibody) have been examined in two communications.[127,128] The degree of the immunological reaction is estimated, for example, from the oxidation current of the products of the enzymic reaction at a platinum electrode.[127] Under these conditons, c_L for the substrate is 10^{-15} M. After suitable treatment of the immunosorbent, it is possible to carry out 500–600 determinations for almost three months with high metrological characteristics.[128]

An analyser based on glucose oxidase immobilised on a gel support as a result of an immunlogical reaction has also been used in the flow-injection version of analysis.[129] Such indirect immobilisation makes it possible to replace the carrier readily and to regenerate easily the system after the determination with only a 5% loss of the initial activity. The entire procedure takes less than an hour. The reversible immobilisation of the enzyme is achieved by a different sequence of reactions including the antigen–antibody interaction.[129] The ranges corresponding to the linearity of the calibration plots are $1.1 \times 10^{-9}-1.1 \times 10^{-5}$ and $1.1 \times 10^{-10}-1 \times 10^{-6}$ M. Three principles are combined in such devices: an enzyme electrode, a flow system, and an immunological reaction.

In all the versions of the IEA examined, the enzyme is used as an antigen or antibody marker, whose redistribution between the solid and liquid phases depends on the concentration of the test compound. New IEA systems, based on the fact that the appearance of the enzyme in solution is a consequence of a specific antigen–antibody interaction, are being developed nowadays.[130] One of the ways of creating such systems involves the incorporation of the enzyme within liposomes on the surfaces of which the antigen is attached chemically. The addition to the system of an antibody and of a complement- (set of enzymes) containing solution leads to the formation of the antigen–antibody complex on the liposome and its lysis by the action of the complement bound to the antibody fragments. The lysis is accompanied by the transfer of the enzyme to the solution. The addition to the system of the antigen to be determined inhibits the lysis as a consequence of the attachment to the liposome of a smaller number of antibody and complement molecules. The rate of appearance of enzyme activity in the solution serves as a characteristic of the initial antigen concentration.[131] The duration of the analysis of theophylline (liposomes with peroxidase) is 15 min and the sensitivity is 4×10^{-9} M for the electrochemical recording of the peroxidase activity in the oxidation of NADH.[132] Apart from enzymes, electrochemically active marker species (ions, substrates) can be incorporated in liposomes.

The principal data characterising the properties and the design of the immunoenzyme electrodes described above are presented in Table 2. It is noteworthy that the chemical amplification of the signal, which occurs under the influence of enzymes, can be used also for the determination of hormones, certain medicinal drugs, neuromediators, cyclic nucleotides, and certain biologically important compounds, whose concentration in the organism is less than 10^{-6} M.[131] A series of reviews has also been devoted to these and other problems concerning the use of immunoenzyme sensors.[20,21,25,26,114,119,133,134]

In conclusion one should note that the problem under discussion is of extremely great current interest. At the present time there exist very many devices (biosensors) of different designs with amperometric indication of the analytical signal and based on immobilised enzymes. In many instances, both potentiometric and amperometric enzyme sensors are constructed for such purposes, the latter finding more extensive applications because they usually exhibit a greater range corresponding to the linearity of the analytical signal and a lower limit of the concentrations which can be determined. Furthermore, in the amperometric version of the biosensor, in contrast to its potentiometric analogue, it is possible to immobilise the enzyme directly on the electrode surface by incorporating it in a polymer film which can be produced in the course of electropolymerisation.

The present review concerning the state of the problem of amperometric biosensors is naturally far from being able to cover exhaustively the entire literature published at the present time. There is no need to compare in it the advantages and disadvantages of a particular biosensor, because each biosensor is usually constructed for the solution of some kind of practical problem, normally operates under specific conditions, and is usually applicable to the determination of specific compounds in a specific medium. One may say with much confidence that detectors with immobilised enzymes, a wide variety of which exist, supplement one another. Only practice can provide an answer to the question of which biosensor is best or worst in each specific case depending on the operating conditions and the nature of the object to be analysed.

The need for the biosensors under consideration is rapidly and continuously increasing and the requirements as regards their operating properties are becoming more stringent. Further development of theoretical and practical aspects of their application involves the expansion of the assortment of the industrially produced enzymes and the improvement of the methods for their

Table 2. Characteristics of immunoenzyme electrodes.

Substance determined	Compounds used		Immobilisation procedure	Electrochemical sensor	Range of concentrations determined	Refs
	AG(AB)	Enzyme (marker)				
Human serum albumin (HSA), insulin	AB (anti-HSA), anti-insulin	Catalase for HSA, glucose oxidase for insulin	AB on capron mesh	Membrane oxygen electrode	Less than 10^{-8} M HSA; Less than 10^{-6} M insulin	[118]
α-Acid glycoprotein	AG	Alkaline phosphatase	Treatment with glutaraldehyde	Carbon paste electrode	1.0–10.0 ng ml^{-1}	[119]
Rabbit immunoglobulin G	Anti-immunoglobulin G	Glucose oxidase—AG marker	AB adsorbed on the surface of a carbon glass electrode	Carbon glass electrode	4×10^{-16} mol cm^{-2} of electrode surface	[120]
Immunoglobulin G	"	Glucose oxidase—AG marker (attached with the aid of *p*-benzoquinone)	Immobilisation on a carrier	Platinum electrode in a flow immunoreactor		[122]
Lidocaine	Antilidocaine	Glucose oxidase with ferrocenium ion—AG marker and mediator simultaneously	Covalent grafting to a carrier	Gold disc working electrode, platinum gas counterelectrode	5–50 mM	[123]
α-Asparaginase	Anti-asparaginase	Horseradish peroxidase—AG marker	Immobilisation of AB to asparaginase in hollows on polystyrene plates	Graphite electrode in a flow analyser	1×10^{-11}–4×10^{-10} M	[125]

immobilisation, an increase in the sensitivity and stability of the electrochemical sensors themselves, and improvement of the materials used for their preparation. Various modifications of the electrode surface play a major role in this connection.[135–136]

It has been suggested that biosensors constitute the future of analytical chemistry and the present revolution in this field of science has been expected for some time. One of the reasons for this view is apparently the large volume of research into biosensors.

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Translated from *Uspekhi Khimii* **60** 913–948 (1991) U.D.C. 547.592.3:541.14:541.128

Norbornadiene–quadricyclane — an effective molecular system for the storage of solar energy

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ABSTRACT. The results of studies on intramolecular interconversions in systems of norbornadiene ⇄ quadricyclane and their derivatives are classified and discussed. The mechanisms of the forward photoreaction and reverse thermal process in relation to the nature of the substituents and carbocycles, type of sensitiser and catalyst, and properties of the medium are discussed in detail and classified. An analysis is made of the influence of these factors on the spectroscopic, kinetic, and thermodynamic properties of this system as an accumulator and converter of light energy. Methods of improving its chararacteristics — light absorption, the quantum yield of the photoreaction, and stability of the photoproduct — have been established.

The bibliography includes 188 references.

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I. Introduction

According to the calculation of specialists, with the most economical consumption of fuel, all of its forms used by man at the present time (coal, oil, natural gas, uranium) will be exhausted after 130 years.[1,2] This period is allotted to changing over to the use of alternative, ecologically clean energy sources — solar, wind, and oceanic energy.

The extent of utilisation of solar radiation is very considerable. Solar energy is used to operate high-temperature units that concentrate a stream of radiation by means of mirrors, where the accumulators of energy used are either physical heat-carriers or inorganic compounds that can undergo cyclic thermal decomposition–synthesis reactions (oxides, hydrates, sulphates, carbonates). Systems of a different type convert radiant energy into electrical, heat, or chemical reaction energy by means of photophysical or photochemical processes.[1,3,4]

At the present time the following methods of photochemical conversion of solar energy (SE) have been widely studied:

— the photocatalytic decomposition of water using metal-complex compounds as catalysts;[2,5]

— the development of "solar photoelectrolysers" based on photoelectron transfers, the photogalvanic effect, stabilisation of the products of photoelectron transfers in the electrical double layer at a phase boundary, etc.;[2,5–7]

— photosynthesis[2,7,8] — the most efficient biochemical method of storing solar energy.

A comparative analysis of the possibilities and prospects of these trends in the use of SE has been carried out in a number of monographs and reviews.[2,4,9–11] An aspect of the abiotic conversion of SE that has been less studied is its storage as strain energy in metastable photoisomers of organic compounds followed by its release in the form of heat energy.

In a number of review articles[12–16] devoted to a study of this aspect of solar energy conversion and an analysis has been carried out of the requirements to be met by a photochromic compound A, its photoform B, and the parameters of the process by which storage and conversion of solar energy occurs.

$$A \underset{\Delta}{\overset{h\nu}{\rightleftarrows}} B + \Delta H. \qquad (1)$$

1. The initial compound A must absorb in the UV and visible region of the spectrum (from 400–600 nm) since more than 50% of the sun's light energy that reaches the earth is distributed over the region 300–700 nm (380–170 kJ per Einstein). The photoisomer B, on the other hand, should be colourless so as to avoid photoinitiation of the reverse reaction. Both components of reaction (1) should be nonluminescent compounds.

2. The energy level of the ground state of compound B formed in photoreaction (1) must lie sufficiently above the level of the ground state of A for the liberation of heat ΔH in the reverse reaction to be considerable (>300 J g^{-1}), exceeding the heat stored in the solar warming (ΔT = 50 °C) of water (ΔH = 209 J g^{-1}), sand (ΔH = 42 J g^{-1}) and salt hydrates (ΔH = 250 J g^{-1}).

3. For prolonged conservation of energy stored by photoisomer B the activation barrier of the thermal transition B → A ($\Delta H^{\pm}$) must be sufficiently high — of the order of 85–105 kJ mol^{-1}.

4. The photochemical reaction A→B must have a high quantum yield, the transition B→A, which liberates stored energy, must be susceptible to catalytic acceleration or thermal initiation. High chemical yields and the absence of by-products are necessary for both processes.

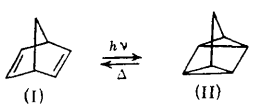
5. Compounds A and B must be sufficiently cheap, available, nontoxic, nonexplosive, incombustible, and chemically stable towards air and atmospheric moisture.

Some of these requirements can be expressed quantitatively in the form of Eqn. (2), which reflects the efficiency of a system that is capable of storing and converting SE.[17-19]

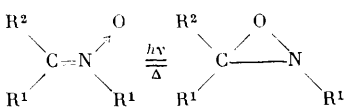
$$\eta_e = \frac{\Delta H \Phi}{E_{h\nu}} \cdot \frac{\int_0^{\lambda_{lim}} I_\lambda(\lambda/\lambda_{lim})d\lambda}{\int_0^{\infty} I_\lambda d\lambda} \eta_{abs} 100, \quad (2)$$

where η_e is the efficiency of the photochrome; ΔH is the difference in enthalpy between the initial compound A and its photoform B; Φ is the quantum yield of photoreaction (1); $E_{h\nu}$ is the energy of the photons (per Einstein) of absorbed light (for λ_{max} of compound A); λ_{lim} is the long-wavelength limit of absorption of compound A; I_λ is the distribution of power of solar radiation by wavelength; η_{abs} is the coefficient of absorption (ratio of the number of photons absorbed by compound A to the total number of photons in the solar spectrum with $\lambda \leqslant \lambda_{lim}$. For a more precise determination of the efficiency of photochromes as SE accumulators it is necessary to take into account the energy capacity of the material W, i.e., the quantity of energy stored per gram of initial compound and the number of working cycles [reaction (1)] without appreciable decomposition of the compound. Quite a wide range of photochromic organic compounds have been studied up to the present time. Amongst the most important reactions of A ⇄ B are the following:

1) valence isomerisation, for example, that of norbornadiene–quadricyclane (3)[20] or nitrone–oxaziridine (4) systems:[21]



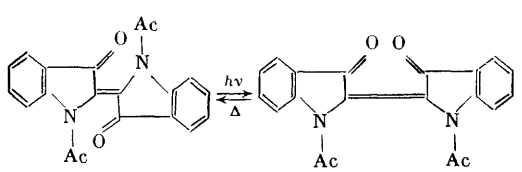
(I) (II) (3)



(III) (IV) (4)

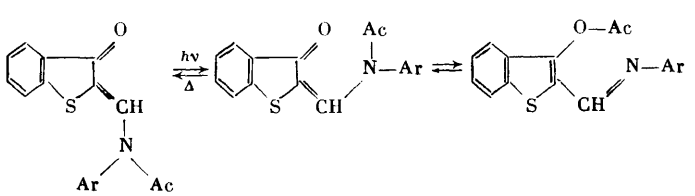
R¹, R² = H, Alk, Ar.

2) geometric (*Z*) ⇄ (*E*) isomerisation, for example, that of indigo derivatives:[22,23]



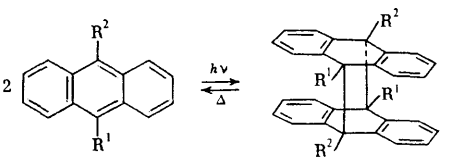
(V, *E*) (V, *Z*)

3) geometric isomerisation followed by intramolecular rearrangement, as in the case of *N*-acylated aminovinyl ketones of the type (VI):[24]



(VI, *Z*) (VI, *E*) (VII)

4) thermally reversible photodimerisation reactions, for example, those of anthracene derivatives:[19]



(VIII) (IX)

R¹, R² = H, Alk.

A summary of the results concerning these and other systems acting as accumulators of light energy appears in a monograph.[25] Table 1 indicates the parameters of some of the most efficient photochromic systems from which it is possible to determine whether they satisfy the requirements imposed on photochemical accumulators of SE.

Cyclic photodecomposition–thermal recombination reactions are also characteristic of certain inorganic systems that can also store light energy. The reaction of nitrosyl chloride can serve as an example:

$$NOCl \underset{\Delta}{\overset{h\nu}{\rightleftarrows}} NO + {}^1/_2Cl_2.$$

Although nitrosyl chloride has optimal spectroscopic data (λ_{lim} = 600 nm) and the quantum yield Φ of the photoreaction is close to unity, it is necessary to separate the photoproducts NO and Cl_2 to prevent too rapid a reverse reaction occuring in parallel with the forward process.

The main advantage of organic photochromes over inorganic ones is the possibility of extensive variation of their molecular structure in order to improve their properties as accumulators and converters of SE, namely: increasing the long-wavelength limit λ_{lim} of the absorption spectrum, increasing the quantum yield Φ of the photoreaction A → B, increasing the exothermicity ΔH of the dark reaction, and the choice of an effective catalyst for the reaction B → A, which causes the liberation of heat.

Intensive investigations in recent years have shown that the most promising development in optimising all of the required parameters is the modification of systems that are characterised by photoinitiated valence isomerisation involving ($2\pi + 2\pi$) cycloaddition, primarily in relation to the readily available norbornadiene derivatives (I). Thus, the main advantage of the norbornadiene–quadricyclane system is the very high exothermicity of the thermally forbidden ($2\sigma + 2\sigma$)-cyclodecomposition of quadricyclane (II) (-110 kJ mol^{-1})[26] (see Table 1). The aim of the present review is to analyse the main approaches to improving the characteristics of this system and to bring them into possibly closer correspondence with the above-mentioned requirements.

II. Optimisation of the spectroscopic properties of the system norbornadiene–quadricyclane

The valence isomerisation of norbornadiene to quadricyclane (3) was first studied by Hammond et al.[20,27] The storage of energy in this photoreaction occurs through the formation of the metastable quadricyclane structure (II), which contains the highly strained cyclobutane and two cyclopropane rings. The following advantages of this photochromic system may be noted: 1) the forward reaction

Table 1. Parameters of certain photochromic systems that can store solar energy.

System	λ_{lim}, nm	Φ	ΔH, kJ mol^{-1}	Q, %	η_A	η_e, %	W, mW g^{-1}	Properties of form B	
								Thermal stability*	Photostability (Φ_{irr})
(I) ⇄ (II) (CuCl sensitiser) CuCl)	388	0.4	110(1200)	14	0.015	0.21	1.75	14 h (140 °C)	~0
(V, *E*) ⇄ (V, *Z*)	610	0.2	34(109)	3.5	0.27	0.95	300	200 s (25 °C)	0.1
(VI) ⇄ (VII) (Ar = Ph)	460	0.6	23(79)	6.2	0.09	0.56	230	20–30 days (25 °C)	0
Photosynthesis	700	0.1	467	26	0.36	8 **			

* Thermal stability — period of half-decomposition for the reaction $B \xrightarrow{\Delta} A$ at the temperature indicated.
** Theoretical value of efficiency; in real systems η_E approximately equals 0.1–0.3%.

can be sensitised and there are effective catalysts for the reverse reaction; 2) the reverse reaction has a high activation barrier (half-decomposition time of (II) is equal to 14 h at 140 °C);[27] 3) the starting products for the synthesis of norbornadiene (I) and its derivatives are amongst those produced by large-scale synthesis; 4) both forms (I) and (II) are liquids, which provides a number of production benefits.

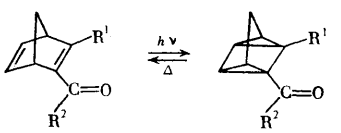
However, there are also considerable disadvantages in system (3). Thus, photochrome (I) has an absorption at too short a wavelength (about 300 nm),[28] in the absence of a sensitiser the quantum yield of the photoreaction is very small, and chemical modification of the structure of norbornadiene often results in irreversible secondary photoreactions.

Thus, in order to improve the properties of the photoconversion of norbornadiene–quadricyclane it is necessary, first of all, to shift the long-wavelength limit of absorption of norbornadiene to longer wavelength in the spectrum [improve λ_{lim} in Eqn. (2)] and at the same time increase the quantum yield of Φ of the photoisomerisation of (I) → (II).

In order to resolve this problem substituents with various chromophoric groups are introduced into the norbornadiene molecule. Three possible ways of "colouring" norbornadiene are known: 1) the introduction of electron-withdrawing substituents or an electron-donating and electron-withdrawing substituent into one of the double bonds of norbornadiene; 2) the introduction of electron-donating and electron-withdrawing substituents into the different double bonds of norbornadiene, resulting in the appearance of a charge-transfer band; 3) the formation of charge-transfer complexes of norbornadiene with transition metal compounds.

1. Norbornadienes containing substituents on one of its C=C double bonds

For the majority of known norbornadiene with simple electron-withdrawing groups (COOH, COOMe, CN, etc.) at the 2- and 3-positions, λ_{lim} does not exceed 365 nm.[29–35] 2-Aroyl-3-aryl-norbornadienes (X),[36] in which charge transfer occurs from the aryl group to the aroyl group thus increasing the efficiency of the photo-reaction for formation of quadricyclanes (XI), absorb at longer wavelength.

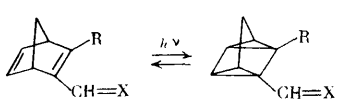


(X) (XI) (5)

R¹, R² = Ar.

Compounds (X) have λ_{max} = 320–370 nm (Table 2), which corresponds to λ_{lim} = 400 nm, while for the norbornadiene (X, *f*), λ_{lim} = 450 nm. Irradiation of norbornadienes (X) with light of wavelength 350 nm yields the corresponding quadricyclanes with high quantum yields (Φ = 0.3–0.6). Electron-donating groups in the aroyl residue assist both an increase in λ_{max} and the quantum yield Φ, while a nitro group, although increasing λ_{max}, sharply reduces the efficiency of photoisomerisation.

3-Phenylnorbornadiene-2-carbaldehyde and its imines (XII) have spectroscopic properties which are similar to compounds (X).[37]



(XII) (XIII) (6)

R = Ar; X = O, NAr.

The absorption maxima of (XII) are grouped in the region of 310–370 nm, the limit of the long-wavelength band reaching 420 nm (Table 2). However, in contrast to norbornadienes (X), the nature of the photoreaction of imines (XII) is determined by the type of solvent; in nonpolar aprotic solvents only isomerisation on the C=N bond occurs, while in proton-donating solvents quadricyclanes (XIII) are formed.

Table 2. Spectroscopic properties of norbornadienes and quantum yields of photoreactions (5)–(11).

Compound (X)	R¹	R²	λ_{max}, nm in MeCN	log ε	λ_{lim}, nm (ε=0)	λ_{irr}, nm	Φ
a	Ph	Ph	325	3.62		350	0.30
b	C_6H_4Me-*p*	Ph	332	3.69		350	0.44
c	C_6H_4OMe-*p*	Ph	348	3.72	~400	350	0.60
d	C_6H_4Cl-*p*	Ph	323	3.69		350	0.36
e	$C_6H_4NO_2$-*p*	Ph	341	4.00		350	0.09
f	C_6H_4OMe-*p*	$C_6H_4NO_2$-*p*	370	3.65	450	366	0.07
g	Ph	β-naphthyl	330	3.73		350	0.32
h	C_6H_4OMe-*p*	C_6H_4Cl-*p*	353	3.74		366	0.50
i	$C_6H_3(OMe)_2$-3,4	C_6H_4Cl-*p*	364	3.73	~400	366	0.41
j	OMe	C_6H_4Br-*p*	353	3.75		366	0.52
k	Me	C_6H_4Br-*p*	337	3.69		366	0.40

Compound (XII)	R	X	λ_{max}, nm in 2-propanol	log ε	λ_{lim}, nm (ε=0)	λ_{irr}, nm	Φ
a	Ph	O	318	4.1	400	313	0.4
b	Ph	NPh	343	4.1	430	365	0.15
c	Ph	NC_6H_4OMe-*p*	365	4.2	440	365	0.1

Compound (XIV)	R¹	R²	λ_{max}, nm in CH_2Cl_2	log ε	λ_{lim}, nm	ε	Φ (λ_{irr}=405 nm)
a	H	H	337	3.44	460	34	0.21
b	Me	H	342	3.50	460	42	0.21
c	Me	Me	345	3.55	460	52	0.22
d	OMe	H	410	3.03	460	480	0.22

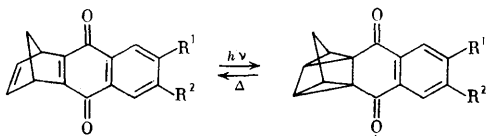
Compound (XVI)	R¹	R²	λ_{max}, nm in aqueous Na_2CO_3 solution	log ε	λ_{lim}, nm (ε=0)	Φ (λ_{irr}=313 nm)
a	H	H	290	3.11	365	0.59
b	Me	H	285	3.30	365	0.52
c	CH_2Ph	H	280	3.49	370	0.59
d	C_6H_9-*t*	H	280	3.40	370	0.54
e	Me	Me	275	3.11	335	0.45
f	$-(CH_2)_4-$		270	3.20	340	0.50
g	Ph	H	307	3.88	430	0.09
h	Ph	Me	270	3.42	360	0.31
i	$-C_6H_4-(CH_2)_2-$		292	3.86	415	0
j	Ph	Ph	270	3.74	405	0
k	CH_2COOH	H	285	3.34	365	0.57

Compound (XX)	λ_{max}, nm in ethanol	log ε	λ_{lim}, nm (ε=0)	Φ (λ_{irr}=334 nm)
a	315	3.83	~380	0.72
b	306	3.92		0.78
c	316	3.93		0.79

Compound (XXII)	λ_{max}, nm (in MeCN)	log ε	λ_{lim}, nm (ε=0)
a	364	3.80	~470
b	314	3.79	~400
c	328	3.64	

Compound (XXV)	R¹	R²	λ_{max}, nm in CH_2Cl_2	log ε	λ_{lim}, nm (ε=0)	Φ (λ_{irr}=546 nm)
a	H	H	495	4.29	580	0.5
b	Me	H	480	4.11	570	0.1
c	Me	Me	470	3.94	550	<0.01

Norbornadienes containing benzo- or naphtho-quinone residues [for example, (XIV)] absorb in the region of 340–410 nm (Table 2) and they have λ_{lim} = ~460 nm.[38,39] Methyl or methoxyl substituents in the quinone part of the molecule displace λ_{lim} to longer wavelengths with a constant quantum yield.

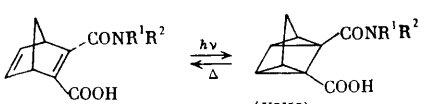


(XIV) (XV) (7)

R¹, R² = H, Me, OMe.

Irradiation of (XIV) with light with λ > 410 nm yields photoproducts (XV) in almost quantitative yield (Φ ~ 0.2). We should note that in earlier studies[40,41] the formation of quadricyclanes was not established.

Carbonyl substituents displace λ_{lim} appreciably to longer wavelengths.[41–45] The presence of carbamoyl and carboxyl groups at the 2- and 3- positions of the norbornadiene molecule makes it possible to carry out the photoisomerisation of (XVI) → (XVII) not only in organic solvents but also in weakly alkaline aqueous solutions.



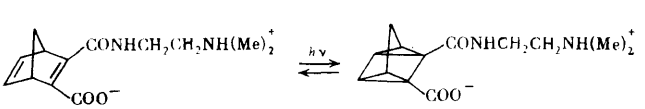
(XVI) (XVII) (8)

R¹, R² = H, Alk, Ar.

In the electronic spectra of compound (XVI) absorption bands occur at 280–340 nm (see Table 2) $\lambda_{lim} \approx 370-400$ nm, while for norbornadiene (XVI, *i*), λ_{lim} = 430 nm. *N*-Alkylamides absorb at longer wavelength than *N,N*-dialkylamides, although they, in turn, are inferior to *N*-arylamides in this respect.

On irradiation of compounds (XVI) in aqueous Na_2CO_3 solutions, quadricyclanes (XVII) are formed with quantum yields of 0.1–0.6. By studying system (XVI) it is possible to establish an important principle of the photochemical behaviour of norbornadienes of this type, namely, displacement of λ_{lim} to longer wavelength in the spectrum results in a decrease in quantum yield Φ of photocyclisation.[45]

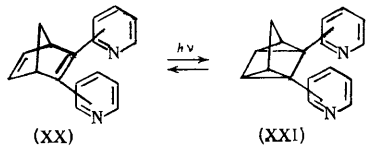
Further modification of carbamoyl-substituted norbornadienes led to the preparation of the first compound that was soluble in water.[46] For the bipolar ion (XVIII), λ_{lim} = 370 nm, but there was no information about the quantum yield of (XIX).[46]



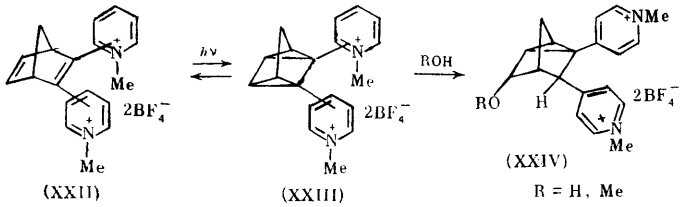
(XVIII) (XIX)

Norbornadienes containing heterocycles or heterocyclic cations as substituents are described in three studies.[47–49] The long-wavelength absorption of dipyridylnorbornadienes (XX) [47,48] reaches $\lambda_{lim} \approx$ 380 nm and irradiation with light of wavelength 334 nm results in

the formation of quadricyclanes (XXI) with high quantum yields (0.7–0.8).



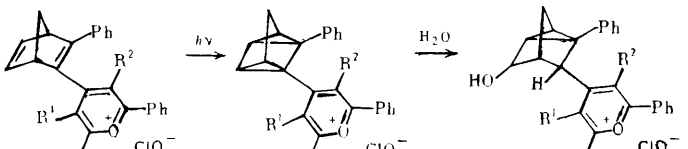
(XX) (XXI) (9)



(XXII) (XXIII) (XXIV) R = H, Me (10)

Quaternary salts of dipyridylnorbornadienes (XXII) have a considerably longer wavelength absorption up to $\lambda_{lim} \sim 470$ nm (see Table 2). However, when they are irradiated with light with $\lambda = 350$ nm, a photostationary state is established between the initial compounds and the photoreaction products in the ratio 12:88 (XXII, *b*) and 30:70 (XXII, *c*), which is apparently due to an absorption in the region of 350 nm that is present in the resulting quadricyclanes. In the presence of traces of water and methanol, norbornadiene (XXII *a*) under these conditions forms the adduct (XXIV).

Record values of λ_{lim} (from 550 to 580 nm) occur in norbornadienes (XXV) containing pyrylium cations at the 2-position[49] (see Table 2). Photoconversion of (XXV) to the corresponding quadricyclanes occurs rapidly and effectively even in diffuse light, but the reaction is very sensitive to traces of moisture, so the final products are adducts (XXVII).



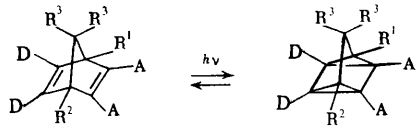
(XXV) (XXIV) (XXVII)

R^1, R^2 = H, Me (11)

2. Norbornadienes with electron-donating and electron-withdrawing substituents on the different double bonds

The theoretical possibility of increasing λ_{lim} in a norbornadiene through a charge-transfer band that occurs by interaction of the electron-donating and electron-withdrawing substituents on the different double bonds was substantiated in two studies.[50,51] The geometric strain in the norbornadiene molecule leads to an interaction of the π-orbitals of the double bonds in the molecule through space, resulting in a considerable convergence of the energy levels of the frontier molecular orbitals.[52,53] This manifests itself spectroscopically in unsubstituted norbornadiene absorbing at longer wavelength than does a compound with two isolated C=C bonds.[28] The presence of electron-donating substituents on one of the two double bonds of norbornadiene and electron-withdrawing substituents on the other causes a further bathochromic shift of the long-wavelength absorption band.

Depending on the nature of the substituents D and A in (XXVIII) molecules, λ_{lim} can vary from 345 to 558 nm (Table 3), and the quantum yield of compounds (XXIX) remains high (0.26–0.96)



(XXVIII) (XXIX)

D = H, Me, Ar; A = CN, COOMe, CONHPh; R^1, R^2, R^3 = H, Me.

A bathochromic shift of the long-wavelength absorption band of norbornadienes (XXVIII) occurs[51,54,55] when the electron-donating and electron-withdrawing capacities of substituents D and A are increased [cf. compounds (XXVIII, *b*) and (XXVIII, *c*); (XXVIII, *d*) and (XXVIII, *f*); (XXVIII, *j*) and (XXVIII, *k*) in Table 3]. The most important characteristic of compounds (XXVIII) is that, in contrast to norbornadienes containing substituents on one of the double bonds, the increase in λ_{lim} is in many cases not accompanied by any significant decrease in quantum yield of the photoreaction (XVIII) → (XXIX). Quadricyclanes (XXIX) are formed quantitatively even in the presence of oxygen in solution. In the opinion of Hirao et al.,[54] norbornadiene (XXVIII, *k*), for which $\lambda_{lim} = 558$ nm, $\Phi = 0.75$, is the most suitable for storage of SE.

Table 3. Spectroscopic properties of donor-acceptor norbornadienes and quantum yields of the photoreaction (XXVIII) $\overset{h\nu}{\rightleftarrows}$ (XXIX).

Compound (XXVIII)	D	A	R^1	R^2	R^3	λ_{lim}, nm (in benzene)	Φ (λ_{irr} = 383 nm)
a	H	CN	H	H	H	345 *	0.59 **
b	Me	CN	Me	H	H	430 *	0.96 **
c	Ph	CN	H	H	Me	494 *	0.95 **
d	Me	CO_2Me	H	H	Me	441	0.66
e	Me, Ph	CO_2Me	H	H	Me	474	0.71
f	Me, C_6H_4OMe-*p*	CO_2Me	H	H	Me	526	0.26
g	C_6H_4OMe-*p*	CO_2Me	H	H	Me	554	0.08
h	Me, C_6H_4OMe-*p*	CONHPh	H	H	Me	528	0.28
i	C_6H_4OMe-*p*	CONHPh	H	H	Me	559	0.05
j	Ph	CO_2Me	Me	Me	H	487	0.56
k	Ph	COEt, CO_2Me	Me	Me	H	558	0.75

* in MeCN; ** λ_{irr} = 313 nm.

Photoconversions of the system (XXVIII) ⇄ (XXIX) can be carried out in poly(methyl methacrylate) films,[55] the magnitude of λ_{lim} and Φ remaining virtually unchanged, and the number of working cycles of (XXVIII) ⇄ (XXIX) without a change in extinction of the initial compound is 10^3. According to the results of Miki et al.,[65] with the same number of cycles the losses of working compound in solution can amount to 20%.

In order to increase the thermal stability of the quadricyclane structures, Hirao and Yamashita[56] proposed the introduction of stabilising acceptor groups (A = CF_3, CF_2Et, CHFEt) into the initial norbornadienes. However, the details of conducting the photoreaction have not been reported.

3. Complexes of norbornadiene with transition metal salts

A further method of increasing λ_{lim} is to use complexes of norbornadiene with different transition metals instead of the unsubstituted compound (I). In this case a new band appears in the electronic spectra of the resulting compounds at a longer wavelength than the absorption compound (I).[15] However, an efficient photoconversion of such systems to quadricyclane (II) only occurs for complexes of norbornadiene with univalent copper salts. The mechanism of such reactions is examined in Section III. We should merely note that λ_{lim} for complexes of norbornadiene with CuX (X = Cl, Br, I, OAc) is no greater than 360 nm. The main disadvantage of this method of inceasing λ_{lim} is the tendency of Cu(I) salts to undergo mild oxidation to bivalent copper salts, which no longer form complexes with norbornadiene.

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By comparing the above approaches to increasing λ_{lim}, the following conclusions can be drawn. The use of norbornadiene complexes with Cu(I) salts displaces λ_{lim} to 360 nm with a satisfactory quantum yield. The main problems of this method are the high sensitivity of the complexes of atmospheric moisture and the lack of scope for varying the structure.

In the case of norbornadienes that contain substituents on one of the two double bonds, λ_{lim} is shifted into the visible region as far as 400–470 nm (even to 580 nm in some cases). The main disadvantage of this method is the sharp decrease in quantum yield Φ of the photoreaction with an increase in λ_{lim}.

By using norbornadienes with electron-donating and electron-withdrawing substituents on the different double bonds it is possible to shift λ_{lim} to even longer wavelength (500–600 nm), and in this case it is possible at the same time to achieve high values of both λ_{lim} and Φ. This approach would appear to have the greatest potential, although, as before, there remain three disadvantages that are difficult to overcome: 1) the reduction in quantity of stored energy per gram of substance because of the increase in molecular weight of the substituted norbornadiene; 2) the relative complexity of the synthesis of such compounds; and 3) their high cost.

III. Methods of increasing the quantum yield of photoisomerisation of norbornadiene to quadricyclane

The photoconversion of unsubstituted norbornadiene to quadricyclane is characterised by quite a low quantum yield (Φ = 0.05),[28,55] but it can be increased substantially with the use of sensitisers. The following methods of sensitisation have been used: 1) formation of complexes between transition metal compounds and norbornadiene that are stable in the electronic ground state; and 2) interaction of a sensitiser (S) in an electronically excited state with norbornadiene (I), resulting in energy transfer and the formation of charge-transfer complexes or the addition-elimination of sensitiser.

In the first case the stable complex that is initially obtained undergoes photoexcitation

$$S + (I) \rightarrow [S\cdots(I)] \xrightarrow{h\nu} S + (II). \qquad (12)$$

The following requirements should be met by the transition metal compound S used as sensitiser:[57]

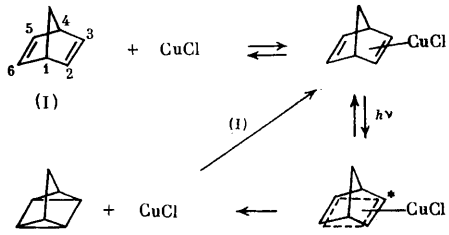
1) The transition metal in compound S must be in a low oxidation state and coordinated with a single norbornadiene molecule (the coordination of S with two norbornadiene molecules assists its dimerisation):

2) the [S···(I)] complex must absorb in the visible region:

3) S must not catalyse the reverse reaction (II) → (I);

4) S must not participate in secondary photochemical reactions.

Despite the fact that many transition metals are capable of forming complexes with norbornadiene,[15] only univalent copper compounds satisfy these requirements to a sufficient degree.[58–62] The photoisomerisation mechanism has been studied in the greatest detail in the case of the complex between norbornadiene and CuCl:



(13)

The initial components—norbornadiene (I) and CuCl—do not absorb in the region >300 nm, whereas the complex formed by them has an intense charge-transfer band with λ_{lim} = 350 nm. Photoexcitation of this complex by light with wavelength 313 nm results in the formation of quadricyclane as the sole product (Φ = 0.2–0.4, depending on the solvent). It is assumed that photoexcitation in the charge-transfer band of the [(I)...CuCl] complex causes the bonds between the C_2-C_3 and C_5-C_6 atoms in norbornadiene to become weaker and the bonds between the C_2-C_6 and C_3-C_5 atoms to become stronger. Subsequent relaxation of the excited state gives either norbornadiene again or quadricyclane. The latter does not form complexes with Cu(I) salts, so catalytic quantities of CuCl are sufficient for conversion of all of the norbornadiene to quadricyclane. The formation of quadricyclane when CuBr, CuI, CuOCOMe,[61,62] and also certain complex Cu(I) compounds are used occurs by a similar mechanism.[63,64] The quantum yields of the photoconversion (I) → (II) on irradiation of complexes of norbornadiene with $CuBr(Py)(PPh_3)$ and $Cu[HB(Pz)_3]$ (Py = pyridine, Pz = 1-pyrazolyl) with light at λ = 313 nm are 0.1–0.2 (in benzene) and (0.37–0.65) (in hexane) respectively, and $\lambda_{lim} \approx 370$ nm.

The second possible way of sensitising the reaction (I) → (II) is by interaction of a sensitiser S with norbornadiene according to the mechanism

$$S + (I) \xrightarrow{h\nu} {}^*S + (I) \rightarrow S + (II). \qquad (14)$$

In the opinion of Juris et al.[57] this type of sensitiser must satisfy the following requirements: 1) not form complexes with norbornadiene in the ground state; 2) absorb in the visible region, with the lifetime of the excited state *S being sufficiently long for the bimolecular reaction (14) to occur; 3) not catalyse the reverse reaction (II) → (I); 4) not participate in secondary photochemical reactions. The latter two requirements match those represented in scheme (12).

Since the conversion of norbornadiene to quadricyclane occurs in a triplet state,[65,66] the greatest efficiency of photoreaction (I) → (II) is to be expected with triplet sensitisation, which consists of the following stages:[67]

$$S \xrightarrow{h\nu} {}^1S \rightarrow {}^3S + (I) \rightarrow S + {}^3(I) \rightarrow (II). \qquad (15)$$

At the first stage the sensitiser S undergoes photoexcitation to a

singlet state, at the second stage the intersystem crossing $^1S \rightarrow {}^3S$ occurs, at the third stage there is a triplet transfer of energy from ^3S to (I), and finally at the fourth stage (II) is formed from triplet-excited (I).

Such a transfer of energy is only favourable for sensitisers with a triplet state energy higher than in norbornadiene (i.e., $E_T > 293$ kJ). However, in this case, as can be seen from Fig. 1,[15] even a small value of the singlet-triplet splitting of such systems will correspond to $\lambda_{lim} \leqslant 400$ nm. The condition $E_T > 293$ kJ is met by a relatively small number of sensitisers,[20,27,68–72] the range of these being mainly limited to carbonyl compounds (Table 4). As expected, the highest values of Φ were found for acetophenone ($E_T = 309.6$ kJ, $\Phi = 0.91$) and benzophenone ($E_T = 289.5$ kJ, $\Phi = 0.45$,[66], 0.8 [69]), with λ_{lim} equal to 366 and 380 nm respectively.

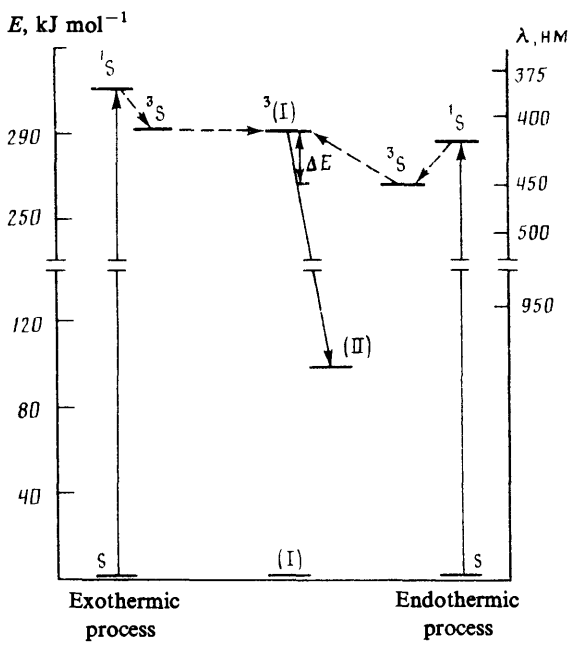
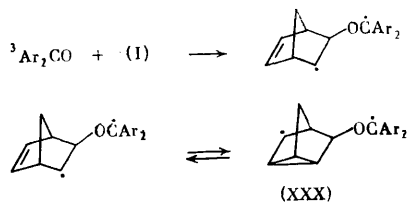


Figure 1. Energy levels of norbornadiene (I) and sensitiser (S).

For sensitisers with $E_T < 293$ kJ the transfer of energy from ^3S to norbornadiene is unfavourable (endothermic process in Fig. 1); nevertheless, efficiency sensitisation of reaction (I) → (II) even occurs in this case, which is due either to the formation of a [*S- - -(I)] complex in an excited state[15] or to the formation of covalent bonds between *S and (I).[73,74] Strong arguments in favour of the latter mechanism have only been established for substituted benzophenones. In fact, in a number of cases the value of Φ is not wholly determined by the magnitude of E_T (Table 4). With similar values of E_T the quantum yield is higher for benzophenones with electron-donating groups (compared to unsubstituted benzophenone) and less for benzophenones with electron-withdrawing groups. Arai et al.[74] conclude from kinetic data that in this case the following process competes with the energy transfer mechanism:



(16)

$$(XXX) \rightarrow (II) + Ar_2CO,$$
$$(XXX) \rightarrow (I) + Ar_2CO.$$

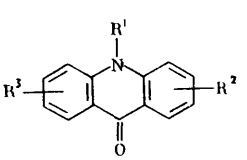
Table 4. Quantum yields of the sensitised photoreaction (I) ⇄ (II).

Sensitiser	E_T, kJ mol^{-1}	λ_{irr}, nm	$\Phi_{(I)\rightarrow(II)}$ (in CH_3CN)
Acetophenone	309.6	313	0.91
4,4'-Dimethoxybenzophenone	294.1	360	0.56
4,4'-Dimethylbenzophenone	290.0	360	0.59
4-Methylbenzophenone	289.5	360	0.50
Benzophenone	289.5	360	0.45
3-Benzoylpyridine	288.7	360	0.36
4-Methoxybenzophenone	288.7	360	0.53
4-Chlorobenzophenone	287.9	360	0.29
4,4'-Dichlorobenzophenone	286.2	360	0.29
4-Hydroxybenzophenone	285.8	360	0.42
2-Benzoylpyridine	282.0	360	0.35
4-Benzoylpyridine	281.2	360	0.40
4-Cyanobenzophenone	280.3	360	0.33
Triphenylene	278.2	360	0.02
Michler's ketone	259.4	360	0.04
4-Phenylbenzophenone	254.0	360	0.23
2-Naphthaldehyde	251.0	313	0.06
2-Acetonaphthone	246.9	313	0.05
Substituted acridinones			
(XXXI, a)	250	366	0.4 *
(XXXI, b)	260	366	0.75 *
(XXXI, c)	260	366	0.5 **
(XXXI, d)	239	366	0.7 ***
(XXXI, e)	240	366	0.4 *

*in DMF; **in toluene; ***in 1,4-dioxan.

However, the most common mechanism of sensitisation is the formation of [*S- - -(I)] complexes between the sensitiser (with $E_T < 293$ kJ) in an excited state and norbornadiene.[15,63]

The substituted acridunones (XXXI) acting by this type of mechanism absorb at longer wavelengths (λ_{lim} = 360–420 nm) than benzophenone[75] and have Φ(I)→(II) = 0.4–0.7 (see Table 4).



(XXXI)

a) R^1 = Me, R^2 = 3-NMe_2, R^3 = 6-NMe_2;
b) R^1 = Me, $R^2 = R^3$ = H;
c) R^1 = H, R^2 = 2-Br, R^3 = 7-Br;
d) R^1 = Me, R^2 = 2-Br, R^3 = 7-Br;
e) $R^1 = R^3$ = H, R^2 = 3,4-C_6H_4.

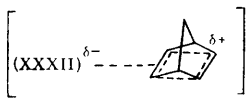
A general disadvantage of using carbonyl-containing compounds for sensitisation of the reaction (I) → (II) is the formation of products obtained by their photoaddition to norbornadiene or quadricyclane.[75–79] Moreover, they promote the polymerisation of norbornadiene, although this can be avoided by adding certain phenols such as 2,6-di-t-butyl-*p*-cresol to the solution.[70,72]

There are also reports on complex compounds of univalent copper that do not form complexes with norbornadiene in the ground state but effectively sensitise the reaction (I) → (II) [80,81] presumably by an endothermic route (Fig. 1) through the thermally activated transfer of energy from S to (I).[15,82] The value of λ_{lim} for $Cu[PPh_2Me]_3BH_4$, $Cu[PPh_3]_2BH_4$, Cu(prophos)BH_4 [prophos = 1,3-bis(diphenylphosphino)propane] is about 330 nm, while the Φ values in benzene at λ_{irr} = 313 nm are equal to 0.56, 0.76, and 0.88 respectively.

By incorporating groups that provide chromaticity into the molecule of the sensitiser Ph_3PCuXL (X = Cl, Br; L = 2,2′-dipyridyl, *o*-phenanthroline, phthalazine, pyridine) it is possible to conduct the reaction (I) → (II) on exposure to light of wavelength 313 nm and 366 nm.[41,83] The quantum yields in ethanol and THF constitute 0.03–0.13 (λ_{irr} = 313 nm) and 0.008–0.011 (λ_{irr} = 366 nm). The use of the compounds $[Cu(PPh_3)_2(dpk)]NO_3$, $[Cu_2I_2(PPh_3)_2(dpk)]$, and $Cu_4I_4(dpk)_3$] (dpk = di-2-pyridyl ketone)[84] as sensitisers results in λ_{lim} being shifted to 500–600 nm and with quantum yields in dichloromethane equal to 0.17, 0.25, and 0.36 respectively (λ_{irr} > 320 nm).

Certain sensitisers can form complexes with norbornadiene in both the ground state and an excited state.[85,86] On irradiation of norbornadiene with light with λ_{irr} > 270 nm in the presence of $Cu_2Br_2(AsPh_3)_3$ and $[CuCl(AsPh_3)]_4$, the quantum yield of the reaction in chloroform is 0.17 and 0.45 respectively, and the limiting value of Φ = 0.75 is reached with high concentrations of norbornadiene.[85] Sensitisation with the complexes $(Ph_2PCH_2CH_2.PPh_2)CuCl$, $(Ph_3P)_3CuX$ and $(MePh_2P)_3CuX$ (X = Cl, Br, I) makes it possible to reach the maximum quantum yield of $\Phi_{(I)\rightarrow(II)}$ = 1.0 in concentrated solution,[86] but dilution sharply reduces the quantum yield.

In a number of studies[57,62,87–89] there are reports on sensitisers containing other transition metals: $Ru(bipy)_3^{2+}$, $Ru(phen)_3^{2+}$, *cis*-$Ir(phen)_2Cl_2^+$, $Rh(phen)^{2+}{}_3$, where bipy = di-2-pyridyl, phen = 1,10-phenanthroline. However, in these cases $\Phi_{(I)\rightarrow(II)}$ does not exceed 0.006 (λ_{irr} = 366 nm). Only in the case of $Ir(bipy)_2.(bipy')^{3+}$ (XXXII) does the quantum yield amount to 0.72, which Grutsch and Kutal[89] relate to the formation of a charge-transfer complex in an excited state



By comparing the properties of the sensitisers described above it may be concluded that when compounds that form a ground state complex with norbornadiene are used, it is difficult to expect large values of λ_{lim} for the system [S- - -(I)], so that a considerable proportion of solar radiation cannot be utilised.

The action of triplet sensitisers such as acetophenone (with E_T > 293 kJ) is limited by the value λ_{lim} = 400 nm. It would appear that the development of sensitisers that have E_T < 293 kJ, absorb in the visible region, and are capable of forming charge-transfer complexes in the excited state with norbornadiene has the greatest future potential.

Although both processes (forward and reverse) for converting norbornadiene to quadricyclane are effected with kinetic control, surmounting the energy barrier of the counter reactions is achieved by different methods. The photochemical forward reaction is complemented by a dark thermal process whose efficiency is determined in many respects by the choice of catalyst.

IV. Catalysis of the thermal reaction quadricyclane → norbornadiene

A necessary condition for creating systems that store light energy is the kinetic stability of the product of the photoreaction. For the thermal conversion of quadricyclanes to norbornadiene, the high value of the energy barrier is dictated by the orbital restriction on the (2σ + 2σ)-cycloaddition reaction. The height of this barrier can be reduced when transition metal compounds and Lewis acids are used as catalysts and also by carrying out the conversion via radical cation intermediates.

Table 5. Catalytic activity of square-planar complex compounds in the isomerisation of quadricyclane to norbornadiene.

Ligand	Electronic structure of metal ion							
	d^5	d^6	d^7	d^8		d^9		d^{10}
	Mn(II)	Fe(II)	Co(II)	Ni(II)	Pt(II)	Cu(II)	Ag(II)	Zn(II)
Phthalocyanine	–	+	+	–	+	–	–	–
Tetraphenylporphyrin			+	+		–	–	–
N,N′-Ethylenebis(salicylidenimine)			+	–		–		–

Note. + = reaction goes to completion; – = no reaction.

1. Catalysis of unsaturated coordination transition metal complexes

The mechanism of catalysis of symmetry-forbidden electrocyclic reactions by transition metals was first analysed by Mango and Schachtschneider[90] and subsequently examined in more recent studies.[91–95] According to three studies[90,94,95] the role of the transition metal is that with a suitable orientation its *d* orbitals can form combined MOs with the delocalised σ-orbitals of the cyclobutane ring of quadricyclane and the π-MOs of the double bonds of norbornadiene. The change in symmetry of the frontier MOs resulting from this leads to a removal of the orbital restriction on the thermal reaction. According to another view of the role of the catalyst,[91] the transition metals make available their orbitals that are intermediate in energy between the HOMOs and LUMOs of the initial compounds and the reaction products, which results in a decrease in the energy of activation of the process, which remains forbidden.

The dependence of the catalytic activity of transition metal complexes on the extent of occupancy of the *d* shell and the geometric configuration was studied by Manassen.[96] It follows from the results given in Table 5 that metal complexes with a d^6–d^8

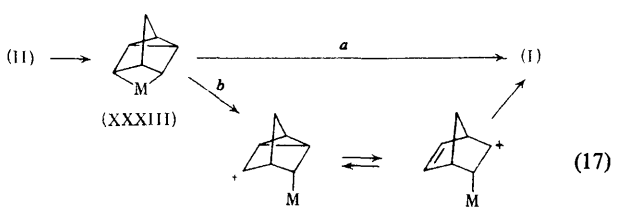
electronic shell in which there is either a vacant d_{zy} orbital or a higher populated p orbital that is similar in energy to an occupied d orbital are effective catalysts. In complex compounds of d^{10} elements [Cu(I), Ag(I)] all of the bonding orbitals are occupied by electrons and these complexes cannot catalyse a concerted opening of the cyclobutane ring.[93]

Another necessary condition for catalytic activity to occur in transition metal complexes is a square-planar structure of their molecules,[96] providing ease in additional coordination.

The available data on the opening of the cyclobutane residue catalysed by transition metal compounds are consistent with a multistage mechanism.[93,97,98] Depending on the properties of the central atom of the metal complexes, two main mechanisms for the multistage catalysed rearrangement of quadricyclane to norbornadiene can be distinguished:

1) an oxidative addition mechanism, which involves the insertion of a metal atom into the strained carbon–carbon bond to form the metallocyclobutane intermediate (XXXIII) followed by elimination of the catalyst[94,99,100] (route *a*);

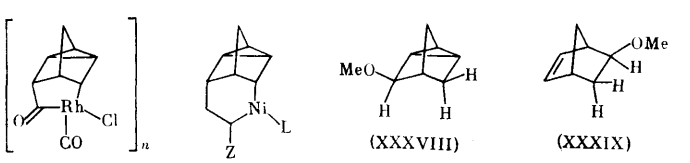
2) a mechanism through which carbocations (XXXIV) and (XXXV) are formed[97,101,102] (route *b*).



(17)

The ability of the catalyst to induce a particular reaction mechanism is determined by the magnitudes of the electron affinity and promotion energy (Table 6). While the first mechanism is typical for the initial members of the series—Ni(0), Pd(0), Pt(0), Rh(I)—the use of metal compounds with large values of these parameters—Pd(II), Pt(II), Cu(I), Ag(I), Zn(II), Hg(II)—leads to the formation of carbocation intermediates (XXXIV) and (XXXV). This is due to the fact that in the metallocycle (XXXIII) the metal atom is in a higher oxidation state and is quite a strong oxidising agent, resulting in heterolytic cleavage of the metal–carbon bond.

The choice between these two mechanisms can be made by analysing the reaction products. For the isomerisation of quadricyclane to norbornadiene catalysed by $[Rh(CO)_2Cl]_2$, complexes of the type (XXXVI) were isolated,[91] being formed by insertion of a carbonyl ligand into the metal–carbon bond of intermediate (XXXIII).



(XXXVI) (XXXVII) (XXXVIII) (XXXIX)

(I)

The formation of subsidiary nickel complexes (XXXVII) as intermediates in the reaction between quadricyclane and bis(acrylonitrilo)nickel has been postulated.[100] It should be noted that the organorhodium compounds (XXXVI) were only detected when rhodium dicarbonyl chloride dimer was used, which may be due to the specific properties of carbon monoxide as a ligand. In other cases the formation of metallocyclic intermediates was not established directly but followed from an analysis of the reaction products and the kinetic data. The formation of the derivatives of nortricyclane (XXXVIII) and norbornene (XXXIX) during isomerisation of quadricyclane by silver(I) and palladium(II) compounds in proton-donating solvents[104] is an argument in favour of reaction (17) occurring by route *b*. A similar dependence of the reaction products on the oxidising properties of the metal ion were found in the isomerisation of cubane catalysed by transition metal compounds.[105]

Table 6. Electron affinities and promotion energies of certain atoms or ions.

Electronic configuration	Atom or ion	Promotion energy, eV*	Electron affinity, eV
d^{10}	Ni(0)	1.72	1.2
d^{10}	Pd(0)	4.23	1.3
d^{10}	Pt(0)	3.28	2.4
d^8	Rh(I)	1.6	7.31
d^8	Ir(I)	2.4	7.95
d^8	Pd(II)	3.05	18.56
d^8	Pt(II)	3.39	19.42
d^{10}	Cu(I)	8.25	7.72
d^{10}	Ag(I)	9.94	7.59
d^{10}	Zn(II)	17.1	17.96
d^{10}	Hg(II)	12.28	18.75
d^{10}	Cd(II)	16.6	16.9

* Energy of transition beween the levels:

$$nd^{10} \rightarrow nd^9(n+1)p \text{ and } nd^8 \rightarrow nd^7(n+1)p.$$

The isomerisation of quadricyclane to norbornadiene catalysed by transition metal complexes was first reported in 1967.[106] It was shown that on treatment of a solution of quadricyclane with di-*m*-chloro-bis(norbornadiene)dirhodium in chloroform at −26 °C the time of half-conversion is 45 min [without a catalyst $\tau_{1/2}$ (140 °C) ≈ 14 h].[27] Other complexes of Rh(I) [90,104,106–109] and also Ni(0) [100,110] and Pd(0) [104,106,108,111] have similar properties.

The rate constants for isomerisation of quadricyclane in the presence of the norbornadiene complex [(I)RhCl], which were obtained by Cassar[99] do not depend on the concentration of norbornadiene and have values of 2.2 mol^{-1} s^{-1} and 1.8 mol^{-1} s^{-1} in chloroform and carbon tetrachloride respectively. However, it was shown previously[112] that this dimeric complex is decomposed by norbornadiene;

$$[(I)RhCl]_2 + 2(I) \rightleftarrows 2(I)_2RhCl. \quad (18)$$

This apparent contradiction was clarified by Taylor and Jennings.[109] From data on the position of equilibrium at different temperatures it follows that at 40 °C it is shifted quite considerably to the left, so there is no effect from norbornadiene. On lowering the temperature the equilibrium concentration of the monomeric complex $(I)_2RhCl$ increases, and because of its greater activity compared to the dimer, the rate of isomerisation increases by a factor of 1.7. The

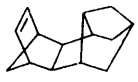
dependence of the equilibrium constant of (18) on temperature with a ratio of (I):$[(I)RhCl]_2$ = 4:1 is given below.

T, K	203	208	213	218	223	228	233
K	1.39	0.73	0.44	0.11	0.07	0.03	0.01

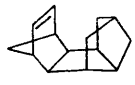
Replacement of a chloride ligand in $[(I)RhCl]_2$ by acetate results in a new equilibrium being established:

$$[(I)Rh(OAc)]_2 + (I) \rightleftarrows (I)_3Rh_2(OAc)_2. \quad (19)$$

Isomerisation of quadricyclane catalysed by the complexes $[(I)Rh(OAc)]_2$ and $(I)_3Rh_2(OAc)_2$ leads to the formation of the novel products (XL) and (XLI):[107]



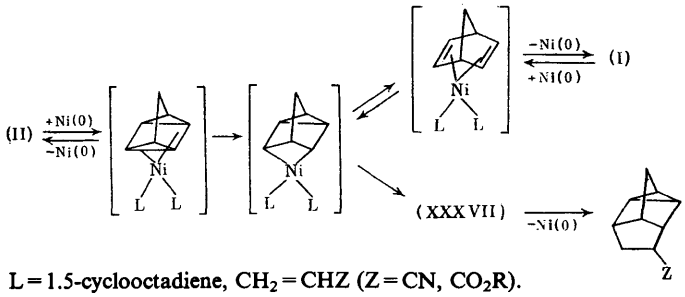
(XL)



(XLI)

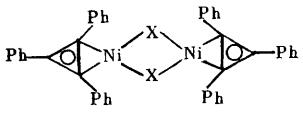
On the other hand, when carbonyl ($[Rh(CO_2)Cl]_2$) and norbornadiene complexes of univalent rhodium are used, norbornadiene is formed in quantitative yield.[104,113]

The formation of by-products (norbornadiene dimers, products of the insertion of ligands into the metal–carbon bond) occurs in the rearrangement of quadricyclane to norbornadiene catalysed by Ni(0) complexes:[100,114]



L = 1.5-cyclooctadiene, $CH_2=CHZ$ (Z = CN, CO_2R).

Derivatives of triphenylcyclopropenylnickel ($Ph_3C_3Ni(CO)X$, X = Cl, Br) (XLII) are active catalysts for the isomerisation of (II) → (I).[110] The initial rate of reaction depends on the concentration of catalyst and quadricyclane and comprises 2–4 (mol cat)$^{-1}$ s^{-1}. The data obtained indicate that the nickel complex (XLII) readily loses its carbonyl ligand and the reactive species is the square-planar dimeric complex (XLII).



(XLIII)

The ability of (XLIII) to form complexes with both quadricyclane and norbornadiene results in steady-state conditions being established.

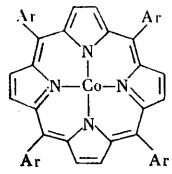
Replacement of the carbonyl in (XLII) by ligands that form stronger bonds with the metal atom [THF, $P(OPh)_3$, $PPhCl_2$, PPh_2Cl, $P(OPr\text{-}iso)_3$, $P(OMe)_3$, py, bipy] and an increase in the ratio of L:Ni in the molecule of the complex compound lead to a reduction in catalyst activity.

The relatively high activity of triphenylpropenylnickel complexes compared to other Ni(II) derivatives (also square-planar) may be due to the tendency of the cyclopropene ring to acquire a positive charge, and at the same time nickel becomes relatively negative. Thus, because of the unusual properties of the cyclopropene ligand, the Ni atom in $Ph_3C_3Ni(L)X$ will be sterically similar to Ni(II) and electronically similar to Ni(0).[110]

Because of the comparatively low value of the promotion energy of the palladium atom (4.23 eV) an oxidative addition mechanism can be proposed for the isomerisation of (I) → (II) catalysed by Pd(0) complexes. Analysis of the reaction products indicates the similarity of the intermediates formed by Rh(I) and Pd(0) complexes.[111]

Thus, only in rare cases do the above-mentioned process for the isomerisation of quadricyclane which are induced by Rh(I), Ni(0), and Pd(0) complexes result in the quantitative formation of norbornadiene. For the most part, by-products are formed.

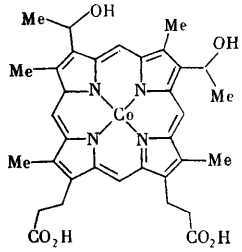
Some of the most widely studied and effective catalysts of the rearrangement of quadricyclanes to norbornadienes are the square-planar unsaturated coordination complexes of cobalt(II) with porphyrin (XLIV)–(LI), phthalocyanine (LII)–(LIV) and bis(azomethane) (LV, n = 2) ligands[51,96] (extending the methylene bridge in complexes (LV) by just one CH_2 group leads to deviation from a planar structure of the chelate centre and a loss of catalytic properties).



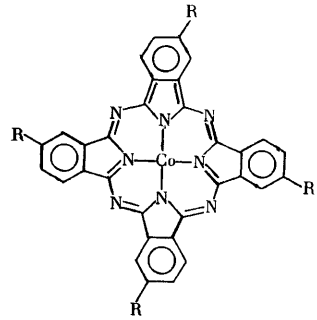
(XLIV) – (L)

(XLIV): Ar = Ph (Co-TPP),
(XLV): Ar = *p*-Me–C_6H_4 [Co-TPP(*p*-Me)],
(XLVI): Ar = *o*-Me–C_6H_4 [Co-TPP(*o*-Me)],
(XLVII): Ar = 2,4,6-$Me_3C_6H_2$ (Co-TMP),

(XLVIII): Ar = *p*-$C_5H_4\overset{+}{N}Me$ (Co-TMPy),
(XLIX): Ar = C_6H_4–SO_3H-*p* (Co-TPPS),
(L): Ar = C_6H_4–CO_2H (Co-TPPC).

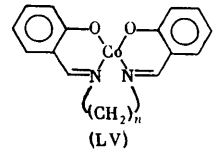


(LI)



(LII) – (LIV)

(LII): R = H (Co-Pc),
(LIII): R = SO_3H (Co-PcS_4),
(LIV): R = CO_2H (Co-PcC_4).



(LV)

The active catalytic site in these molecules occurs in the axial position (relative to the plane of the chelate CoN_4- or CoN_2O_2-centre); shielding of this reduces the efficiency of the catalyst:[115,116]

Co-TPP ~ Co-TPP(*p*-Me) > Co-TPP(*o*-Me) > Co-TMP.

In studies of the catalytic activity of Co(II) porphyrin and phthalocyanine complexes it was found that: 1) introduction of electron-withdrawing substituents into the ligand molecule increases the efficiency of the catalyst;[51,117] 2) the catalysts are effective in both aqueous solution and organic media (except for pyridine bases, which block the axial positions of the complexes);[96,118] 3) cobalt(II) porphyrin complexes in aqueous solution are more active than phthalocyanine complexes because of the ability of the latter to undergo aggregation.[118]

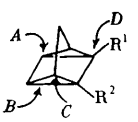
An increase in the hydrophobic properties of quadricyclanes—replacement of amide and carboxyl hydrogen atoms by alkyl or aryl groups—increases their reactivity, since the process that limits the rate of isomerisation in aqueous solution is approach of the quadricyclane to the hydrophobic environment of the active site of Co(II) porphyrin catalysts (Table 7).[118]

Table 7. Second-order rate constants for isomerisation of quadricyclanes (XVII).

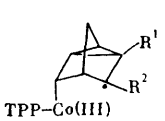
$CONR^1R^2$	k, $mol^{-1}\,s^{-1}$		Refs.
	Co-TPPC in $D_2O-Na_2CO_3$	Co-TPP in $CDCl_3$	
$CONH_2$	2.6	7.6	[116]
CONHMe	2.8		[118]
$CONHC_4H_9$-t	2.5		[116]
$CONMe_2$	3.9	4.5	
$CONCH_2CH_2CH_2CH_2$	6.9		[116]
CONHPh	6.7	6.4*	[118]
$CONHC_6H_4Cl$-*p*	7		[44]
$CONHC_6H_4Me$-*p*	6		[44]
$CONHC_6H_4OM$-*p*	7		[44]
$CONHCH_2Ph$	5.6		[116]
CONMePh	61.6	3.7	[116]
$CONHCH_2COOH$	2.0		[116]
COOMe	22.3	7.5	[116]
COOH	9.6		[116]

* in acetone-d_6.

It follows from the data given in Table 8 that an increase in steric hindrance to the approach of substrate and catalyst along direction *A* in (LVI) significantly reduces the rate of isomerisation. This direction of attack by cobalt(II) porphyrin catalysts is different from the direction of attack on quadricyclane by rhodium and nickel catalysts (routes *B* and *C*):[99,100]



(LVI)

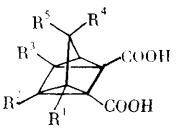


(LVII)

The ability of cobalt(II) porphyrin complexes to catalyse the isomerisation of quadricyclane is due to the presence of an unpaired electron in the d_{z^2} orbital of cobalt(II).[119] The existing literature data[120,121] are consistent with a radical mechanism for the process which involves the formation of the radical intermediates (LVII).

The advantage of cobalt catalysts is their quantitative conversion of quadricyclanes to norbornadienes in both organic solvents and water, but at the same time it should be borne in mind that there is a possibility of cobalt(II) being oxidised to cobalt(III), whose square pyramidal complexes, although more active,[122–124] are capable of inducing side reactions.

Table 8. Rate constants for isomerisation of substituted quadricyclanes (Co-TPPC, D_2O/Na_2CO_3)



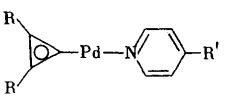
R^1	R^2	R^3	R^4	R^5	k, $mol^{-1}\,s^{-1}$
H	H	H	H	H	$1\cdot10$
Me	H	H	H	H	$4\cdot10$
H	Me	H	H	H	$7\cdot10^{-3}$
H	Me	Me	H	H	$<5\cdot10^{-3}$
H	H	H	Me	H	$2\cdot10$
H	H	H	H	Me	$1\cdot10^{-3}$
H	H	H	Me	Me	$9\cdot10^{-4}$

2. Carbocation mechanism of isomerisation

It was shown earlier that when transition metal complexes with a high electron affinity and promotion energy are used as catalysts, the reaction occurs via the formation of carbocation intermediates.

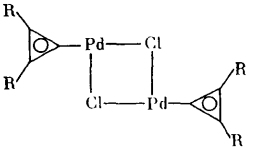
The ratio of isomerisation products of quadricyclane when the reaction is carried out in the presence of palladium dichloride and its complex compounds depends on the nature of the solvent used; in aprotic media only norbornadiene is formed,[104,111,126] while in proton-donating solvents (in methanol, for example) there is a mixture of products consisting of norbornadiene (40%), methanol adducts, and compounds of an undetermined structure.[104]

The Pd(II) cyclopropene derivatives (LVIII)–(LXI) are effective catalysts of the quadricyclane → norbornadiene process.[125]



(LVIII)–(LXIII)

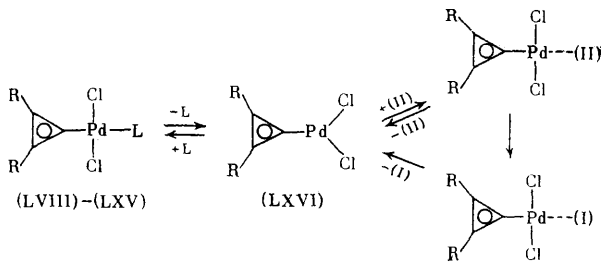
(LVIII): R = t-C_4H_9 R^1 = H; (LXI): R = iso-C_3H_7, R^1 = H;
(LIX): R = t-C_4H_9, R^1 = Me; (LXII): R = iso-C_3H_7, R^1 = Me;
(LX): R = t-C_4H_9, R^1 = CN; (LXIII): R = iso-C_3H_7, R^1 = CN.



(LXIV), (LXV)

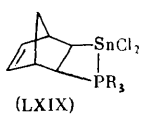
(LXIV): R = t-C_4H_9;
(LXV): R = iso-C_3H_7.

The catalytic activity of the complexes (LVIII)–(LX), (LXIV), and (LXV) is comparable to the activity of $[(I)RhCl]_2$, but in contrast to the latter they are not susceptible to oxidation. The active species in this case are unsaturated coordination complexes of the type (LXVI).



The efficiency of catalysts of this type depends on the tendency of the initial forms to dissociate—an increase of the electron-withdrawing properties of the ligands increases the catalytic activity. The dimeric complexes (LXIV) and (LXV) are more active than the monomeric (LVIII)–(LXIII) because of their higher dissociation constants.

The values of the ionisation potential and electron affinity of tin(II) (11 ± 5 and 14.6 eV respectively) provide an indication that Sn(II) ions are moderately good acceptors and poor donors of electrons. Hence it may be expected that metallocyclobutane complexes of the type (XXXIII, M = Sn) will be unstable. Only one form of complex between $SnCl_2$ and norbornadiene was detected using ^{119}Sn NMR.[126] The activation parameters for isomerisation of (II) → (I) catalysed by $SnCl_2$ are: $\Delta G^{\neq} = 94.05$ kJ mol^{-1}; $\Delta H^{\neq} = 58.10$ kJ mol^{-1}, $\Delta S^{\neq} = -120$ J deg^{-1} mol^{-1}. The less negative value of the entropy of activation compared to that for $PdCl_2$ (-230 J deg^{-1} mol^{-1}) may result from a reaction mechanism that is different from that represented by scheme (17). The bonding of $SnCl_2$ in the complexes with phosphine ligands $Me_3P{=}SnCl_2$ (LXVII) and $Ph_3P{=}SnCl_2$ (LXVIII) increases the catalytic activity of Sn(II) compounds—the half-conversion time of (II) → (I) in these cases is about 5 s (compared to 1 min for $SnCl_2$). Adducts (LXIX) or charge-transfer complexes may be reaction intermediates.[127]



The conversion of quadricyclane to norbornadiene accelerated by $HgCl_2$ that occurs in quantitative yield at 18–20 °C has also been reported.[128] The process mechanism involves chloromercuration of the substrate during a rapid initial stage in which 60% conversion is achieved [the Hg(II) compound acts as a catalyst]. Further conversion takes place slowly and is represented by zero-order kinetics.

The action of Ag(I) ions on quadricyclane and its derivatives has been reported in sufficient detail.[104,129–133] It was found[129] that the formation of norbornadiene, nortricyclane (XXXVIII), and norbornene (XXXIX) is accompanied by the reduction of Ag(I) ions, which is due to higher value of the ionisation potential of Ag(I) (7.57 eV)[101,129] compared to quadricyclane (7.40 eV).[134] Quadricyclanes with electron-withdrawing substituents have higher ionisation potentials, which inhibits the reduction of Ag(I).

The formation of carbocation species can occur not only via cyclic intermediates but also by direct addition of a catalyst ion to the substrate,[130] as in the case of catalysis by protic acids.[51,54,130,135,136]

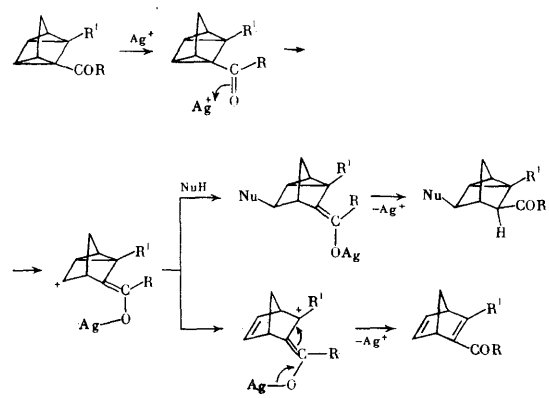
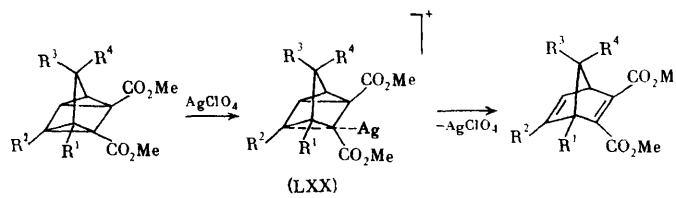


Table 9. Rate constants for isomerisation in reaction (20) catalysed by Ag(I).

R^1	R^2	R^3	R^4	$k^* \times 10^{-5}$, mol^{-1} s^{-1}, at: 25 °C	60 °C
H	H	H	H	1	30
Me	H	H	H	1	30
H	Me	H	H	$2.4 \cdot 10^3$	–
H	H	Me	H	1	40
H	H	H	Me	0	1
H	H	Me	Me	0	0.7

* Apparent initial second-order rate constants.

A different view is expressed in studies by Maruyama and Tamiaki.[131–133] It follows from the results given in Table 9 [131] that an increase in steric hindrance that makes *exo* attack by the catalyst on the 2-position of quadricyclane difficult results in a considerable slowing down of the reaction, since in this case attack by silver ions occurs along direction *D* (see above) to form the cation (LXX).



(20)

The reaction mechanism does not change when organic solvents are replaced by water.[132] The introduction of methyl substituents into the 6-position of quadricyclane-2,3-dicarboxylic acids and their esters considerably increases the rate of their isomerisation [through stabilisation of intermediate (LXX)] and it suppresses side reactions involving the addition of nucleophiles.

The rearrangement of 2,3-bis(trifluoromethyl)quadricyclane to the corresponding norbornadiene in the presence of a tungsten catalyst ($PhWCl_3-AlCl_3$) occurs with yields that are almost quantitative.[137]

3. Heterogeneous catalysis

The processes presented above involving valence isomerisation of quadricyclanes to the corresponding norbornadienes are carried out under conditions of homogeneous catalysis, which may have only limited practical application. In order to achieve a cyclic recurrence of the process of storage and release of light energy by the norbornadiene–quadricyclane system, it is necessary to fulfil at least two conditions—separation of the catalyst and the light-sensitive medium and to achieve a yield of virtually 100% for the thermal reaction. It follows from an analysis of the literature data that this is feasible under conditions of heterogeneous catalysis.[138] Transition metal complex compounds immobilised on various types of supports and also inorganic compounds were investigated as catalysts of this type.

While crystal hydrate chlorides of Sn(II) and Pd(II) are effective catalysts under conditions of homogeneous catalysis, only anhydrous salts of these metals are active during heterogeneous catalysis,[140] which is due to the blocking of the active sites on the surface of crystals of the catalyst by water molecules.

Anhydrous copper(II) sulphate has similar properties to those of anhydrous Sn(II) and Pd(II) chlorides,[140] while in the case of copper(II) halides a secondary redox process occurs, giving nortricyclane halides and univalent copper salts (with sufficiently high concentrations of CuX_2 this process predominates). The catalytic activity of copper salts results from the formation of charge-transfer complexes between quadricyclane and CuX_2 in which both rearrangement to norbornadiene and the reduction of Cu(II) to Cu(I) and addition of halogen to quadricyclane may occur.

Table 10. Classification of oxides according to their ability to accelerate the isomerisation of (XXIX, *j*).

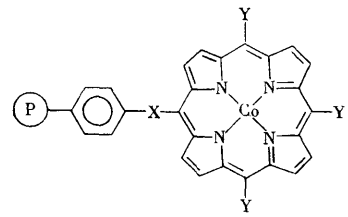
Group of catalysts	Time of reaction for the given group of catalysts	Oxide*
I	10 min	ReO_3 (24.7), MoO_3 (23.4), WO_3 (22.1), As_2O_5 (22.0), Sb_2O_5 (20.9), PtO_2 19.8, RuO_2 (19.8), TeO_2 (18.9), V_2O_5 (17.6), Nb_2O_5 (17.6)
II	24 h	Ta_2O_5 (16.5), SiO_2 (16.2), GeO_2 (16.2), SnO_2 (16.2), PbO_2 (16.2)
III	isomerisation has not occurred after 24 h	Rh_2O_3 (15.4), MnO_2 (13.5), TiO_2 (13.5), Sb_2O_3 (13.3), Bi_2O_3 (13.3), Tl_2O_3 (12.6), Fe_2O_3 (12.6), Ni_2O_3 (12.6), ZrO_2 (12.6), In_2O_3 (11.9), Co_3O_4 (11.4), Cr_2O_3 (11.2), Ga_2O_3 [11.2), HgO (9.5), AgO (9.5), CuO (9.5), CdO (8.5), ZnO (8.0), BaO (4.5)

* Electronegativity values of metals (χ_i) are given in brackets.

Inorganic oxides have the ability to accelerate effectively the isomerisation of quadricyclane to norbornadiene.[140–142] It was demonstrated that the catalytic activity of the latter varies in the same way as the electronegativity value of the metal[142] (Table 10). Such a correlation makes it possible to assume that the metal oxides act in the same manner as a proton, whose behaviour has been described by Hirao et al.,[54] namely, the first stage of catalysis is attack by the metal on the carbonyl oxygen atom. An increase in solvating power of the solvent reduces the activity of the catalyst, and a solvent such as pyridine completely suppresses it. The use of an oxide mixture increases the efficiency of the catalytic system (a mixture of TiO_2 and ZnO correspond approximately to SiO_2 in efficiency), which is due to the increase in acidic properties of such a mixture.[143,144]

Immobilised transition metal complexes also have the ability to catalyse the isomerisation of (II) → (I).[145–147] The catalysts of this type known at the present time are obtained either by the adsorption of transition metal compounds on various types of supports or by their complexation with polymer-bound ligands.

The properties of covalently bonded Co(II) complexes have been studied by different groups of chemists.[118,14]



(LXXI)–(LXXIX)

P = polymer support

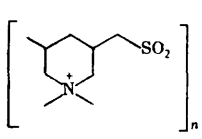
Compound	–X–	Y
(LXXI)	–NHCO–	CO_2Me
(LXXII)	$-NHSO_2-$	SO_2Me
(LXXIII)	$-CH_2NHCOC_6H_4-$	$C_6H_4CO_2H$-*p*
(LXXIV)	$-CH_2COC_6H_4-$	$C_6H_4CO_2H$-*p*
(LXXV)	$-COC_6H_4-$	$C_6H_4CO_2H$-*p*
(LXXVI)	$-CH_2-\overset{+}{N}(C_6H_4)-$	C_6H_4Me-*p*
(LXXVII)	$-CH_2-\overset{+}{N}Me_2-C_6H_4-$	4-C_5H_4N
(LXXVIII)	$-CH_2-\overset{+}{N}Me_2-C_6H_4-$	$C_6H_4NMe_2$-*p*
(LXXIX)	$-CH_2NHC_6H_4-$	$C_6H_4NH_2$-*p*

During the reaction the catalyst gradually loses its activity, which is due to the partial oxidation of Co(II) as well as its reaction with impurities. Treatment of the spent catalyst with reducing agents increases its activity. The rate of isomerisation of quadricyclane by such catalysts is virtually independent of the residue X, but the properties of the latter determine the stability of the catalyst under different conditions. Catalysts (LXXI)–(LXXIV) are hydrolysed in aqueous alkaline solution.

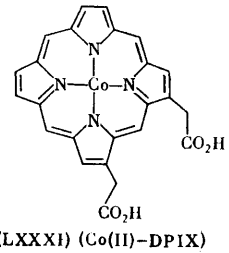
In addition to polymer-bound cobalt complexes, heterogeneous catalysts obtained by adsorption of complexes (XLIV)–(LV) on ion-exchange resins and inorganic materials have been studied.[118] In contrast to catalysts of the type (LXXI)–(LXXIX), Co(II) phthalocyanine and porphyrin complexes immobilised on carbon are less prone to a loss of activity during the process. Thus, for Co-TPPC (see IV.1) it is halved only after 10^4 cycles. Simple washing of the spent catalyst with boiling tetrahydrofuran completely restores the catalyst's efficiency.

Square-planar Co(II) complexes immobilised on aluminium oxide modified with polyaminosulphone (LXXX) are very promising

catalysts for the isomerisation of quadricyclanes. As in the case of cobalt porphyrins immobilised on carbon

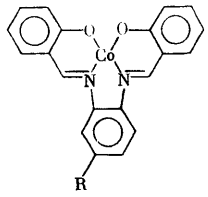


(LXXX) (PAS)



(LXXXI) (Co(II)-DPIX)

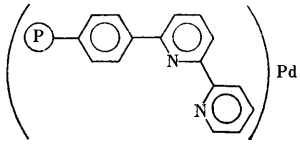
they are sufficiently effective, undergo slow deactivation, and are readily regenerated by heating under vacuum at 200 °C. However, the catalysts Co(II)-TPS/PAS/Al_2O_3 and Co(II)-DPIX/PAS/Al_2O_3 are not very active towards substituted quadricyclanes,[149] which is due to the steric repulsion between the equatorial ligands and the polysubstituted nortricyclane derivative (LVII). Complexes Co(II) such as (LV) (n = 2) and (LXXXII)–(LXXXV), with ligands that are more flexible than porphyrins, do not have these disadvantages.[150] In addition to activated carbon and alumina, poly(methacrylic acid), Florisil, magnesium silicate, and silica are also suitable as supports.



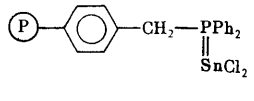
(LXXXII): R = H,
(LXXXIII): R = Me,
(LXXXIV): R = CO_2Me,
(LXXXV): R = CO_2H

(LXXXII)–(LXXXV)

The disadvantage noted for polymer-bound Co(II) porphyrin complexes are also typical for Pd(0), Pd(II), Sn(II) complexes fixed on polystyrene.



(LXXXVI)



(LXXXVII)

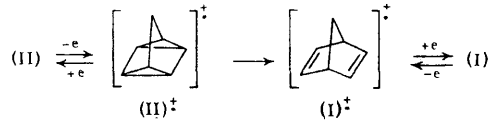
Thus, complex (LXXXVI) is deactivated during isomerisation as a result of oxidation and leaching of the metal.[127,128,152] Initially this catalyst is 30 times more active than palladium on carbon, but after two cycles their activities become equal.

Even less successful was the attempt to fix [Pd(MeCN)Cl_2] on a diphenylphosphine derivative of polystyrene. The activity of this type of catalyst proved to be much lower than for soluble [Pd(PPh_3)Cl_2] and it decreased even further on repeated introduction of this catalyst into the cycle.[152]

4. Radical cation mechanism for isomerisation

The barrier for many pericyclic reactions that occur via radical cation intermediates is known to be low in comparison with the barrier of similar reactions between neutral molecules.[153,154] When applied to the present problem of the catalysis of the isomerisation of quadricyclane, this method of lowering the activation barrier has the additional advantage of the ability of a radical cation of norbornadiene to oxidise quadricyclane and hence to the involvement of a redox chain mechanism.[155–160]

The generation of a radical cation of quadricyclane can be achieved, firstly, by oxidation of substrate with a photochemically generated oxidising agent,[161–165] secondly, by oxidising it with electronically excited sensitisers,[166,167] and finally, by electrochemical anodic oxidation of quadricyclane.[168] In each of these cases the $(II)^{+\cdot}$ radical cation is isomerised to the corresponding norbornadiene derivative $(I)^{+\cdot}$, which participates in the development of a redox chain reaction, so that the quantum yield (or yield based on current) of the reaction is greater than 1 (the isomerisation of quadricyclane to norbornadiene catalysed by dimethyldioxirane is also a chain process).[169]



$(II)^{+\cdot}$ $(I)^{+\cdot}$

Ikezawa and Kutal[161] showed that irradiation of n-type semiconductors (CdS, TiO_2, ZnO) in the presence of quadricyclane results in the formation of norbornadiene [$E^{Ox}_{1/2}(I)$ = 1.56, $E^{Ox}_{1/2}(II)$ = 0.91 V relative to a standard calomel electrode (SCE)].[162] The role of the oxidising agent in such systems is fulfilled by photogenerated holes that migrate to the surface of the semiconductor (Fig. 2*a*).

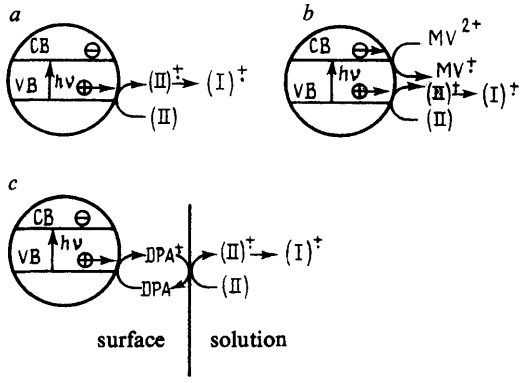


Figure 2. Schematic representation of the radical-cation mechanism of isomerisation of (II) → (I) on the surface of a semiconductor being irradiated. Adopted notation: CB = conductivity band; VB = valence band; MV^{2+} = methylviologen dication; DPA = diphenylamine.

The yield of norbornadiene is inversely proportional to the width of the forbidden band and varies in the series CdS > TiO_2 ⩾ ZnO. It can be increased by the addition of a methylviologen dication, which binds photogenerated electrons and thus prolongs the lifetime of the holes in the valence band (Fig. 2*b*). Addition of diphenylamine (DPA) ($E^{Ox}_{1/2}$ = 0.83 V), which acts as intermediate agent between the holes of the valence band and the quadricyclane molecules in solution (Fig. 2*c*) slightly increases the yield of norbornadiene. However, the ability of $DPA^{+\cdot}$ to dimerise to *N,N'*-diphenylbenzidine inhibits the cyclic processes [a more suitable intermediate agent may be tri-*p*-tolylamine ($E^{Ox}_{1/2}$ = 0.75 V)]. Although the attempts undertaken did lead to an increase in the yield of norbornadiene, the latter was still small (6–10%).

The results on the dependence of the rate of isomerisation of quadricyclane on the presence of oxygen in the system, obtained by Draper and de Mayo,[170] are different from those published by Kutal.[169] They found that when zinc was used, the rate of formation of norbornadiene increased in the presence of oxygen, which was due to the increase in lifetime of the photoinduced hole through bonding of an electron in a superoxide radical anion.[171] When CdS and TiO_2 were used the reverse effect occurred.[161,170,172,173] This may be due to predominating concurrent processes that involve the reduction of a radical cation by the superoxide anion, blocking of the surface of the semiconductor, and also the donation of an electron by chemisorbed oxygen to the photoinduced hole. The dark formation of norbornadiene (about 30%) in the presence of CdS was also detected.

Dichloronorbornadienepalladium molecules that are excited on exposure to radiation can act as oxidising agents. Irradiation of (I)$PdCl_2$ complexes in the presence of quadricyclane leads to isomerisation of the latter to norbornadiene with a yield exceeding 85%.[167,168,174] The quantum yield of the process is inversely proportional to the value of the half-wave oxidation of the strained hydrocarbon and for unsubstituted quadricyclane reaches a value of several hundred (Table 11), which is clear evidence in favour of a redox chain mechanism. For organic sensitisers the quantum yield is less than 1.[88,158,166,175–177]

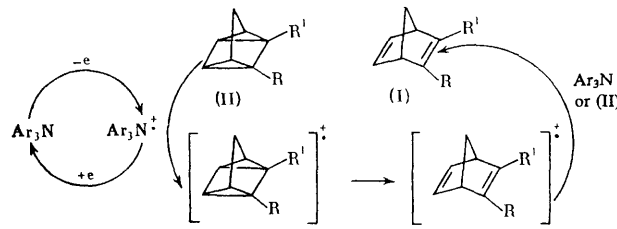
Table 11. Quantum yields of isomerisation of substituted quadricyclanes in the presence of (I)$PdCl_2$ (solvent—CH_2Cl_2, λ_{irr} = 405 nm).

Compound	$E^{Ox}_{1/2}$, V (vs. SCE)	Φ
Quadricyclane	0.91	230
2-Carbomethoxyquadricyclane	1.2	3.0
2,3-Dicarbomethoxyquadricyclane	1.64	0.06

Table 12. Electrochemical conversion of (II) → (I) (solvent—CH_2Cl_2).

Quantity of electricity passed through solution, $F \times 10^5$	Quantity of (II) before electrolysis, mol × 10^3	Quantity of (I) obtained mol × 10^3	Yield based on current	Quantity of (I) + (II) after electrolysis
2.1	0.97	0.16	7.6	1.02(±1.8%)
2.1	0.97	0.14	6.7	0.94(±0.7%)
0.89	0.42	0.056	6.3	–
4.1	1.52	0.45	11	1.83(±1.5%)

In the isomerisation processes examined above a preliminary stage—derivation of the active form of the catalyst—is required. A more convenient method is the direct generation of $(II)^{+\cdot}$ by anodic oxidation. The results obtained by Kutal et al.[168] (Table 12) show that: 1) electrolysis is quite suitable for obtaining norbornadiene; 2) the reaction is a catalytic process; 3) the yield based on current increases with an increase in concentration of quadricyclane; and 4) the conversion is sufficiently selective. A drawback of this method is contamination of the anode with a polymer film, which inhibits further reaction. This can be remedied with the use of an intermediate agent such as triarylamine, which is first oxidised at the anode and then reacts with quadricyclane.[178,179]



Better results were obtained for unsubstituted quadricyclane in the presence of tri-*p*-bromophenylammonium hexachloroantimonate ($E^{Ox}_{1/2}$ = 1.05 V). The introduction of substituents into the quadricyclane molecule and the use of the salts $(p\text{-}C_6H_4Br)_3N^+GaCl_4^-$ and Ph_3PMeX^- (X = $SbCl_6$, $GaCl_4$) increases the isomerisation time considerably and reduces the yield of product.[180]

5. Comparative properties of catalysts

It may be concluded from an analysis of the literature data on the efficiency of catalysts for the isomerisation of quadricyclane to norbornadiene that those with the greatest potential are square-plane complexes of bivalent cobalt. Their activity under conditions of both homogeneous and heterogeneous catalysis is usually comparable to the activity of compounds of other transition metals and in a number of cases substantially exceeds it. Moreover, when Co(II) catalysts are used, side reactions are absent in virtually all cases, in contrast to catalysis with cobalt(III) compounds. Amongst the disadvantages of catalysts of this type it is necessary to include the ease with which the oxidative process Co(II) → Co(III) takes place and the reduced efficiency of Co(II) towards quadricyclanes that are substituted with electron-withdrawing groups. These disadvantages do not occur in the carboxyl derivatives (LXXXV) on inorganic supports (activated carbon, alumina). An undoubted advantage of catalysts (LXXXV) is the possibility of regenerating them by relatively simple methods.

Metal oxides have very promising catalytic properties, but as yet no data exists on the possibility of carrying out cyclic processes with them.

Electrochemical oxidation of quadricyclanes is a fairly convenient method of accelerating the isomerisation of quadricyclanes to the corresponding norbornadienes. In the opinion of Gassman et al.,[178,179] some of these systems are feasible for use in real cases. Nevertheless, we should note that the conditions for the quantitative derivation of norbornadienes with this method have so far not been found.

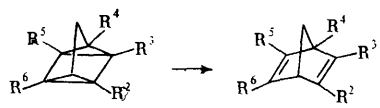
V. Exothermicity of the thermal reaction

As was mentioned in Section II, the exothermicity of the isomerisation of quadricyclane to norbornadiene satisfies the requirements imposed on photochemical materials that can store solar energy—it amounts to ~10^3 kJ kg^{-1}. The introduction of

substituents, while improving the spectroscopic properties of norbornadiene, results in an increase in molecular weight and hence causes a worsening of the energy parameters of the system.

The amount of energy accumulated by the photochemical isomerisation of norbornadienes to the corresponding quadricyclanes is determined both indirectly (from the difference between the heats of hydrogenation[181–183] and combustion[184] of both isomers) and by direct methods (by different scanning calorimetry[185] through measuring the enthalpy of isomerisation of quadricyclanes by homogeneous and heterogeneous catalysts[26,44,118,150] and by photocalorimeter). Photocalorimetry involves the measurement of energy absorbed by the system when the photoreaction is conducted directly in a calorimeter.[186] The results obtained are given in Table 13.

Table 13. Heats of isomerisation of the process



R^2	R^3	R^4	R^5	R^6	ΔH, kJ mol^{-1}	Refs.
H	H	H	H	H	96*	
H	H	H	CONHPh	CO_2H	59±4	[44, 118]
H	H	H	$CONHC_6H_4Cl$-*p*	CO_2H	60±4	[44]
H	H	H	$CONHC_6H_4Me$-*p*	CO_2H	60±5	[44]
H	H	H	$CONHC_6H_4OMe$-*p*	CO_2H	59±4	[44]
H	H	H	CONHMe	CO_2H	52±4	[44]
H	H	H	CO_2Me	CO_2Me	105.4±14.6	[186]
H	H	H	CO_2Me	CO_2Me	77.1±1	[185]
H	H	H	CN	CN	92.0±9.6	[186]
Me	Me	Me	CN	CN	88.0±8.0	[151, 186]
Me	Me	H	CO_2Me	CO_2Me	80	[51]
Me	Me	H	CN	CN	88	[51]
Me	Me	H	CN	CN	92	[51]

*Average value given. The values obtained by different methods are (in kJ mol^{-1}): 100,[181] 91.42,[182] 91.63,[183] 41.64,[184] 88.7 ± 0.8,[185] 110 ± 1, 113 ± 1,[26] 92 ± 4,[185] 59 ± 4,[186] 81 ± 1.[118]

The experimentally determined values of the heats of isomerisation of quadricyclane (ΔH) are virtually independent of the method used, except in two cases.[184,186] The low value of ΔH = 59 ± 4 kJ mol^{-1} obtained by calorimetry is attributed to an interaction of norbornadiene and quadricyclane with the sensitiser (acetophenone).

A comparison of the exothermicities of the rearrangements of substituted quadricyclanes shows that the introduction of methyl, cyano, and carboxymethyl groups has hardly any effect on the value of ΔH, whereas carboxyl and carboxamide groups reduce it by ~20 kJ mol^{-1}.

VI. Conclusion

The practical value of the system norbornadiene (I) ⇄ quadricyclane (II), if it is characterised by high values of λ_{lim} and Φ, is obvious. Information is available[51] on engineering studies carried out in Japan aimed at developing small-scale experimental systems operating on norbornadiene to heat buildings, garden houses, and greenhouses and to generate electrical energy.

However, in progressing towards the large-scale utilisation of heat energy liberated by the catalytic conversion of quadricyclane to norbornadiene there are certain difficulties, in particular those of an economic nature. The operating scheme of a system for absorbing solar energy followed by the production of low-pressure steam[12,13,187] is depicted in Fig. 3. Norbornadiene stored in tank *1* is transmitted by pump *2* at a pressure slightly above atmospheric through a planar collector *3* (possibly with an immobilised sensitiser). The quadricyclane obtained by the photoreaction is stored in tank *4*, from which it can pass at a required pressure (pump *5*) into heat-exchanger *6*. The latter is necessary only if the reverse reaction (II) → (I) is carried out thermally (for example, on heating quadricyclane to 140 °C). The heat liberated is used to obtain low-pressure steam (or hot water) in reactor-boiler *7*, which is supplied with immobilised catalyst *8* in order to carry out the conversion of (II) → (I).

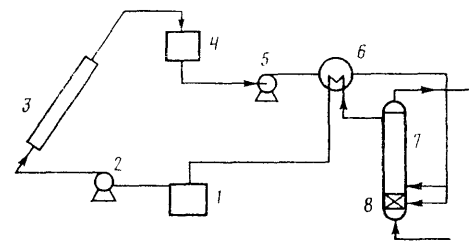


Figure 3. Operating scheme of a system for absorbing solar energy and the production of low-pressure steam (hot water): *1*, *4*, storage tanks; *2*, *5*, pumps; *3*, collector; *6*, heat-exchanger; *7*, reactor-boiler; *8*, immobilised catalyst.

Table 14. Cost of the unit shown in Fig. 3 with output of 100 kW (at 1981 prices).[187]

Equipment	Dimensions	Cost, in dollars
Collector *3*	Area 116000 m^2, depth 2 cm	2320000
Storage tanks *1* and *4*	120 m^3 each	60000
Heat-exchanger *6*	length 102 m	2500
Reactor-boiler *7*	27 tubes each of length 4.7 m	15000
Pumps *2* and *7*	—	4000
	Total	2410000

The norbornadiene used in such a system must be stable so that a large number of cycles of (I) ⇄ (II) can be achieved. 1440 cycles is considered to be the optimum number (corresponding to 99.99%

regeneration of norbornadiene per cycle and a total degree of discoloration of the initial material of 25%), and the cost of norbornadiene should not exceed 0.003 dollars per gram according to 1979 estimates.[188] We should note that in the light of the results of Yoshida et al.,[51,55] the required degree of cyclic recurrence does not seem impracticable nor does the reduction in price of the production of substituted norbornadienes (Table 14).

Taking into account the fact that the cost of steam obtained on such a system is substantially higher (by a factor of about 50) than the cost of steam produced by alternative methods, the main direction of efforts at the present time remains the development of less powerful small-scale units.

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Translated from *Uspekhi Khimii* 60 949–981 (1991) U.D.C. 661.491

Kinetics and mechanism of the oxidation of organic compounds with hydrogen peroxide

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ABSTRACT. The literature data on the kinetics and mechanism of the oxidation of organic compounds of various nature with hydrogen peroxide in aqueous solution have been analysed. A generalised kinetic scheme is described for the radical–chain decomposition of hydrogen peroxide in the presence of organic compounds for which a rate equation for the process has been found by the method of quasi-steady-state concentrations for long chains. Partial expressions have been obtained for the rate of oxidation of various organic compounds with hydrogen peroxide allowing for the nature of the organic compound.

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I. Introduction

Hydrogen peroxide is an available and effective oxidising agent and is widely used as a bleaching agent in the textile,[1] cellulose–paper industries[2] and in other fields.[3–5] Dilute solutions of hydrogen peroxide are used in medicine as an antiseptic and a disinfectant.[6,7] In addition H_2O_2 is used in the preparation of organic peroxides,[8] in the purification of effluent from substances oxidisable under mild conditions such as phenols,[9] and in the delignification of wood pulp.[10]

Hydrogen peroxide is a component of oxidation–reduction systems which are sources of free radicals in the initiation of free radical processes.[11]

Hydrogen peroxide is widely used as an initiator of radical polymerisation processes with unsaturated monomers[12] and also in the grafting of them to cellulose or its derivatives[13] and to water-soluble lignin preparations.[14] The efficiency of graft polymerisation and the extent of grafting are determined to a significant extent by the initiation stage which in fact is the reaction of hydrogen peroxide and its radicals with the initial polymer and with its macroradicals with subsequent interaction of the radicals obtained with the monomer.

Decomposition of hydrogen peroxide by radicals resulting on oxidation of certain oxygen-containing organic compounds (alcohols for example) with oxygen leads to further initiation of oxidation processes and co-oxidation of organic substances.[15]

Hydrogen peroxide often reacts with various types of organic compounds when used as an oxidising agent. Without a study in depth of the chemical mechanism of such practically important processes it is impossible to find optimum conditions for carrying them out, to effect target-directed control of them or to increase their efficiency.

II. Initiation of the oxidation of oxygen-containing organic compounds by hydrogen peroxide

Depending on conditions, the decomposition of hydrogen peroxide in aqueous media proceeds by a radical–chain or ion–molecule mechanism and by a heterogeneous catalytic mechanism on the reactor surface.[16–22] Hydrogen peroxide reacts with organic compounds in aqueous solution predominantly by a radical–chain mechanism which is indicated by the inhibition of such processes by unsaturated monomers and other acceptors of free radicals. Initiation with hydrogen peroxide of the radical–chain oxidation of oxygen-containing organic substances may occur by homolysis of H_2O_2 according to reaction (1) or by the direct interaction of hydrogen peroxide with the organic compound.[15]

$$H_2O_2 \rightarrow 2^{\cdot}OH, \qquad (1)$$

The energy of activation for the homolysis of H_2O_2 according to reaction (1) is close to the energy for the decomposition of the O–O bond in hydrogen peroxide (202 kJ mol^{-1}). In particular the energy of activation for the process in the gas phase at 470–540 °C, when decomposition of unimolecular H_2O_2 predominates, is in the range 170–210 kJ mol^{-1} which is close to the theoretical limit.[23] In an aqueous medium at fairly low temperatures it is significantly less, of the order of 84 kJ mol^{-1}.[21,24]

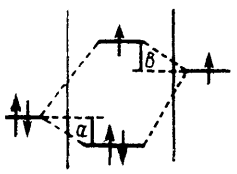
The reduction in the energy of activation may be explained by the formation of a complex of hydrogen peroxide with the solvent. The possibility of complex formation with the participation of hydroxyl-containing compounds has been shown.[24,25] If the H_2O_2 molecule participates in the formation of hydrogen bonds as a proton donor then the H–O and O–O bonds in it will be weakened, as was noted for hydroperoxides.[26]

In organic solvents capable of forming hydrogen bonds with H_2O_2 the decomposition of hydrogen peroxide with the formation of $^{\cdot}OH$ radicals is characterised by a reduced energy of activation

(84–105 kJ mol^{-1}) in comparison with the O–O bond energy in hydrogen peroxide.[27] This is explained by the interaction of H_2O_2 with hetero atoms of the solvent and by the formation of hydrogen bonds which generate favourable conditions for the interaction of electrons from the solvent (Solv) with the unbonded orbital of the radical arising on fission of H_2O_2. This leads to the formation of a complex.

$$\text{Solv...H—O—O—H...Solv} \rightarrow 2(\text{Solv...}^{\cdot}\text{OH}). \quad (2)$$

The energy level diagram for the complex between a hydroxyl radical and the electron-donating solvent is shown in Fig. 1. It is known that the splitting of energy levels on complex formation is greater the closer they are to one another, i.e. in the case in question the energy of complex formation grows with the increase in basicity of the solvent[28] and must increase in the series ketone–alcohol–water.



Solvent Complex Radical

Figure 1. Diagram of the energy levels of a complex between a radical and an electron-donating solvent.[27]

Several physicochemical investigations also show the formation of complexes of hydrogen peroxide with water. Liquidus diagrams for the system hydrogen peroxide–water indicate the presence of two eutectic points for the mixtures of ice–$H_2O_2.2H_2O$ and $H_2O_2.2H_2O$–solid hydrogen peroxide.[29] A deviation was established in such complexes for the atomic concentration (number of atoms per unit volume) from that calculated by the additivity rule.[30] A maximum is observed in the dielectric constant–composition isotherms for this $H_2O_2.2H_2O$ complex.[31]

At low concentrations of hydrogen peroxide in water the decomposition process is described by a kinetic equation which is first order with respect to H_2O_2.[10,25] When investigating the decomposition of concentrated solutions of hydrogen peroxide it was discovered that an increase in the water concentration in the system leads to a growth in the ratio of reaction rate to initial H_2O_2 concentration.[1] The order of the reaction with respect to water found from the data[1] proved to be 1.99 ± 0.41.[22] It was suggested[22] that the decomposition of H_2O_2 in water proceeds through the stage of forming the complex $H_2O_2.2H_2O$.

$$H_2O_2 + 2H_2O \underset{k_{-к}}{\overset{k_к}{\rightleftharpoons}} H_2O_2 \cdot 2H_2O, \quad (3)$$

$$H_2O_2 \cdot 2H_2O \xrightarrow{k_d} 2^{\cdot}OH \cdot H_2O. \quad (4)$$

The concentration of complex at steady-state-concentrations is

$$[H_2O_2 \cdot 2H_2O] = k_к (k_{-к} + k_d)^{-1} [H_2O_2][H_2O]^2. \quad (5)$$

From which it is possible to obtain an expression for the rate of decomposition of H_2O_2

$$w = k_к k_d (k_{-к} + k_d)^{-1} [H_2O_2][H_2O]^2, \quad (6)$$

which corresponds with the experimental data.[1]

The reduction in activation energy to 84 kJ mol^{-1} for the decomposition of hydrogen peroxide in aqueous solution may therefore be explained by the formation of a complex of H_2O_2 with water.

It may be shown that at low concentrations of hydrogen peroxide when $k_K (k_{-K} + k_d)^{-1}[H_2O]^2 \gg 1$, the position of the equilibrium is shifted practically completely to the side of forming the complex, so that $[H_2O_2.2H_2O]_0 = [H_2O_2]_0$ and the rate is practically equal to

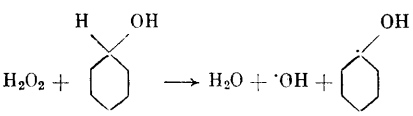
$$w = k_d [H_2O_2], \quad (7)$$

which corresponds with the experimental data.[22]

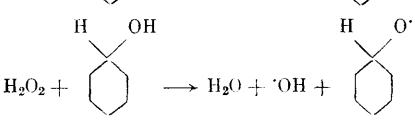
In the opinion of authors,[32] who studied the decomposition of H_2O_2 in cyclohexanol solution at 120–140 °C, the initiation of the oxidation of cyclohexanol with hydrogen peroxide may include the reactions given below:

$$H_2O_2 \rightarrow 2^{\cdot}OH \ (\Delta H = 210 \text{ kJ mol}^{-1}), \quad (8)$$

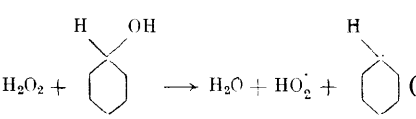
$$2H_2O_2 \rightarrow {}^{\cdot}OH + H_2O + HO_2^{\cdot} \ (\Delta H = 95 \text{ kJ mol}^{-1}), \quad (9)$$



$(\Delta H = 57 \text{ kJ mol}^{-1})$, (10)



$(\Delta H = 141 \text{ kJ mol}^{-1})$, (11)



$(\Delta H = 265 \text{ kJ mol}^{-1})$. (12)

The rate found experimentally for the initiation of the oxidation of cyclohexanol with hydrogen peroxide is described by the expression[32]

$$w_i = k_1 [H_2O_2] + k_2 [H_2O_2]^2, \quad (13)$$

where

$$k_1 = 8.9 \times 10^6 \exp(-98700/RT), \text{ sec}^{-1},$$

$$k_2 = 6.8 \times 10^9 \exp(-122000/RT), \text{ litre mol}^{-1} \text{ sec}^{-1}. \quad (14)$$

The initiation of the oxidation of propan-2-ol with hydrogen peroxide is represented[33] by a reaction of first order with respect to H_2O_2 with rate constant

$$k_1 = 1.1 \times 10^7 \exp(-96600/RT), \text{ sec}^{-1}. \quad (15)$$

Since

$$E_{act} \geqslant \Delta H, \quad (16)$$

for endothermic reactions, the second term in expression (13) may correspond to reaction (9). Consequently the first term in expression (13) may correspond to reactions (8), (10)–(12).

In the opinion of the investigators[32,33] the formation of radicals from H_2O_2 by unimolecular decomposition [reaction (8)] in a non-aqueous medium requires a significant consumption of energy (about 210 kJ mol^{-1}) and must proceed very slowly. The observed

activation energy for the initiation of oxidation of alcohols with hydrogen peroxide is significantly lower and is about 100 kJ mol^{-1}. The latter enabled the authors to propose that this reaction proceeds with the participation of alcohols [reactions (10)–(12)] disposed to form complexes with H_2O_2. However the heat of reaction for (11) and (12) is significantly greater than that of reaction (10) and approaches the heat of reaction for H_2O_2 homolysis. Consequently it was proposed[32] that radicals may be formed only by the bimolecular reaction (10). In addition a hypothesis has also been expressed[32,33] as to the possibility of carrying out a trimolecular reaction through the stage of complex formation.

$$H_2O_2 + 2ROH \rightleftharpoons ROH\ldots\underset{\underset{H}{|}}{O}\!\!-\!\!\underset{\underset{H}{|}}{O}\ldots HOR \longrightarrow 2H_2O + 2RO^{\cdot}. \quad (17)$$

Thermodynamic calculations[32,33] allowing for the stability of the O–H bond in the alcohol, the O–O in H_2O_2 and the H–O in water showed that

$$\Delta H = 2\times 428 + 210 - 2\times 495 = 76 \text{ kJ mol}^{-1}. \quad (17A)$$

It follows that reaction (17) is also energetically more advantageous than reactions (8), (9), (11) and (12) and the size of its heat of reaction relates to the experimentally found activation energy in accordance with expression (16).

In order to determine the reaction order with respect to alcohol for the initiation of oxidation of alcohols with hydrogen peroxide experiments were carried out using dilution of the reaction mixture with an inert solvent (chlorobenzene or decane).[32] However the results obtained, as calculated by the investigators, did not permit an unequivocal answer to the problem posed, since the dilution of the reaction mixture over wide limits (2–10 times) caused practically no change in reaction rate. This may be explained by the fact that in non-polar solvents, in which the solubility of hydrogen peroxide is insignificant, the latter is in the form of associates with cyclohexanol.

Investigation of the kinetics of the decomposition of hydrogen peroxide in an aqueous solution of phenol[25] at 115–160 °C showed that the initiation reaction rate was

$$w_i = k_1 [H_2O_2] + k_2 [H_2O_2][C_6H_5OH], \quad (18)$$

where

$$k_1 = 7.1\times 10^8 \exp(-99500/RT), \text{ sec}^{-1},$$

$$k_2 = 7.3\times 10^{10} \exp(-111000/RT), \text{ litre mol}^{-1} \text{ sec}^{-1}. \quad (18A)$$

The proportionality of the reaction rate in the first step to the concentrations of both peroxide and of phenol at an excess of the latter enabled the suggestion,[25] that initiation of the reaction of hydrogen peroxide and phenol is predominantly a bimolecular reaction.

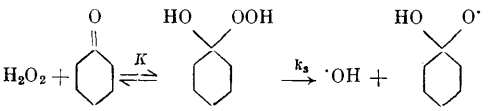
$$H_2O_2 + C_6H_5OH \rightarrow {}^{\cdot}OH + H_2O + C_6H_5O^{\cdot}. \quad (19)$$

It may be proposed that this reaction also includes a complex-forming step.

A thermodynamic calculation of the heat of reaction allowing for the bond stability in phenol (336 kJ mol^{-1}) led[25] to a value of ΔH = 50 kJ mol^{-1}, which according to (16) is in satisfactory agreement with the value of the activation energy found experimentally.

A feature of the decomposition of hydrogen peroxide in alcohols in the presence of ketones, in particular for cyclohexanol in the presence of cyclohexanone,[34] is the ability of the latter to form peroxides and hydroperoxides with H_2O_2 and consequently the initiation of oxidation may be described by the reactions

$$2ROH \ldots H_2O_2 \xrightarrow{k_1} 2RO^{\cdot} + 2H_2O, \quad (20)$$



(21)

The initiation rate of the process in this case is[34]

$$w_i = k_1 [H_2O_2] + k_3 [R(OOH)OH]. \quad (22)$$

The authors[34] noted that the rate of the unimolecular decomposition of the resulting hydroperoxide significntly exceeds the decomposition rate of hydrogen peroxide. Considering that the concentration of cyclohexanone hydroperoxide is proportional to the concentration of both hydrogen peroxide and of cyclohexanone

$$[R(OOH)OH] = K [H_2O_2] [R{=}O], \quad (23)$$

and the experimentally found overall initiation rate is proportional to the concentration of active oxygen, then the apparent rate constant for initiation may be described by

$$k_i = \frac{w_i}{[H_2O_2] + [R(OOH)OH]} = \frac{k_1 + k_3 K [R{=}O]}{1 + K [R{=}O]} \quad (24)$$

This permitted experimental determination of the rate constants of the individual reactions

$$k_1 = 8.9\times 10^6 \exp(-98700/RT), \text{ s}^{-1},$$

$$k_3 = 2.2\times 10^4 \exp(-68000/RT), \text{ s}^{-1}, \quad (24A)$$

and the equilibrium constant

$$K = 2.2\times 10^{-5} \exp(28100/RT), \text{ litre mol}^{-1}. \quad (24B)$$

The formation of acetone hydroperoxide on reaction of hydrogen peroxide with acetone has been observed.[35] At an acetone:H_2O_2 ratio <0.07 the hydroperoxides $(CH_3)_2C(OH)OOH$ and $(CH_3)_2C(OOH)_2$ were mainly formed but a further increase of this ratio as a result of interaction of hydroperoxides led to the appearance of peroxide $HOOC(CH_3)_2OOC(CH_3)_2OOH$ as a product.

Aliphatic acids are also inclined to form hydroperoxides. The reaction forming peroxyacids from hydrogen peroxide and acids is first order with respect to both components.[36–39] It is necessary to record that the reaction is reversible. For example the rate constant for the direct reaction of H_2O_2 with formic acid at 20 °C is 2.1 × 10^{-4} litre mol^{-1} s^{-1} and for the reverse 2.4 × 10^{-4} litre mol^{-1} s^{-1}.[36]

It has been recorded that sulphuric acid catalyses the formation of peroxyacids.[38] A study of the reaction of hydrogen peroxide with several aliphatic acids showed that the the reaction rate is determined mainly by the length and structure of the hydrocarbon radical of the acid. Comparison of the kinetics of forming mono-, di- and trichloroperoxyacetic acids[39] indicated that the reaction rate constants increased with the increase in the number of chlorine atoms in the acid molecule.

It may be concluded from the above that the activation energy for the decomposition of hydrogen peroxide in the presence of water and of hydroxyl-containing organic compounds may be significantly lower than the energy for fission of the O–O bond in hydrogen peroxide because of the formation of a complex between H_2O_2 and the hydroxyl-containing compound. The reduction of the activation

energy for hydrogen peroxide decomposition in the presence of ketones is explained by the formation of organic peroxides and hydroperoxides.

III. Interaction of hydroxyl radicals with organic substances

On oxidation of organic substances with hydrogen peroxide by a radical mechanism an important role is played by their reaction with hydroxyl radicals. Reaction may occur either through addition of ·OH radicals at a multiple bond or by direct abstraction of a labile hydrogen atom from the organic substance with the formation of a molecule of water or as a result of 'adhesion' of the hydroxyl radical to the aromatic ring. In particular the initiation by ·OH radicals of the polymerisation of unsaturated monomers has been fairly well studied. This includes the addition of hydroxyl radicals to substances containing double bonds.[12]

The addition of hydroxyl radical to benzene and some of its derivatives is also possible,[40–43] as a result of which hydroxy derivatives of cyclohexadiene are formed. The course of hydroxylation of benzene, its halogen derivatives and phenol was shown in a study[40] of the IR spectra of the radicals obtained in aqueous organic media under the action of a pulse of electrons.

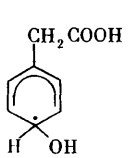
The reaction of benzene and its derivatives with hydroxyl radicals occurs by addition of the latter to the aromatic ring with a rate constant of 4.3×10^9 litre mol^{-1} s^{-1} (at 23 °C). In the presence of oxygen of the air, the nascent radicals add oxygen with the formation of peroxy radicals which in turn decompose into phenol or its derivatives and $HO_2^{\cdot}$ radicals.[40]

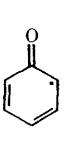
In view of the high reactivity of ·OH radicals displayed on direct addition of them to the aromatic ring of benzene and its derivatives, the rate constants of these reactions may be expected to be close to one another.[41] In reality the rate constants for the addition of hydroxyl radicals to benzene, toluene and benzoic acid at 25 °C lie within a fairly narrow range (2.1 to 3.3) $\times 10^9$ litre mol^{-1} s^{-1}.

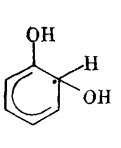
Rate constants for the addition of hydroxyl radicals to several benzene derivatives have been measured[42] and it was shown that they are reduced on going from amino and hydroxy substituted derivatives to nitro and sulphonate derivatives.

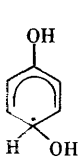
The interaction of hydroxyl radicals with phenylacetic acid[44] leads, according to ESR data, to the formation of radical (I). In acidic medium (I) decomposes with the formation of carbon dioxide, water and the benzyl radical.

The addition of hydroxyl radicals to phenol leads to the formation of various products depending on the solution pH.[43] Radicals (II) are formed in acid solution at pH $\approx$ 1. An increase of pH to 3.9–7 leads to the appearance of hydroxycyclodienyl radicals (III) and (IV) which are ionised in alkaline solution.

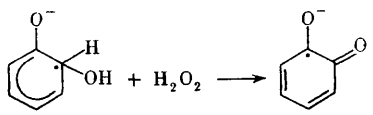

(I)


(II)

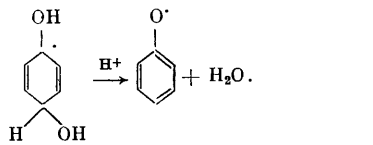

(III)


(IV)

Under the action of hydrogen peroxide the latter are oxidised by the following reaction.[43]

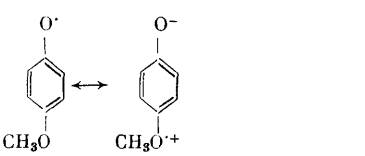

(25)

It was proposed[43] that on interaction of phenol with ·OH radicals in acid media, phenoxyl radicals arise as a result of the elimination of water from the resulting hydroxy-cyclodienyl radicals by the following reaction.

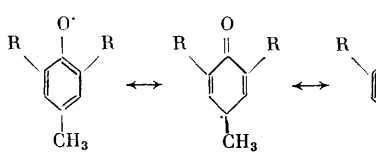

(26)

A broad review of the methods of preparation, structure and isomerisation of phenoxyl radicals resulting on reaction of phenol and its derivatives with hydroxyl radicals has appeared.[45] It was shown that the electron density in phenoxyl radicals is distributed over the aromatic ring and substituent atoms. In phenoxyl radicals the carbon atoms of the ring and the substituent atoms in the *ortho* and *para* positions may be reaction centres in addition to the phenoxyl oxygen.

Study of the ESR spectra of several phenoxyl radicals has enabled their hyperfine structure to be analysed and splitting constants have been found for ring protons and nuclear substituents. Methoxyl and some other similar groups reduce the splitting constants for the ring protons particularly in the *ortho* position to a far greater extent than alkyl groups. This implies that a significant portion of the electron density of such radicals is located on the two oxygen atoms.


(27)

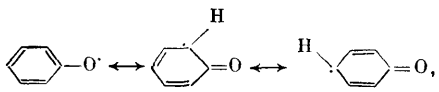
Introduction of a deuterium isotopic label into the hydroxyl group[47] and into the *p*-methyl group of ionol[48] enabled rearrangement of phenoxyl radicals containing a methyl group in the *para* position to benzyl radicals (R = t-C_4H_9) to be demonstrated with rearrangement of hydrogen from the *p*-methyl group to oxygen.


(28)

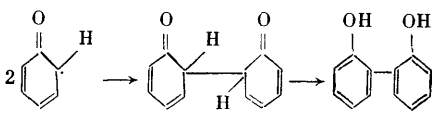
The possibility of such a rearrangement was also confirmed by ESR spectroscopic investigations of the kinetics of the consumption of *p*-alkylphenoxyl radicals.[45]

The dimerisation of phenoxyl radicals on oxidative oligomerisation of phenol is also accompanied by migration of a proton.[49] According to IR spectroscopic data phenolic structural units linked by C–C bonds in the *ortho* and *para* positions are found in the resulting oligomer. The process occurs stepwise by dimerisation of

phenoxyl radicals with subsequent enolisation according to the following scheme.

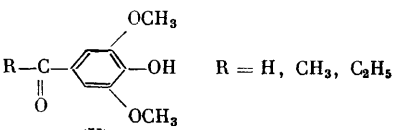


(29)



(30)

Compounds of type (V)



(V)

give stable phenoxyl radicals with an average half-life of about 5 h. In the case of vanillin and its derivatives no ESR signals or only weak ESR signals were observed.[50] The stability of phenoxyl radicals of the syringyl series is explained, in the opinion of the authors,[50] by the presence of two *ortho* substituents and a CO group in the *para* position (in vanillin there is only one *o*-methoxy group). Stable phenoxyl radicals are slowly converted into red products, probably *o*-quinones.

Hammett's rule, which describes the relationship of reaction rate constants to the type of substituent (Figs. 2 and 3), is obeyed in addition reactions of hydroxyl radicals to various derivatives of benzene and benzoate ion. The size of the reaction constant ρ is close to −0.4 which shows the electrophilic character of the ·OH radical in these reactions.[42]

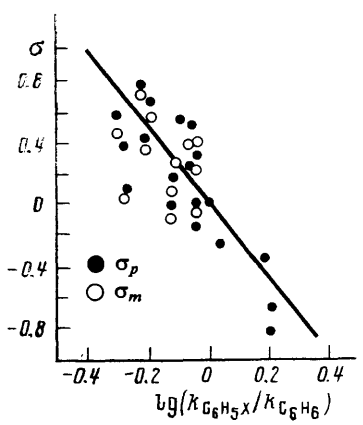


Figure 2. Relationship between the logarithm of the relative rate constant for the reaction of hydroxyl radical and a substituted benzene and the Hammett constant for the substituent.[42]

The reaction of ·OH with aldehydes has been investigated.[51] The interaction of hydroxyl radicals with acrolein and methacrolein occurs by addition of ·OH at the double bond, while reaction with crotonaldehyde includes abstraction of a hydrogen atom from the methyl group.

The kinetics of the consumption of hydroxymethyl radicals formed by reaction of methanol with ·OH radicals obtained by photolysis of hydrogen peroxide has been studied by ESR.[52] The following scheme was proposed for the process:

$$H_2O_2 \xrightarrow{h\nu} 2^{\cdot}OH, \quad (31)$$

$$^{\cdot}OH + CH_3OH \rightarrow {}^{\cdot}CH_2OH + H_2O, \quad (32)$$

$$2^{\cdot}OH \rightarrow H_2O_2, \quad (33)$$

$$^{\cdot}OH + {}^{\cdot}CH_2OH \rightarrow CH_2(OH)_2, \quad (34)$$

$$2^{\cdot}CH_2OH \rightarrow HOCH_2CH_2OH. \quad (35)$$

The rate constant for reaction (35), equal to 3.5×10^8 litre mol^{-1} s^{-1} was measured by flash photolysis and recording of the kinetics of the decrease in the ESR signal.[53] The rate constants for reactions (33) and (34) were found to be 1.5×10^8 and 2.8×10^8 litre mol^{-1} s^{-1} respectively (at 213 K). The rate constant for reaction (32) was 8.4×10^8 litre mol^{-1} s^{-1}.

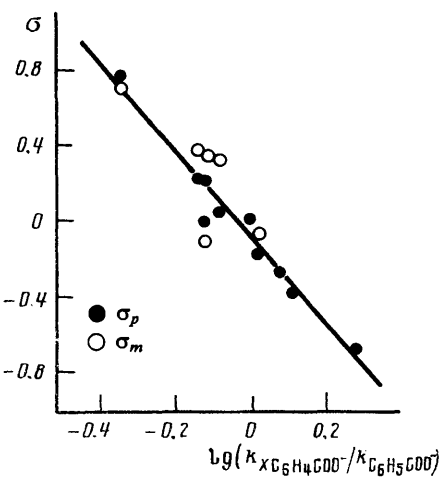


Figure 3. Relationship between the logarithm of the relative rate constant for the reaction of hydroxyl radical and a substituted benzoate ion and the Hammett constant for the substituent.[42]

The structure of the radicals resulting from the reaction of organic acids and ethers with hydroxyl radicals has also been investigated by ESR.[54] In the reaction between ·OH radicals and aliphatic acids and their halogen and hydroxy derivatives, removal of a hydrogen atom is mainly observed with the formation of a radical with the unpaired electron on the carbon atom in the α-position to the carboxyl group. However in the case of formic and malonic acids removal of a hydrogen atom from the carboxyl group occurs. The reaction is accompanied by decarboxylation in the latter case. Acids containing double bonds, such as maleic and methacrylic, add hydroxyl radicals at the multiple bond with the formation of a radical with an unpaired electron on the adjoining carbon atom. When reacting ethers with hydroxyl radicals, radicals are mainly formed with an unpaired electron on the α-carbon atom in relation to oxygen.

Analysis of the reaction between alcohols and ·OH radicals[55] showed that reaction (36) only occurred to a small extent. Process (37) predominates (more than 90%) for methanol, ethanol and propan-2-ol. Reaction (38) is also possible for *n*-propanol, *n*-butanol and isobutanol.

$$R_2CH—CH(R')—OH + {}^{\cdot}OH \begin{cases} \longrightarrow R_2\dot{C}H—CH(R')—O^{\cdot} & (36) \\ \longrightarrow R_2CH—\dot{C}(R')—OH & (37) \\ \longrightarrow R_2\dot{C}—CH(R')—OH & (38) \end{cases}$$

Several rate constants have been found for the removal of a hydrogen atom from aliphatic compounds by hydroxyl radicals.[56] When reacting ·OH radicals with aliphatic acids the reaction rate constant increases with the increase in the number of hydrogen atoms in the acid molecule. This constant may be calculated by the additivity rule for partial activities of hydrogen atoms in various positions in relation to the carboxyl group. The contributions to the reaction rate constant of H atoms in the α-position to the carboxyl group of CH_3COO^-, RCH_2COO^- and R_2CHCOO^-, are 0.14×10^8, 1.75×10^8 and 5.3×10^8 litre mol^{-1} s^{-1} (per atom) respectively and the contributions of H atoms of CH_3R, RCH_2R and R_2CHR groups in other positions are 0.36×10^8, 3.0×10^8 and 8.4×10^8 litre mol^{-1} s^{-1} (per atom) respectively. It is necessary to note that cyclic carboxyl-containing compounds are less reactive than the corresponding acyclic compounds.

Alcohols possess greater reactivity than acids when reaction with ·OH radicals, however the character of the relationship of reaction rate constant to hydrocarbon chain length is preserved.[56] The partial contributions of the activity of hydrogen atoms in the α-positions of CH_3OH, RCH_2OH and R_2CHOH groups are 1.8×10^8, 5.0×10^8 and 8.8×10^8 litre mol^{-1} s^{-1} respectively. An increase in the number of hydroxyl groups in the alcohol molecule leads to a reduction in reaction rate which is explained by hydration of the alcohol.

The reaction rate constants measured for the reaction of hydroxyl radicals with ethers[56] were, in contrast to the constants given in study,[57] somewhat lower than the reaction rate constants for the corresponding alcohols.[56] The partial activities of hydrogen atoms in the α-position of CH_3OR, RCH_2OR, $(RO)_2CH_2$, $(RO)_2CHR$ and $ROCR_2CH_2OH$ groups are 0.6×10^8, 1.4×10^8, 0.5×10^8, 0.9×10^8 and 1.65×10^8 litre mol^{-1} s^{-1} respectively. A good correlation was also recorded between the rate constants for the reaction of hydroxyl radicals with the aliphatic compounds investigated and the Hammett constants for substituents. The value for the ρ factor was −0.96, i.e. the ·OH radical attacks the aliphatic compound as an electrophilic reagent.

The reaction of aliphatic compounds of various classes with ·OH radicals obtained on radiolysis of water by ^{60}Co has been studied and a series of rate constants for these reactions has been found.[57] In particular it was established that the additivity rule for the contributions of CH_2 groups of the compounds investigated to the reaction rate constant was fulfilled only for a fairly small group of substances containing up to 4–6 carbon atoms. On further increasing the hydrocarbon chain length the growth in reaction rate constant slowed (Fig. 4). A significant increase in rate constant was also recorded for the reaction of hydroxyl radicals with amines and carboxylic acids depending on the increase in pH, the greatest values being achieved in the region of the pK_a of the acid. Evidently this confirms that carboxylate radicals (and not radicals with an unpaired electron on adjacent carbon atoms) are formed predominantly by the reaction of hydroxyl radicals according to the reaction

$$RCOO^- + {}^{\cdot}OH = RCOO^{\cdot} + OH^-, \quad (39)$$

and the one-electron oxidation of the carboxylate ion of a salt to the corresponding carboxyl radical occurs more readily than removal of a hydrogen atom from the carboxyl group of the corresponding carboxylic acid.

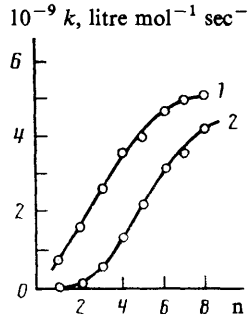


Figure 4. Relationship of the rate constants for the reaction of hydroxyl radicals with *1*, aliphatic alcohols and *2*, dicarboxylic acids to the number of atoms in the hydrocarbon chain.[57]

IV. Decomposition of hydrogen peroxide in the presence of oxygen-containing aliphatic compounds

Study of the kinetics of the oxidation of organic compounds with hydrogen peroxide using ESR showed that decomposition of hydrogen peroxide by radicals of organic compounds is observed in addition to the formation of radicals of organic substances by reaction with hydroxyl radicals (see section III) and recombination of the radicals under specific conditions.

Two types of radicals (VI) and (VII) were detected when investigating the kinetics of oxidation of dimethoxymethane with the system hydrogen peroxide–titanium(III) using ESR spectroscopy.[58]

$$Ti(III) + H_2O_2 \rightarrow Ti(IV) + OH^- + {}^{\cdot}OH, \quad (40)$$

$${}^{\cdot}OH + CH_3OCH_2OCH_3 \rightarrow \underset{(VI)}{{}^{\cdot}CH_2OCH_2OCH_3} + H_2O, \quad (41)$$

$${}^{\cdot}OH + CH_3OCH_2OCH_3 \rightarrow \underset{(VII)}{CH_3O\dot{C}HOCH_3} + H_2O. \quad (42)$$

The change of radical concentration with time showed that the order of the reaction with respect to radicals was close to $^3/_2$. Rate constants for the consumption of radicals (VI) and (VII) calculated from the Arrhenius equation were respectively

$$k_1 = 4 \times 10^{14} \exp(-61800/RT) \text{ litre}^{1/2} \text{ mol}^{-1/2} \text{ s}^{-1}, \quad (43)$$

$$k_2 = 1 \times 10^{14} \exp(-54300/RT) \text{ litre}^{1/2} \text{ mol}^{-1/2} \text{ s}^{-1}. \quad (44)$$

The rate of consumption of radicals did not depend on the initial titanium(III) concentration and was proportional to the initial H_2O_2 concentration in the first stages. Gas chromatographic analysis of the reaction products showed the presence of formaldehyde, formic

acid and methanol. Dimers of dimethoxymethane were not detected, on the basis of which the authors came to the conclusion that chain termination by radicals (VI) and (VII) does not occur in practice.[58]

It was also established by ESR spectroscopy that the decomposition of radicals (VI) and (VII) did not play an appreciable role. Based on the data, a kinetic scheme for the process was proposed which included reactions (40)–(42) and provided for the decomposition of H_2O_2 by reactions (45) and (46) and possible chain termination with the participation of radicals (VI), (VII) and ·OH.

$$\cdot CH_2OCH_2OCH_3 + H_2O_2 \rightarrow HOCH_2OCH_2OCH_3 + \cdot OH, \quad (45)$$

$$CH_3O\dot{C}HOCH_3 + H_2O_2 \rightarrow CH_3OCH(OH)OCH_3 + \cdot OH, \quad (46)$$

$$\cdot CH_2OCH_2OCH_3 + \cdot OH \rightarrow HOCH_2OCH_2OCH_3, \quad (47)$$

$$CH_3O\dot{C}HOCH_3 + \cdot OH \rightarrow CH_3OCH(OH)OCH_3. \quad (48)$$

However the orders found for the reactions are not substantiated by an analysis of the given kinetic scheme.[58]

The oxidation of propan-2-ol by the H_2O_2–Ti(III) system has been investigated.[59] The formation of radicals of two types, viz. $(CH_3)_2\dot{C}OH$ (VIII) and $\cdot CH_2CH(CH_3)OH$ (IX), was shown by ESR spectroscopy. With an excess of hydrogen peroxide in the system the kinetic relationships of the change of radical concentration with time are linearised by a first order equation or an order of $^3/_2$ with respect to radicals. The order with respect to hydrogen peroxide for radicals (VIII) and (IX) proved to be 1.1 and 1.2 respectively. The investigators proposed that consumption of these radicals occurs in reactions causing decomposition of peroxide.

$$\underset{(VIII)}{(CH_3)_2\dot{C}OH} + H_2O_2 \rightarrow (CH_3)_2CO + \cdot OH + H_2O, \quad (49)$$

$$\underset{(IX)}{\cdot CH_2CH(CH_3)OH} + H_2O_2 \rightarrow CH_2{=}C(CH_3)OH + \cdot OH + H_2O. \quad (50)$$

The product of the second reaction is the enol form of acetone. The heats of reaction for (49) and (50) (ΔH) are –205 and –165 kJ mol^{-1} and the energy of activation 48.1 and 48.5 kJ mol^{-1}.

At low hydrogen peroxide concentrations, consumption of alcohol radicals occurs according to a second order equation which indicates the bimolecular termination of these radicals. However the authors considered that the radicals resulting from reactions (49) and (50) have relatively low reactivity in relation to the substrate, consequently the radical–chain process does not play an appreciable role. There remains the unclarified reasons for the different reactivity of ·OH radicals formed by reactions (49) and (50) and by reaction (40) of titanium(III) with H_2O_2.

It has been noted[60] that at a low rate of initiation, corresponding to a low titanium(III) concentration, the concentration of radicals (IX) exceeds the concentration of radicals (VIII) and at a high initiation rate, corresponding to a high titanium(III) concentration, the reverse relationship is observed in the initial stages. It was proposed that radicals (VIII) participate in a radical–chain process occurring at low rates of initiation and the chain length increases with the growth in concentration of hydrogen peroxide. Evidently this indicates that only radicals (VIII) may cause additional decomposition of hydrogen peroxide.

The change in concentration of radicals as a function of reactant concentration in the oxidation of propan-2-ol by hydrogen peroxide has been described.[61] This process was initiated by oxidation–reduction systems containing H_2O_2 and a metal of variable valency, such as vanadium(IV), titanium(III), chromium(II) or iron(II). On increasing the hydrogen peroxide concentration in the system the concentration of propan-2-ol radicals passed through a maximum (Fig. 5), while an increase in the variable valency metal concentration led to a significant drop in the concentration of radical (VIII) and practically no change in the concentration of radical (IX). The change of concentration of alcohol radicals obtained on radiolysis of H_2O_2 as a function of the initial reactant concentrations indicated that decomposition of H_2O_2 by radicals (VIII) may be possible at various ranges of reactant concentration. A mechanism for the process was proposed, analogous to that described previously, the only difference being that chain termination by alcohol radicals predominates over termination of the latter by reaction with ·OH radicals. It was shown that chain length in the hydrogen peroxide decomposition process grows according to the increase of hydrogen peroxide concentration.

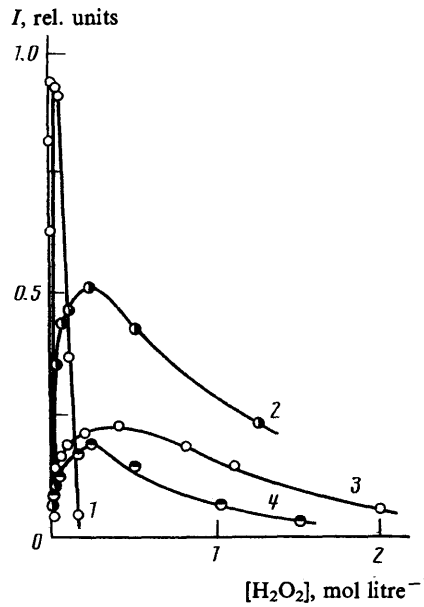


Figure 5. Relative intensity of the ESR signal for radicals formed in reactions of hydrogen peroxide with propan-2-ol in the presence of *1*, titanium(III) at pH 1, *2*, vanadium(IV) at pH 3, *3*, iron(II) at pH 1 and *4*, at pH 3. Concentrations of propan-2-ol and metal were 2.5 mol litre^{-1}.[61]

Investigation of the influence of the concentration of $HO_2^{\cdot}$ radicals on the concentration of alcohol radicals in this system showed[61] that perhydroxyl radicals show no appreciable influence on the content of other radicals. Consequently the authors considered hydroxyl radicals to be the main reactive species.

The mechanism of the interaction of hydrogen peroxide with alcohols has been investigated with initiation of the process by radiolysis of H_2O_2.[62] The concentration of propan-2-ol radicals in the system was found by ESR spectroscopy. With an increase in hydrogen peroxide concentration the overall content of radicals in the system was practically unchanged, while the ratio of the concentrations of radicals (IX) and (VIII) was increased. An

increase in the rate of initiation by increasing the radiation intensity led to growth of both these parameters. On increasing the propan-2-ol concentration the concentration of radical (IX) and the overall concentration of radicals passed through maxima even at low alcohol content while the concentration of radical (VIII) grew constantly. The authors considered[62] that the oxidation of propan-2-ol proceeded by a radical–chain mechanism, comprising decomposition of peroxide according to reaction (53) and termination with the participation of radicals (VIII) and (IX) (54)–(56).

$$^{\cdot}OH + (CH_3)_2CH{-}OH \xrightarrow{k_s} H_2O + (CH_3)_2\dot{C}{-}OH, \quad (51)$$

$$^{\cdot}OH + (CH_3)_2CH{-}OH \xrightarrow{k_{s1}} H_2O + {}^{\cdot}CH_2CH(OH)CH_3, \quad (52)$$

$$(CH_3)_2\dot{C}{-}OH + H_2O_2 \xrightarrow{k_{in}} {}^{\cdot}OH + H_2O + (CH_3)_2CO, \quad (53)$$

$$2(CH_3)_2\dot{C}{-}OH \xrightarrow{k_t} \quad (54)$$

$$(CH_3)_2\dot{C}{-}OH + {}^{\cdot}CH_2CH(OH)CH_3 \xrightarrow{k_t} \text{chain termination.} \quad (55)$$

$$2{}^{\cdot}CH_2CH(OH)CH_3 \xrightarrow{k_t} \quad (56)$$

It was claimed that in view of the high initiation rate the chain length was not large, the concentrations of radicals (VIII) and (IX) were comparable and chain termination by all radicals is possible. An expression for the ratio of the concentrations of the radicals in the system was derived on the basis of the given scheme.[62]

$$[IX]/[VIII] = k_{s1}k_{in}\,(k_s + k_{s1})^{-1}(2k_t w_i)^{-1/2}[H_2O_2] \quad (57)$$

(w_i is the initiation rate) which was confirmed by the experimental data (Fig. 6).

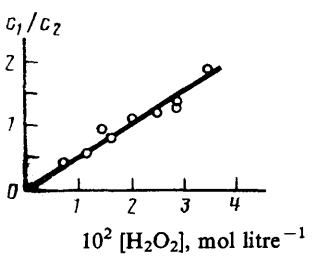


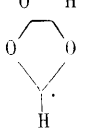
Figure 6. Dependence of the relative concentrations of $^{\cdot}CH_2CH.(OH)CH_3$ (c_1) and $(CH_3)_2\dot{C}OH$ (c_2) radicals on hydrogen peroxide concentration during photolysis of the latter in an aqueous solution of 0.68 mol litre^{-1} acetone and 0.65 mol litre^{-1} propan-2-ol at 30 °C.[62]

Indirect confirmation of the lack of participation of radical (IX) in the decomposition of H_2O_2 is the observation that t-butyl alcohol does not cause decomposition.

An analogous mechanism has been proposed to describe the reaction of hydrogen peroxide with other oxygen-containing compounds (methanol, ethanol, tetrahydrofuran, dioxan, diethyl ether, etc.). Some rate constants for the decomposition of peroxide are given in Table 1.

When initiating the reaction of hydrogen peroxide with alcohols with the H_2O_2–titanium(III) system radical decomposition of peroxide was observed only at high concentrations of it and the chain length was not very large.[63] This is evidently linked with the high rate of the reaction between H_2O_2 and titanium(III). Similar results have been obtained elsewhere.[64]

Table 1. Rate constants for the decomposition of hydrogen peroxide by various radicals at 20 °C.

Radical	$10^{-4}k$, litre mol^{-1} s^{-1}	Refs.
$^{\cdot}CH_2OH$	35	[62]
	5	[63]
	4	[66]
	2.3	[67]
	4	[68]
$CH_3\dot{C}HOH$	18	[64]
	15	[69]
$(CH_3)_2\dot{C}OH$	51	[62]
	50	[63]
$^{\cdot}CO_2^-$	70	[70]
	3	[67]
	6	[67]
$CH_3\dot{C}HOCH_2CH_3$	5.5	[67]
$^{\cdot}CH(OCH_3)_2$	110	[67]

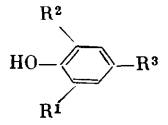
The decomposition of hydrogen peroxide may therefore take place under the action of radicals in which an unpaired electron is present on the α-carbon atom of oxygen-containing compounds. The chain length in this process may vary within wide limits depending on the initiation rate.

The rate constant for the decomposition of hydrogen peroxide by radicals of organic compounds may be increased by reducing the oxidation–reduction potential of the latter. This is observed in their interaction with benzoyl peroxide.[65]

V. Oxidation of phenolic compounds with hydrogen peroxide

Interest in this question is linked with the need to clarify the mechanism of action of phenolic antioxidants, the mechanism of the initiation by hydrogen peroxide of graft polymerisation of monomers to natural polyphenolic compounds such as lignin and its derivatives,[14] and also the chemical mechanism of the delignification of wood by hydrogen peroxide.[10] Lignin macromolecules of coniferous wood contain structural units of 4-hydroxy-3-methoxyphenylpropane (guaiacylpropane) and there are also 4-hydroxy-3,5-dimethoxyphenylpropane (syringylpropane) structures in wood lignins from deciduous species.[71] Consequently phenolic compounds

may serve as the simplest models of the guaiacyl and syringyl structures of lignin units.



$R^1 = H,\ OCH_3;\ R^2 = OCH_3;$
$R^3 = H,\ CH_2OH,\ CHO$ etc.

(X)

The kinetics of the oxidation of guaiacol (X, $R^1 = OCH_3$, $R^2 = R^3 = H$) with hydrogen peroxide at pH 4.0 in an inert atmosphere have been investigated.[22] Guaiacol markedly accelerates the decomposition of H_2O_2, the order of the reaction with respect to the latter is close to 1 and with respect to guaiacol to $^1/_2$, the effective energy of activation being 90 kJ mol^{-1}. Monomer (acrylamide) slows the reaction rate to the rate of decomposition of H_2O_2 in water, which indicates a radical–chain mechanism for the process and its initiation by homolysis of hydrogen peroxide.

To substantiate the results obtained, a kinetic scheme was proposed[22] for the peroxide oxidation of guaiacol and other phenols which provides for the formation of phenoxyl radicals, their subsequent isomerisation into aryl radicals and the decomposition of H_2O_2 under the action of the latter.

$$H_2O_2 \cdot 2H_2O \xrightarrow{k_d^t} 2{}^{\bullet}OH + 2H_2O, \quad (58)$$

$$^{\bullet}OH + Ar{-}OH \xrightarrow{k_s} Ar{-}O^{\bullet} + H_2O, \quad (59)$$

$$Ar{-}O^{\bullet} \xrightarrow{k_r} {}^{\bullet}Ar{-}OH, \quad (60)$$

$$^{\bullet}Ar{-}OH + H_2O_2 \xrightarrow{k_{in}} {}^{\bullet}OH + Ar', \quad (61)$$

$$^{\bullet}Ar{-}OH + {}^{\bullet}OH \xrightarrow{k_{12}} \text{chain termination}, \quad (62)$$

where Ar′ is the oxidation product of the phenolic compound. Eqn. (63) for the consumption of H_2O_2 is obtained from this scheme using quasi-steady-state concentrations.

$$w = k_d \{^1/_2 + (^1/_4 + k_s k_{in} (k_d k_{12})^{-1}[Ph])^{1/2}\}[H_2O_2], \quad (63)$$

where [Ph] is the concentration of phenolic compound. It may be rearranged into (64) which is in agreement with the experimental data.

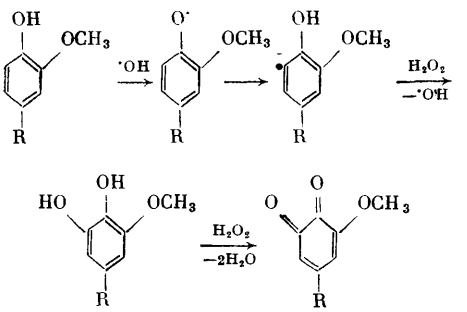
$$w^2/(k_d [H_2O_2]^2) - w/[H_2O_2] = (k_s k_{in}/k_{12})[Ph]. \quad (64)$$

If the rate of decomposition of H_2O_2 by (61) is significantly greater than the rate of its homolysis then Eqn. (63) reduces to expression (65) which corresponds to the order of the reaction found experimentally.[22]

$$w = (k_d k_s k_{in}/k_{12})^{1/2}[Ph]^{1/2}[H_2O_2]. \quad (65)$$

Proposals on the mechanism of initiation by hydrogen peroxide of the grafting of monomers to lignin were also made on the basis of kinetic investigations on the polymerisation of monomers in the presence of phenolic compounds modelling the structural units of lignin.[72–74] A comparison of the influence of guaiacol and veratrole (*o*-dimethoxybenzene),[72] vanillin sulphonate (3-methoxy-4-hydroxybenzyl sulphonate), *p*-hydroxybenzyl sulphonate and veratryl sulphonate (3,4-dimethoxybenzyl sulphonate),[73] guaiacol and 2,6-dimethoxyphenol[74] on the rate of polymerisation of monomers led investigators to the conclusion that the kinetics of the process depend on the presence of a phenolic hydroxyl and a vacancy in the *ortho* position to the phenol in the structure of the model compound.[75]

The kinetic scheme (58)–(62) also provides for homolytic fission of the OH bond of the phenolic compound with subsequent isomerisation of phenoxyl radicals having no substituent in the *ortho* position into aryl radicals capable of inducing chain decomposition of H_2O_2.[76]



(66)

According to this scheme, the accumulation of quinones must correspond to the reduction in the content of phenolic hydroxyls and is not accompanied by demethylation of the starting material. The formation of one mole quinone must consume two moles H_2O_2. However functional analysis of the oxidation products of guaiacol showed,[76] that the reduction in content of phenolic hydroxyls is in good agreement not only with the accumulation of quinone but also with the fall in methoxy group content and the consumption of hydrogen peroxide (Table 2), which contradicts the scheme (66). In the oxidation of guaiacol to quinone an equimolecular (and not double) quantity of H_2O_2 is consumed and the quinone is formed predominantly by demethylation of guaiacol and not as a result of the formation of appropriate bonds in the vacant *ortho* (or *para*) positions to the phenolic hydroxyl as shown in the scheme (66).[76]

Table 2. Relationship between the functional composition (in mmol g^{-1} guaiacol) of the oxidation products of guaiacol and hydrogen peroxide concentration.[76]

$[H_2O_2]$, mmol g^{-1} guaiacol	[OH]	[OCH_3]	[Quinones]	$-\Delta$[OH]	$-\Delta$[OCH_3]
0	8.06	8.06	0	0	0
1.90	6.61	6.51	1.40	1.45	1.55
3.81	4.66	3.96	3.56	3.40	4.10

Footnote. Reaction conditions: guaiacol concentration 161 mmol litre^{-1}, temperature 70 °C, reaction time 1.5 h.

These concepts were confirmed by investigations on the kinetics of the interaction of hydrogen peroxide with phenol, veratrole and syringaldehyde (3,5-dimethoxy-4-hydroxybenzaldehyde), compounds which model the structures with vacant *ortho* and *para* positions relative to a free phenolic hydroxyl and to a hydroxyl included in an ester bond. The investigations showed that of these only syringaldehyde was able to cause decomposition of H_2O_2 (Fig. 7). Consequently in order to carry out the radical–chain decomposition of peroxide the presence of an unsubstituted phenolic hydroxyl

group in the benzene ring is necessary the presence in the ring of other substituents and a vacant position *ortho* or *para* to them is not obligatory.[76]

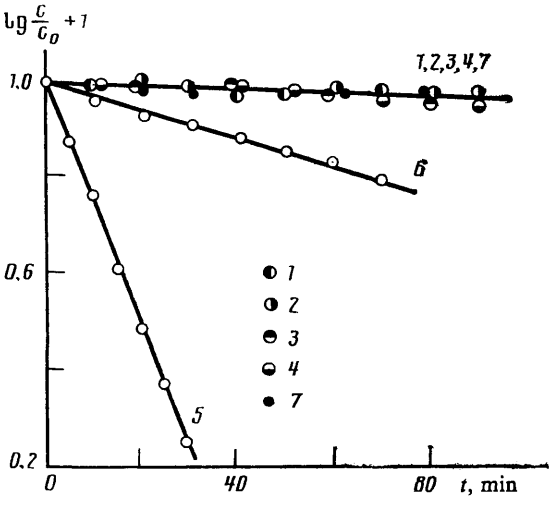
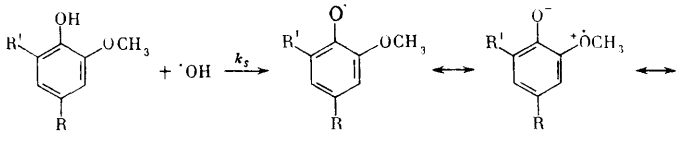


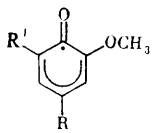
Figure 7. Semilogarithmic plot of the kinetic curves for the consumption of H_2O_2 *1*, in water, in solutions of *2*, veratrole, *3*, phenol, *4*, guaiacol in the presence of acrylamide 0.141 mol litre^{-1}, *5*, guaiacol, *6*, syringic aldehyde, and *7*, syringic aldehyde in the presence of acrylamide 0.282 mol litre^{-1} at pH 4, 70 °C, and initial concentrations of H_2O_2 1.06 mmol litre^{-1} and of phenolic compound 4.03 mmol litre^{-1}.[76]

Allowing for what has been said, the experimental data[22,76] may be described by the kinetic scheme (67)–(70) which includes the decomposition of H_2O_2 by the phenoxyl radical according to reaction (69) since the electron density of its unpaired electron is distributed predominantly between the two oxygen atoms[46] (see section III).

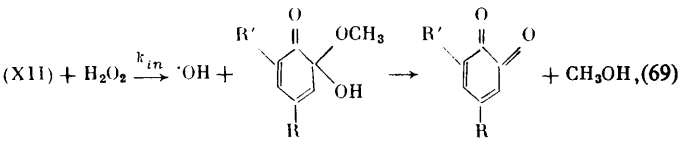
$$H_2O_2 \cdot 2H_2O \xrightarrow{k_d} 2{}^{\cdot}OH + 2H_2O, \qquad (67)$$



(XI) (XII)



(68)



$$(XII) + {}^{\cdot}OH \xrightarrow{k_{12}} \text{chain termination.} \qquad (70)$$

Calculations on this scheme using quasi-steady-state concentrations for the interaction of H_2O_2 with guaiacol (XI, R, R′ = H) lead to Eqn. (63) compatible with the kinetic results presented above.

Investigation of the oxidation of vanillin with hydrogen peroxide[77] enables assessment of the effect of carbonyl and methoxy groups in addition to a phenolic hydroxyl in the benzene ring on the kinetics of the process. Vanillin may also serve, as a first approximation, as a model of the guaiacol structural units of lignin with carbonyl groups in the side chain. The rate of consumption of H_2O_2 in the presence of vanillin is greater than the rate of decomposition of peroxide in water under analogous conditions and markedly less than in a solution of guaiacol. Experiments with acrylamide added to the system confirmed the radical–chain mechanism of the reaction. Experiments were also carried out on the oxidation of benzaldehyde and of mixtures of it with guaiacol in order to clarify the influence of substituents in the benzene ring on the kinetics of the process. These showed the ability of aldehyde groups to interact with hydroxyl radicals with the formation of radicals causing no chain decomposition of H_2O_2.

A study of the functional composition of the oxidation products of vanillin with hydrogen peroxide showed[76] that the quantity of quinones formed corresponds approximately to the reduction in the content of hydroxyl and methoxyl groups, carbonyl groups are oxidised to carboxyls, and the consumption of H_2O_2 corresponds to the overall accumulation of quinone and carboxyl groups (Table 3). Vanillic acid was identified in the oxidation products by thin layer chromatography.

This indicates that two reaction centres participate in the oxidation of vanillin, viz. the phenolic hydroxyl and the aldehyde group.

Table 3. Relationship between the functional composition (in mmol g^{-1} vanillin) of the oxidation products of vanillin with hydrogen peroxide and the concentration of the latter.[76]

$[H_2O_2]$, mmol g^{-1} vanillin	[COOH]	[OH]	[OCH_3]	[Quinones]	[COOH]+ [Quinones]	−Δ[OH]	−Δ[OCH_3]
0	0	6.53	6.57	0	0	0	0
1.75	0.93	5.80	6.09	0.72	1.65	0.73	0.48
3.50	2.02	5.44	5.68	1.22	3.24	1.09	1.11
7.00	4.13	4.64	4.26	2.14	6.27	1.89	2.31

Footnote. Reaction conditions: vanillin concentration 63.4 mmol litre^{-1}, temperature 80 °C, reaction time 6 h.

The reaction is first order with respect to hydrogen peroxide since the initial rate of H_2O_2 consumption is proportional to its concentration (Fig. 8). The relationship of the apparent reaction rate constant to vanillin concentration has a complex character. It increases with the growth in concentration of the latter tending to a limiting value (Fig. 9) so that the reaction order with respect to vanillin is changed from $^1/_2$ to zero. The apparent activation energy is 97 kJ mol^{-1}.

The data enable the oxidation of vanillin (XI, R = CHO, R′ = H) with hydrogen peroxide to be described by the kinetic scheme

(67)–(70) supplemented by reaction equations (71) and (72) for the oxidation of vanillin at the aldehyde group.

$$HO{-}C_6H_3(OCH_3){-}CHO + {}^{\cdot}OH \xrightarrow{k_{s1}} \rightarrow HO{-}C_6H_3(OCH_3){-}\dot{C}O + H_2O, \quad (71)$$

$$HO{-}C_6H_3(OCH_3){-}\dot{C}O + {}^{\cdot}OH \xrightarrow{k_{12}} HO{-}C_6H_3(OCH_3){-}COOH. \quad (72)$$

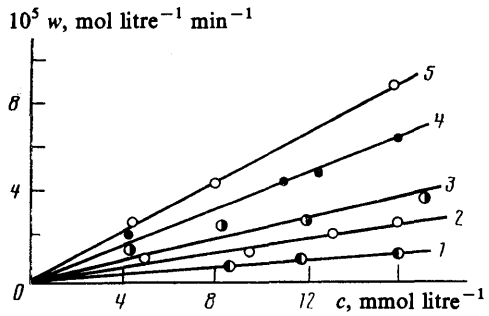


Figure 8. Relationship between the rate of consumption of H_2O_2 during the oxidation of vanillin and the initial concentration of hydrogen peroxide at 70 °C and initial vanillin concentrations of *1*, 0.66, *2*, 3.29, *3*, 6.58, *4*, 32.9, *5*, 65.8 mmol litre^{-1}.

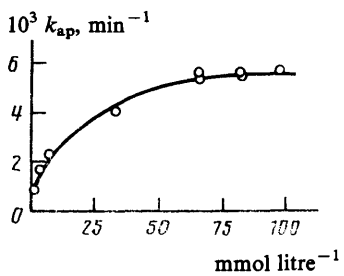


Figure 9. Influence of the initial vanillin concentration during its oxidation by H_2O_2 on the apparent rate constant for the consumption of hydrogen peroxide at 70 °C.

A mathematic model for the kinetics of the process may be obtained from schemes (67)–(72) using quasi-steady-state concentrations.

$$w = k_{ap}[H_2O_2], \quad (73)$$

where w is the rate of H_2O_2 consumption in the oxidation of vanillin.

$$k_{ap} = (2k_{12})^{-1}\{(F^2 + 4k_d k_{in} k_s k_{12}[Ph])^{1/2} - F\},$$
$$F = k_{in}k_{s1}[Ph] - k_d k_{12}. \quad (74)$$

Eqn. (73) is in agrement with the kinetic results given in Fig. 8.

At low vanillin concentrations $k_{in} \gg k_d k_{12}(4k_s[Ph])^{-1}$ and expression (73) simplifies to

$$w = (k_d k_s k_{in}/k_{12})^{1/2}[Ph]^{1/2}[H_2O_2], \quad (75)$$

which is in agrement with the experimentally found partial reaction orders (at vanillin concentrations up to 33 mmol litre^{-1}).

At fairly high vanillin concentrations the relationship (76) may be obtained by expansion of (73) into an exponential series and corresponds to the partial reaction order found by experiment under these conditions.

$$w = k_d(1 + k_s/k_{s1})[H_2O_2]. \quad (76)$$

It is seen from Fig. 9 that the apparent reaction rate constant tends to a limit on increasing the vanillin concentration. It may be shown that the limit of function (74) is determined by the expression

$$\lim_{[Ph]\to\infty} k_{ap} = k_d k_s / k_{s1}. \quad (77)$$

Combinations of rate constants for the individual reactions $k_d k_s/k_{s1}$ and k_s/k_{s1}, equal to 5.56 × 10^{-3} min^{-1} and 12.5 respectivley (at 70 °C), are found from the data given in Fig. 9 using Eqn. (77).

Transformation of relationship (74) leads to the equation

$$(k_{ap} + k_d)/[Ph] = -k_{in}k_{s1}/k_{12} + (k_d k_{in} k_s/k_{12})\,(1/k_{ap}), \quad (78)$$

which describes the kinetic data well as is evident from Fig. 10. The relationships of the rate constants for the individual reactions are found from the intercept and the slope of the straight line in Fig. 10 and $k_d k_s/k_{s1}$, k_s/k_{s1}, $k_d k_{in} k_s/k_{12}$, $k_{in}k_s/k_{12}$ are 6.38 × 10^{-3} min^{-1}, 14.4 and 1.70 × 10^{-3} litre mol^{-1} min^{-2} and 3.84 litre mol^{-1} min^{-1} respectively at 70 °C. The values obtained from Eqns. (77) and (78) are close to one another. This indicates the adequacy of the mathematical model (73) and (74) describing the kinetic experimental data for the oxidation of vanillin with hydrogen peroxide over a wide range of reactant concentrations.

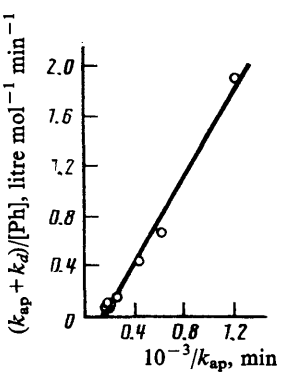


Figure 10. Relationship between the apparent reaction rate constant for the oxidation of vanillin with hydrogen peroxide and vanillin concentration at 70 °C in the coordinates of Eqn. (78).

A feature of the hydrogen peroxide oxidation of vanillyl alcohol (4-hydroxy-3-methoxybenzyl alcohol), modelling the structural units of lignin with benzyl hydroxyls, is the transfer in the initial stage of the reaction centre from the phenolic oxygen of the aromatic ring to

the carbon atom in the α-position.[78] This is indicated by the constant nature of the content of phenolic hydroxyls in the initial stage of the reaction and the correspondence of the quantity of H_2O_2 reacted to the overlall accumulation of carbonyl and carboxyl groups (Table 4) (vanillin was identified as the product of oxidation of vanillyl alcohol by thin layer chromatography).

Table 4. Change of functional composition (in mmol g^{-1} vanillyl alcohol) of the oxidation products of vanillyl alcohol with hydrogen peroxide in relation to the quantity of H_2O_2 reacted.[78]

Quantity of H_2O_2 reacted, mmol $litre^{-1}$ vanillyl alcohol	$[OH_{phenol}]$	$[OCH_3]$	[COOH]	[CHO]
0	6.49	6.47	0	0
0.39	6.49	6.38	0	0.45
0.98	6.49	6.43	0	0.92
1.23	6.57	6.43	0.08	1.01
1.47	6.63	6.46	0.17	1.13

Footnote. Reaction conditions: vanillyl alcohol concentration 66.1 mmol $litre^{-1}$, H_2O_2 concentration 87.5 mmol $litre^{-1}$, temperature 80 °C.

The kinetic investigations showed the acceleration of hydrogen peroxide decomposition in aqueous media in the presence of vanillyl alcohol. Acrylamide suppressed the decomposition of peroxide which indicates the radical–chain mechanism of the process. Partial orders of the reaction were 1 with respect to peroxide and $^1/_2$ with respect to vanillyl alcohol. The apparent activation energy was 92 kJ mol^{-1}.

The results obtained are in agreement[78] with the kinetic scheme (79)–(85). In this, attack by the radical initiator of the phenolic hydroxyl and the C–H bond of the alcohol group is proposed, then rearrangement (82) of phenoxyl to benzyl radical, which was confirmed by ESR spectroscopic investigations on the kinetics of the consumption of *p*-alkylphenoxyl radicals (see section III).[45,79]

$$H_2O_2 \cdot 2H_2O \xrightarrow{k_d} 2\,{}^{\cdot}OH + 2H_2O, \tag{79}$$

$$^{\cdot}OH + HO{-}C_6H_3(OCH_3){-}CH_2OH \xrightarrow{k_s} {}^{\cdot}O{-}C_6H_3(OCH_3){-}CH_2OH + H_2O, \tag{80}$$

$$^{\cdot}OH + HO{-}C_6H_3(OCH_3){-}CH_2OH \xrightarrow{k_{s1}} HO{-}C_6H_3(OCH_3){-}\dot{C}HOH + H_2O, \tag{81}$$

$$^{\cdot}O{-}C_6H_3(OCH_3){-}CH_2OH \xrightarrow{k_r} HO{-}C_6H_3(OCH_3){-}\dot{C}HOH, \tag{82}$$

$$HO{-}C_6H_3(OCH_3){-}CHOH + H_2O_2 \xrightarrow{k_{in1}} {}^{\cdot}OH + HO{-}C_6H_3(OCH_3){-}CHO + H_2O, \tag{83}$$

$$\left.\begin{aligned} {}^{\cdot}O{-}C_6H_3(OCH_3){-}CH_2OH + {}^{\cdot}OH &\xrightarrow{k_{12}} \\ HO{-}C_6H_3(OCH_3){-}\dot{C}HOH + {}^{\cdot}OH &\xrightarrow{k_{13}} \end{aligned}\right\} \text{chain termination.} \tag{84, 85}$$

Using a quasi-steady-state approach for long chains and the condition that

$$k_r\,(k_s + k_{s1})\,k_{13} \gg k_{in1}k_sk_{12}\,[H_2O_2] \tag{86}$$

It follows that

$$w = \{k_dk_{in1}\,(k_s + k_{s1})/k_{13}\}^{1/2}[Ph]^{1/2}[H_2O_2], \tag{87}$$

which is in agreement with the partial reaction orders given above.

The kinetics have also been investigated for the reaction of hydrogen peroxide with the phenolic carboxylic acids (X), containing a phenolic hydroxyl and a carboxylic acid group, viz. ferulic (R^1 = H, R^2 = OCH_3, R^3 = CH=CH–COOH), syringic (R^1 = R^2 = OCH_3, R^3 = COOH), gallic (R^1 = R^2 = OH, R^3 = COOH) and protocatechuic (R^1 = H, R^2 = OH, R^3 = COOH) acids.[80,81]

It was established that the rate of consumption of H_2O_2 in a solution of ferulic acid increases with the increase in acid concentration (in the range 0.05–15.5 mol $litre^{-1}$) and in a solution of gallic acid the reaction rate increases with the increase in concentration of the latter only up to 0.29 mmol $litre^{-1}$ and then remains practically constant. In the presence of a monomer (acrylic acid) a reduction in the rate of the process practically to the rate of homolysis of peroxide in water indicates the radical–chain character of the reaction and its initiation by homolysis of H_2O_2.

From the initial rate of consumption of peroxide in the presence of the phenolic acids mentioned the reaction order found with respect to H_2O_2 was close to 1, with respect to ferulic acid to $^1/_2$, with respect to protocatechuic and syringic acids it was zero and with respect to galic acid it varied from $^1/_2$ (at concentrations up to 0.29 mmol $litre^{-1}$) to zero (at higher concentrations). The apparent activation energies for the oxidation of ferulic and gallic acids were 72 and 79 kJ mol^{-1} respectively. The data obtained[81] are in agreement with the kinetic scheme of (88)–(96) which proposes the formation of carboxyl and aryl radicals in addition to phenoxyl radicals.

$$H_2O_2 \cdot 2H_2O \xrightarrow{k_d} 2\,{}^{\cdot}OH + 2H_2O, \tag{88}$$

$$^{\cdot}OH + HO{-}Ar{-}COOH \xrightarrow{k_s} H_2O + {}^{\cdot}O{-}Ar{-}COOH, \tag{89}$$

$$^{\cdot}OH + HO{-}Ar{-}COOH \xrightarrow{k_{s1}} H_2O + HO{-}Ar{-}COO^{\cdot}, \tag{90}$$

$$^{\cdot}O{-}Ar{-}COOH \xrightarrow{k_r} HO{-}Ar{-}COO^{\cdot}, \tag{91}$$

$$HO{-}Ar{-}COO^{\cdot} \xrightarrow{k_c} CO_2 + HO{-}Ar^{\cdot}, \tag{92}$$

$$^{\cdot}O{-}Ar{-}COOH + H_2O_2 \xrightarrow{k_{in}} {}^{\cdot}OH + \text{products}, \tag{93}$$

$$\left.\begin{aligned} {}^{\cdot}O{-}Ar{-}COOH + {}^{\cdot}OH &\xrightarrow{k_{12}} \\ HO{-}Ar{-}COO^{\cdot} + {}^{\cdot}OH &\xrightarrow{k_{13}} \\ HO{-}Ar^{\cdot} + {}^{\cdot}OH &\xrightarrow{k_{14}} \end{aligned}\right\} \text{chain termination} \tag{94, 95, 96}$$

Although oxidation of syringic aldehyde leads to the formation of stable phenoxyl radicals, the oxidation of syringic and sinapic (R_1 = R_2 = OCH_3, R_3 = CH=CH–COOH) acids leads to the observation of only a weak ESR signal[50] since seemingly their phenoxyl radicals are capable of conversion into reactive carboxyl and aryl radicals.[81] These facts point in favour of the occurrence of reactions (91) and (92). The reaction products of (93) are *o*-quinones which was confirmed by their colour reactions with ethylenediamine.

An expression was obtained from the kinetic scheme (88)–(96) for the rate of the radical–chain decomposition of H_2O_2 by the method of quasi-steady-state concentrations.[80,81]

$$w = k_{in}\{(F_1^2/4 + F_2)^{1/2} - F_1/2\}[H_2O_2], \quad (97)$$

$$F_1 = k_r(k_s + k_{s1})[Ph](k_{in}k_{12}[H_2O_2])^{-1} + k_s k_{12}^{-1}[Ph],$$

$$F_2 = k_d(k_s + k_{s1})(k_{in}k_{12})^{-1}[Ph].$$

At low concentrations of the phenolic carboxylic acid the expression (97) is simplified and takes the form of (98),[81] which corresponds to the experimental data given above for the decomposition of hydrogen peroxide in the presence of ferulic and gallic (at concentrations below 0.29 mmol litre^{-1}) acids.

$$w = \{k_{in}k_d(k_s + k_{s1})/k_{12}\}^{1/2}[Ph]^{1/2}[H_2O_2]. \quad (98)$$

At higher concentrations of phenolic carboxylic acids and hydrogen peroxide the Eqn. (97) is transformed into (99).[81] The empirical partial reaction orders given above for the hydrogen peroxide oxidation of protocatechuic, syringic and gallic acids (at concentrations of the latter above 0.29 mmol litre^{-1}) are in agreement with this equation.

$$w = \{k_d(k_s + k_{s1})/k_{s1}\}[H_2O_2]. \quad (99)$$

The oxidation of lignosulphonic acid (LSA) with hydrogen peroxide is first order with respect to H_2O_2 and about $^1/_2$ with respect to LSA. The apparent activation energy (58 kJ mol^{-1}) is significantly less than in the oxidation of model compounds of lignin.[82] The deceleration of the reaction by stable 2,2,6,6-tetramethylpiperidin-1-oxyl radicals indicates its radical–chain mechanism.

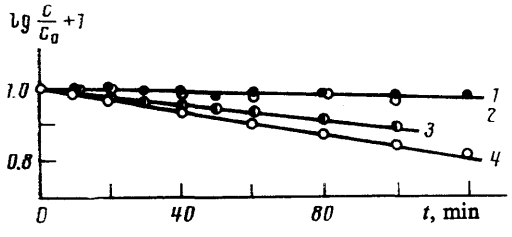


Figure 11. Semilogarithmic plot of the kinetic curves for the consumption of H_2O_2 in *1*, water, in solutions of lignosulphonic acid methylated *2*, with dimethyl sulphate and *3*, with diazomethane and *4*, in a solution of the initial LSA at concentrations of H_2O_2 2.6 mmol litre^{-1} and LSA 4.24 mmol litre^{-1} at 70 °C.[83]

An absorption band in the IR spectrum of LSA oxidised with peroxide appears at 1730 cm^{-1}, characteristic of a carbonyl group.[83] With an increase in the initial H_2O_2 concentration the content of acidic OH^- and carbonyl groups in the reaction products increases significantly, the quantity of quinone groups increases insignificantly and the content of methoxy groups is almost unchanged. This supports the hypothesis that the oxidation of LSA with hydrogen peroxide occurs in the side chain to a significant extent. In order to clarify whether phenolic hydroxyls participate in the oxidation, the kinetics of the interaction of H_2O_2 with lignosulphonic acid were investigated[83] after only the acidic OH groups had been methylated with diazomethane or after all the hydroxyl groups had been methylated with dimethyl sulphate. In the first case the rate of peroxide consumption was somewhat lower than in a solution of the initial unmethylated LSA but in the second case it approached the rate of decomposition of H_2O_2 in water (Fig. 11). This supports the proposal that the decomposition of hydrogen peroxide occurs only partially with the participation of phenoxyl radicals but to a significant extent with the participation of radicals with an unpaired electron in the side chain.

The kinetic scheme of (100)–(106) corresponds to the results obtained. In this it is proposed that the accumulation of carbonyl compounds and quinones occurs by reactions (103) and (104) and of acidic OH groups by secondary oxidation processes.

$$H_2O_2 \cdot 2H_2O \xrightarrow{k_d} 2{}^{\cdot}OH + 2H_2O, \quad (100)$$

$${}^{\cdot}OH + HO{-}C_6H_3(OCH_3){-}R(X)H \xrightarrow{k_s} {}^{\cdot}O{-}\underset{(XIII)}{C_6H_3(OCH_3)}{-}R(X)H + H_2O, \quad (101)$$

$${}^{\cdot}OH + HO{-}C_6H_3(OCH_3){-}R(X)H \xrightarrow{k_{s1}} HO{-}\underset{(XIV)}{C_6H_3(OCH_3)}{-}\dot{R}(X) + H_2O, \quad (102)$$

$$(XIII) + H_2O_2 \xrightarrow{k_{in}} {}^{\cdot}OH + O{=}\langle\rangle{-}R(X)H + CH_3OH, \quad (103)$$

$$(XIV) + H_2O_2 \xrightarrow{k_{in1}} {}^{\cdot}OH + HO{-}C_6H_3(OCH_3){-}RO + \text{products}, \quad (104)$$

$$\left.\begin{array}{ll}(XIII) + {}^{\cdot}OH \xrightarrow{k_{12}} & (105)\\ (XIV) + {}^{\cdot}OH \xrightarrow{k_{13}} & (106)\end{array}\right\} \text{chain termination.}$$

An equation was obtained for the rate of consumption of H_2O_2 in LSA solution[83] from this scheme using a kinetic model for unbranched radical–chain processes[84] in a quasi-steady-state approach for long chains.

$$w = (k_s + k_{s1})(k_d k_{in} k_{in1})^{1/2}(k_s k_{in1} k_{12} + k_{s1} k_{in} k_{13})^{-1/2}[LSA]^{1/2}[H_2O_2]. \quad (107)$$

This is in agreement with the reaction orders with respect to LSA and hydrogen peroxide found experimentally.

On reacting hydrogen peroxide with nitrolignin (NL) the reaction order with respect to H_2O_2 was close to 1 and with respect to NL close to $^1/_3$, the apparent energy of activation was 75 kJ mol^{-1}.[24] The marked deceleration of H_2O_2 consumption in a solution of NL under the influence of an unsaturated monomer indicated the radical–chain mechanism of the reaction and the fact that the reaction rate in this case exceeds the rate of peroxide homolysis points in favour of initiation of the process by an associate of nitrolignin with hydrogen peroxide according to reaction (108).

According to data from gel permeation chromatography (GPC) the polydispersity (from 2.96 to 10.30) and the mean molecular mass MW (from 3190 to 11470) of nitrolignin are increased by oxidation with hydrogen peroxide. In the opinion of the authors,[24] this occurs as a result of recombination of NL macroradicals by chain termination reactions (112)–(114). The kinetic scheme proposed[24] involves the isomerisation of an aroxyl radical having a vacant *ortho*

position into an aryl radical (criticism of such ideas is given above). The possibility of carrying out the previously considered rearrangement of aroxyl radical into a radical with an unpaired electron in the side chain is disregarded.[78] Allowing for what has been said the kinetic scheme for the oxidation of NL with peroxide may be described by the equations

$$H_2O_2 + HO{-}Ar{-}RH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2O_2 \ldots HO{-}Ar{-}RH \xrightarrow{k'} 2{}^{\cdot}OH + HO{-}Ar{-}RH, \quad (108)$$

$${}^{\cdot}OH + HO{-}Ar{-}RH \xrightarrow{k_s} H_2O + {}^{\cdot}O{-}Ar{-}RH, \quad (109)$$

$${}^{\cdot}O{-}Ar{-}RH \xrightarrow{k_r} HO{-}Ar{-}R^{\cdot}, \quad (110)$$

$$HO{-}Ar{-}R^{\cdot} + H_2O_2 \xrightarrow{k_{in}} {}^{\cdot}OH + \text{products}, \quad (111)$$

$$\left.\begin{aligned} 2{}^{\cdot}O{-}Ar{-}RH &\xrightarrow{k_0} \\ {}^{\cdot}O{-}Ar{-}RH + HO{-}Ar{-}R^{\cdot} &\xrightarrow{\sigma k_0} \\ 2HO{-}Ar{-}R^{\cdot} &\xrightarrow{\sigma^2 k_0} \end{aligned}\right\} \text{chain termination} \quad (112)\text{–}(114)$$

It is possible to obtain an equation for the rates of the radical–chain decomposition of H_2O_2 from the given scheme using quasi-steady-state concentrations taking geometric means and corresponding to that given previously.[24]

$$w = \frac{k_{in}k_r(2k/k_0)^{1/2}[NL]^{1/2}[H_2O_2]^{3/2}}{k_{in}[H_2O_2] + \sigma k_r + \sigma(2kk_0[NL][H_2O_2])^{1/2}}, \quad (115)$$

where $k = k_1k'(k_{-1} + k')^{-1}$. Proceeding from the proposed different contributions of radicals with an unpaired electron in the side chain and aroxyl radicals to chain termination, the reaction order with respect to NL and H_2O_2 must be intermediate between 0 and $^1/_2$ and between $^1/_2$ and $^3/_2$ respectively according to expression (115).[24] This is in agreement with the partial reaction orders found empirically, so that in the system investigated radicals with an unpaired electron in the side chain and aroxyl radicals from nitrolignin evidently participate in chain termination. High molecular weight fractions of NL appear as a result and this was confirmed by GPC data.

The oxidation with hydrogen peroxide of water-soluble lignin derivatives and of compounds modelling units of its structure proceeds according to a radical–chain mechanism with the participation of both phenolic hydroxyls and of functional groups in the side chain.

VI. Analysis of the kinetic scheme for radical–chain oxidation of phenolic compounds with hydrogen peroxide

The results of the kinetic investigations considered above enable the conclusion to be drawn that the interaction of hydrogen peroxide with organic substances, particularly phenolic compounds, usually proceeds by a radical–chain mechanism. This is indicated by the acceleration of peroxide decomposition in the presence of organic compounds, the frequently encountered fractional partial reaction orders, the dependence of the form of the rate equation on the relative concentrations of organic compound and peroxide and by the sensitivity of the reaction to the action of small amounts of catalysing or inhibiting substances.

The kinetic schemes given above for the oxidation of phenolic compounds with hydrogen peroxide are in fact partial variants of the general scheme of (116)–(126) which comprises chain initiation by homolysis of peroxide (116), interaction of hydroxyl radicals with the phenolic compound with the formation of phenoxyl radicals (117) and radicals with an unpaired electron in the side chain (118), rearrangement of the former to the latter (119), decomposition of hydrogen peroxide by these radicals (120) and (121) and chain termination with the participation of these radicals and of hydroxyl radicals.

$$H_2O_2 \cdot 2H_2O \xrightarrow{k_d} 2{}^{\cdot}OH + 2H_2O, \quad (116)$$

$${}^{\cdot}OH + HO{-}Ar{-}R(X)H \xrightarrow{k_s} H_2O + {}^{\cdot}O{-}Ar{-}R(X)H, \quad (117)$$

$${}^{\cdot}OH + HO{-}Ar{-}R(X)H \xrightarrow{k_{s1}} H_2O + HO{-}Ar{-}\dot{R}(X), \quad (118)$$

$${}^{\cdot}O{-}Ar{-}R(X)H \xrightarrow{k_r} HO{-}Ar{-}\dot{R}(X), \quad (119)$$

$${}^{\cdot}O{-}Ar{-}R(X)H + H_2O \xrightarrow{k_{in}} {}^{\cdot}OH + \text{products}, \quad (120)$$

$$HO{-}Ar{-}\dot{R}(X) + H_2O_2 \xrightarrow{k_{in\,1}} {}^{\cdot}OH + \text{products}, \quad (121)$$

$$\left.\begin{aligned} {}^{\cdot}O{-}Ar{-}R(X)H + {}^{\cdot}OH &\xrightarrow{k_{12}} \\ HO{-}Ar{-}\dot{R}(X) + {}^{\cdot}OH &\xrightarrow{k_{13}} \\ 2{}^{\cdot}O{-}Ar{-}R(X)H &\xrightarrow{k_{22}} \\ {}^{\cdot}O{-}Ar{-}R(X)H + HO{-}Ar{-}\dot{R}(X) &\xrightarrow{\sigma k_{22}} \\ 2HO{-}Ar{-}\dot{R}(X) &\xrightarrow{\sigma^2 k_{22}} \end{aligned}\right\} \text{chain termination} \quad (122)\text{–}(126)$$

The rate equation for each process depends mainly on the chain length and on the relative contributions of chain propagation reactions (117)–(121). It is expedient in this connection to conduct an analytical calculation of the given kinetic scheme using the quasi-steady-state concentrations under conditions when the chain length is sufficiently large.

1. Analytical calculation of a kinetic scheme with the long-chain approach

A general rate equation for long-chain oxidation of phenolic compounds with hydrogen peroxide has been derived using a kinetic model of the unbranched radical–chain process.[84] It is possible to represent the topology of the kinetic scheme (116)–(126) by the diagram shown in Fig. 12. The total chemical reaction proceeds by three routes, i.e. the first includes reactions (117) and (120), the second reactions (118) and (121) and the third reactions (117), (119) and (121).

The overall rate equation for the consumption of hydrogen peroxide is obtained by summation of the rates for each route.[83]

$$w = (2k_dk_{in\,1})^{1/2}(k_s + k_{s1})\,F_3[Ph]^{1/2}[H_2O_2]/(2F_3F_4 + F_5F_6)^{1/2}, \quad (127)$$

where

$$F_3 = k_r + k_{in}[H_2O_2],\ F_4 = k_{12}k_{in\,1}k_s[H_2O_2] + k_{13}(k_{s1}F_3 + k_rk_s),$$
$$F_5 = k_{22}k_s[Ph],\ F_6 = k_{in\,1}k_s[H_2O_2] + \sigma(k_{s1}F_3 + k_rk_s). \quad (128)$$

It may be shown that on satisfying the condition

$$[Ph] \gg 2F_3F_4/(k_{22}k_sF_6) \quad (129)$$

chain termination by substrate radicals according to reactions

(124)–(126) predominates. In this case equation (127) is transformed into (130).

$$w = (2k_d k_{in\,1})^{1/2}(k_s + k_{s1})\,(k_{22}k_s)^{-1/2}F_3[H_2O_2]/F_6^{1/2}. \quad (130)$$

However from this expression a first order equation with respect to peroxide, compatible with the experimental data, may be derived when $k_{in} = 0$ and $k_{in1} = 0$ [i.e. reactions (120) and (121) for the chain decomposition of H_2O_2 at any reaction centre do not play an appreciable role], which contradicts the result given in section V.

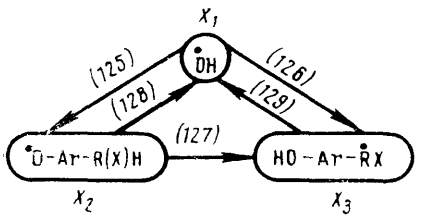


Figure 12. Diagram representing the topology of the kinetic scheme for the oxidation of phenolic compounds with hydrogen peroxide.

At the same time under conditions the reverse of (129) chain termination by hydroxyl radicals [reactions (122) and (123)] must predominate and the reaction rate will be described by Eqn. (131), following from (127).

$$w = (k_d k_{in\,1})^{1/2}\,(k_s + k_{s1})\,F_3\,[Ph]^{1/2}[H_2O_2]/F_4^{1/2}. \quad (131)$$

Partial reaction orders with respect to peroxide and to substrate may be obtained from the equation given and correspond to the results of experiments. This points in favour of the hypothesis on the preference under selected experimental conditions (see section V) for chain termination by reactions (122) and (123). In reality is follows from Eqn. (131) that the reaction order with respect to substrate is $^1/_2$, but with respect to peroxide it may be less, equal to or greater than 1 depending on the peroxide concentration and the values of the rate constants for the individual reactions (117)–(123). Such partial reaction orders were observed on oxidation of lignosulphonic acid, vanillyl alcohol and guaiacol. It may be shown that the rate equations obtained for these processes (see section V) are partial instances of the general dependence (131).

For example $k_r = 0$ in the system lignosulphonic acid–hydrogen peroxide (this is indicated by kinetic data on the oxidation of initial and methylated LSA, see Section V). Under this condition Eqn. (131) is in fact transformed into (107).

It follows from the data given in Section V on the change of functional composition of the products that $k_{in} = 0$ for the oxidation of vanillyl alcohol with hydrogen peroxide. In this case, allowing for the condition (86), Eqn. (131) is simplified to (87).

Finally, on oxidising guaiacol, which has only one reaction centre due to the absence of a side chain, it is possible to set rate constants k_r and k_{s1} to zero. Eqn. (131) is then transformed into (65). This confirms the correctness of Eqn. (131), which may aid (by drawing on results obtained by other methods) an adequate choice for the kinetic scheme and the corresponding expressions for reaction rates.

2. Analysis of a kinetic scheme at an arbitrary chain length

On oxidising certain phenolic compounds (vanillin, phenolic carboxylic acids) with hydrogen peroxide a first order is retained with respect to H_2O_2 while the order with respect to the organic substance may vary depending on the reaction conditions. This is not explained within the framework of the long-chain approach.

It is possible to analyse the kinetic scheme for the process at arbitrary chain length by the method of quasi-steady-state concentrations. However it is impossible to solve the system of nonlinear equations for the quasi-steady-state in explicit form in the present case consequently it was proposed to reduce it from a stationary reaction rate to a kinetic polynomial.[85] Application of such an approach to the kinetic scheme (116)–(123) enables the following polynomial to be obtained in the form represented by the equation:

$$F_7^2F_8 = c_1 + c_2/[H_2O_2] + c_3F_7F_8 + c_4F_7 + c_5[Ph]\,F_7/k_d, \quad (132)$$

where

$$c_1 = k_{in}k_{in\,1}(k_s + k_{s1})^2(k_{12}k_{13})^{-1},\ c_2 = k_r k_{in\,1}(k_s + k_{s1})^2(k_{12}k_{13})^{-1},$$
$$c_3 = -(k_s + k_{s1})\,k_r k_{12}^{-1},\ c_4 = (k_{in}/k_{12} + k_{in\,1}/k_{13})\,(k_s + k_{s1}),$$
$$c_5 = -(k_{in}k_{s1}/k_{12} + k_{in\,1}k_s/k_{13}),$$
$$F_7 = w\,[H_2O_2]^{-1}[Ph]^{-1},\ F_8 = wk_d^{-1}[H_2O_2]^{-1} - 1. \quad (133)$$

The kinetic polynomial (132) may be used in the analysis of the results obtained for discriminating between the kinetic hypotheses and in the choice of a variant of the kinetic scheme (116)–(123) for appropriate experiment. The following partial cases are considered.

1. If rearrangement of phenoxyl radicals into radicals with an unpaired electron in the side chain (119) is not feasible then substitution of $k_r = 0$ in polynomial (132) leads to the expression

$$F_7^2F_8 = c_1 + \left\{c_4\frac{w}{[H_2O_2]} + \frac{c_5}{k_d}\left(\frac{w}{[H_2O_2]}\right)^2\right\}\frac{1}{[Ph]} \quad (134)$$

In this case the dependence of reaction rate on the concentration of phenolic compound (at constant initial H_2O_2 concentration) must be linear in the coordinates of Eqn. (134) and enables exclusion of Eqn. (119) from the kinetic scheme (Table 5).

2. If $k_r = 0$ and $k_{in1} = 0$ also, i.e. the radicals with an unpaired electron in the side chain do not cause decomposition of hydrogen peroxide (121), then allowing for (133) $c_1 = 0$ and expression (134) reduces to Eqn. (135). It also follows from this that the experimental data in the coordinates of Eqn. (134) must be described by a straight line passing through the origin of coordinates.

$$F_7F_8 = c_4 + (c_5k_d^{-1}[H_2O_2]^{-1})\,w. \quad (135)$$

In this case the relationship between reaction rate and the concentration of the phenolic compound (at constant initial H_2O_2 concentration) must be linear in the coordinates of Eqn. (135). The passing of the straight line of (134) through the origin indicates fulfilment of the conditions $k_r = 0$ and $k_{in1} = 0$ and enables reactions (119) and (121) to be excluded from the overall kinetic scheme (Table 5).

3. If the condition $k_{s1} = 0$ is fulfilled in addition to $k_r = 0$ and $k_{in1} = 0$ then $c_5 = 0$ and Eqn. (135) is transformed into

$$wF_8/[H_2O_2] = (k_{in}k_s/k_{12})\,[Ph]. \quad (136)$$

It also follows from this that the experimental straight lines must be parallel to the abscissa axis in the coordinates of Eqn. (135) and must pass through the origin in the coordinates of Eqn. (134). Linearity of the experimental data in the coordinates of Eqn. (136)

combined with the line of (135) being parallel to the abscissa axis and the line of (134) passing through the origin indicates that the conditions $k_r = 0$, $k_{in1} = 0$ and $k_{s1} = 0$ are fulfilled and reactions (118), (119) and (121) may be excluded from the overall kinetic scheme (Table 5).

Table 5. Discrimination between kinetic hypotheses when oxidising phenolic compounds with hydrogen peroxide in aqueous solution.

Variant number	Determining conditions	Linear relationships	Discriminating reactions
1	$k_r = 0$	(134)	(119)
2	$k_r = 0$, $k_{in\,1} = 0$	(134) *, (135)	(119), (121)
3	$k_r = 0$, $k_{in\,1} = 0$, $k_{s\,1} = 0$	(134) *, (135) **, (136) *	(118), (119), (121)
4	$k_{in\,1} = 0$	(137)	(121)
5	$k_{in} = 0$	(138)	(120)

*The straight line in the coordinates of the given equation passes through the origin.
**The straight line in the coordinates of the given equation is parallel to the abscissa axis.

4. If only the condition $k_{in1} = 0$ is fulfilled then polynomial (132) allowing for (133) reduces to the equation

$$F_7F_8 = c_4 + (c_3/[H_2O_2] + c_5/k_d)\,F_8. \qquad (137)$$

Linearity of the data in the coordinates of Eqn. (137) indicates the fulfilling of the condition $k_{in1} = 0$ and points in favour of excluding reaction (121) from the overall kinetic scheme (Table 5).

5. If there is no decomposition of hydrogen peroxide by phenoxyl radicals, i.e. $k_{in} = 0$, then when $k_{ap} \gg k_d$ the kinetic polynomial (132) is transformed into the linear relationship

$$[Ph]/(k_{ef}^2[H_2O_2]) = (c_6 - c_7) + c_8(k_{ef}/[Ph]),$$

Where

$$c_6 = \{k_{in\,1}/k_{13} + k_r/(k_{12}[H_2O_2])\}\,k_{12}k_{13}\,(k_dk_{in\,1}k_r)^{-1}(k_s + k_{s1})^{-1},$$
$$c_7 = k_{s1}k_{12}\,(k_dk_r)^{-1}(k_s + k_{s1})^{-2},$$
$$c_8 = k_{12}k_{13}\,(k_dk_{in\,1}k_r)^{-1}(k_s + k_{s1})^{-2}. \qquad (138)$$

Linearity of the experimental data in the coordinates of Eqn. (138) indicates that $k_{in} = 0$ and points in favour of the exclusion of reaction (120) from the experimental scheme (Table 5).

The analysis of the kinetic polynomial (132) enables a purpose-directed discrimination to be made between kinetic hypotheses and may facilitate appreciably the choice by experiment of an appropriate variant of the kinetic scheme (116)–(123). Such an approach enables a simplified kinetic scheme of the actual process being investigated to be obtained from the complete scheme (116)–(123) by discarding individual reactions which make little contribution to the kinetics of the process.

What has been said enables the kinetic polynomial (132) to be used for the analysis of the kinetic scheme for the oxidation of phenolic compounds with hydrogen peroxide and may give desirable information on the mechanism of the process under investigation. This is illustrated by some examples.

When oxidising guaiacol with hydrogen peroxide linear relationships are observed for (134), (135) and (136). The straight lines in the coordinates of (134) and (136) pass through the origin of coordinates (Fig. 13, *1*) and (Fig. 14, *3*) and the straight line in coordinates of Eqn. (135) is parallel to the abscissa axis (Fig. 14, *1*). This corresponds to case 3 (Table 5) and indciates that reactions (118), (119) and (121) do not play a significant role in this system. In reality the structure of the guaiacol molecule and the change in its functional composition in the process of peroxide oxidation (see Section V) confirm this conclusion. What has been said enables exclusion of reactions (118), (119) and (121) from the kinetic scheme (116)–(123) and is in agreement with the scheme for the oxidation of guaiacol considered in Section V. When $k_r = 0$, $k_{in1} = 0$ and $k_{s1} = 0$ the general Eqn. (132) reduces to expression (63).

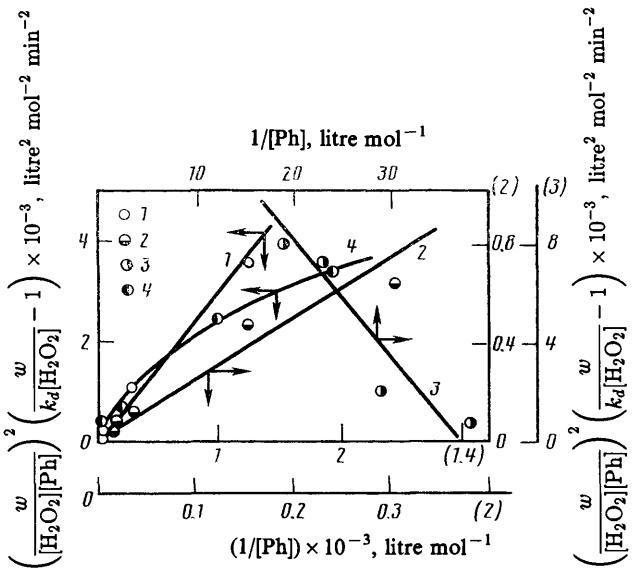


Figure 13. Relationship of the rates of oxidation with hydrogen peroxide of *1*, guaiacol, *2*, vanillin, *3*, LSA and *4*, ferulic acid to the concentration of phenolic compound in the coordinates of Eqn. (134) at 70 °C.[22,76,81]

Similarly when oxidising ferulic acid with hydrogen peroxide the relationship (134) is not linear (Fig. 13, *4*) but relationship (137) is linear (Fig. 15, *1*) which corresponds to case 4 (Table 5). The latter indicates that induced decomposition of H_2O_2 by reaction (121) does not occur in practice in the system being investigated. This enables reaction (121) to be excluded from the kinetic scheme (116)–(123) and is in agreement with the oxidation scheme for phenolic carboxylic acids given in Section V. When $k_{in1} = 0$ the overall Eqn. (132) is transformed into expression (97).

Investigation of the kinetics of the interaction of H_2O_2 with LSA and its methylated derivatives showed that in this system chain decomposition of peroxide by radicals in the side chain and by phenoxyl radicals occurs (see Section V). In this case a linear relationship was observed for (134) while the straight line did not pass through the origin of coordinates (Fig. 13, *3*). This

corresponds to case 1 (Table 5) and indicates that reaction (119) does not play an appreciable role in the system under investigation. What has been stated enables exclusion of reaction (119) from the overall scheme (116)–(123) and is in agreement with the kinetic scheme for the oxidation of LSA considered in Section V.

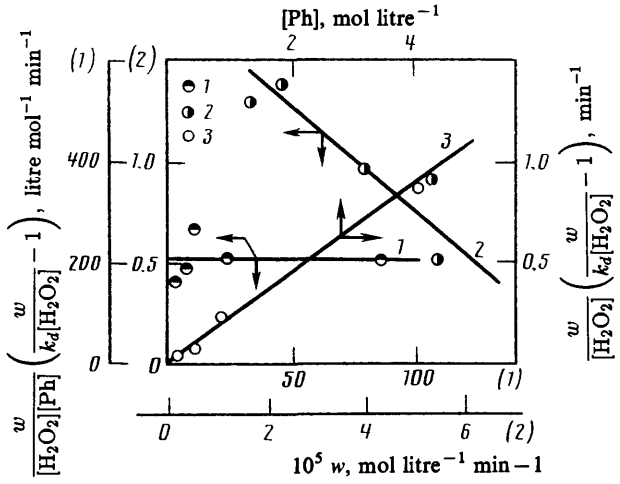


Figure 14. Relationship of the reaction rates of hydrogen peroxide with *1*, *3*, guaiacol and *2*, vanillin to their concentrations in the coordinates of Eqn. (135) *1*, and *2*, and of Eqn. (136) (*3*) at 70 °C and a hydrogen peroxide concentration of 1.06 mmol litre^{-1}.[22,76]

When oxidising vanillin with hydrogen peroxide a linear relationship was observed for (134) and (135). Although the straight line drawn from the experimental data in the coordinates of Eqn. (134) passes through the origin of coordinates, the straight line in coordinates of Eqn. (135) is not parallel to the abscissa axis (Fig. 13, *2*; Fig. 14, *2*) This corresponds to case 2 (Table 5) and indicates that reaction (119) and the decomposition of H_2O_2 by radicals with an unpaired electron on the carbon atom of the carbonyl group (121) do not make significant contributions to the kinetics of the process. These conclusions are confirmed by data on the kinetics for the decomposition of hydrogen peroxide in solutions of benzaldehyde, guaiacol, and mixtures of them (see Section V). Consequently reactions (119) and (121) may be excluded from the overall kinetic scheme in this case which is in agreement with the scheme given in Section V for the oxidation of vanillin. When k_r = 0 and k_{in1} = 0, the general Eqn. (132) reduces to expression (71).

Analysis of the functional composition of the oxidation products of vanillyl alcohol with hydrogen peroxide showed that the content of phenolic hydroxyls and methoxyl groups was practically unchanged in the oxidation process, while the alcohol is oxidised to a carbonyl group (see Section V). This indicates that the decomposition reaction (120) does not make an appreciable contribution to the kinetics of the process. The linearity of relationship (138) (Fig. 15, *2*) confirms this conclusion and enables assignment of this system to case 5 (Table 5). Reaction (120) may therefore be excluded from the overall kinetic scheme (116)–(123) in agreement with the oxidation scheme for vanillyl alcohol represented in Section V. When k_{in} = 0 and allowing for (86) the overall Eqn. (132) is transformed into expression (87).

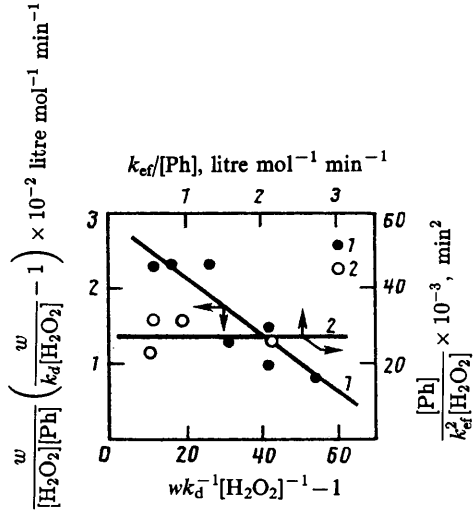


Figure 15. Relationship of the rates of oxidation with hydrogen peroxide of *1*, ferulic acid and *2*, vanillyl alcohol to reactant concentration in the coordinates of *1*, Eqn. (137) and *2*, Eqn. (138) at 70 °C.[78,81]

The rate equations given in Section V for the oxidation of phenolic compounds with hydrogen peroxide are partial cases of the general relationship (132) obtained by analysis of the kinetic scheme (116)–(123). This confirms the correctness of the chosen kinetic schemes to describe the oxidation processes of phenolic compounds with hydrogen peroxide in aqueous medium.

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Translated from *Uspekhi Khimii* **60** 982–1004 (1991) U.D.C. 543.51

Mass spectrometry of derivatives and heterocyclic analogues of 9,10-dihydroanthracene

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ABSTRACT. The fragmentation of derivatives of 9,10-dihydroanthracene and of its heterocyclic analogues containing atoms of O, S, N, P, Si, As, Se and Te at positions 9 and/or 10 is examined. The conditions reviewed are electron impact and chemical ionisation with recording of positive and negative ions. It has been shown that depending on its nature, the heteroatom may be eliminated together with substituents from the molecular ion or a substituent may be lost both as a radical and together with an additional H atom. The fragmentation of compounds in which the substituting groups are adjacent to the hetero atom is explained by the '*peri*-effect'. The elimination of substitutents from phenylene rings, at the *meso* position and at the hetero atom occurs in a similar manner to elimination in the corresponding aromatic derivatives.

The bibliography contains 114 references.

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I. Introduction

Derivatives of 9,10-dihydroanthracene and its heterocyclic analogues are widely distributed in nature. The anthracyclines, which are antibiotics possessing antitumour activity, belong to this class. The aglycone of the anthracyclines is a tetrahydronaphthacenequinone which contains an anthraquinone fragment. Phenothiazine derivatives possess various physiological activities and are applied in medicine as antihistamine preparations, for the treatment of Parkinsonism and also for the treatment of psychiatric disorders (Aminazine). Antibiotics of the actinomycin series possess strong bactericidal properties and contain a dibenzoxazine (phenoxazine) ring in the molecule. Up to the present a large number of analogues of 9,10-dihydroanthracene have been synthesised which contain in positions 9 and 10 not only the traditional heteroatoms O, N, S and P but also the elements Si, Se, Te, As, etc.

While possessing specific chemical properties the derivatives of 9,10-dihydroanthracene and its heterocyclic analogues also differ in their specific fragmentation under conditions of electron impact (EI). First there are processes eliminating fragments of the central ring, leading to its contraction and the formation of dibenzohetarene ions. No less important fragmentation processes are fission of this ring and elimination of substituents depending on their nature and disposition in the molecule. Knowledge of the rules for dissociation on ionisation is necessary when studying the reactivity of ions in the gas phase and in the solution of structure-analytical problems (the establishment of the composition and structure of molecules, the determination of trace amounts of the appropriate physiologically active compounds and the products of their metabolism).

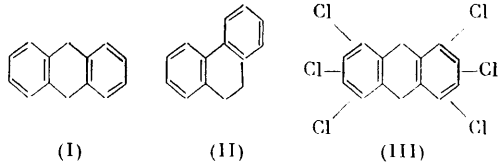
There are no special reviews in the literature of studies in which the features of the dissociation of 9,10-dihydroanthracenes and their heterocyclic analogues on ionisation have been correlated and systematised. The EI mass spectra of anthraquinones are considered only in old monographs[1,2] and the mass spectral characteristics of individual types of heterocyclic analogues of 9,10-dihydroanthracene have been given in a monograph.[3] It should be noted that in this review the EI method is implied even when not specially stipulated.

II. 9,10-Dihydroanthracene and its derivatives

The mass spectrum of 9,10-dihydroanthracene (I) contains three most significant peaks corresponding to the ions M^+, $[M-H]^+$ and $[M-2H]^+$ with a ratio of intensities 92:100: 63. A similar triplet of peaks also dominates the mass spectrum of 9,10-dihydrophenanthrene (II), however in this case the ratio of intensities is 100:55:30. The higher intensity peak for the $[M-H]^+$ ion in the case of compound (I) is explained by the fact that on elimination of a hydrogen atom from a methylene group a carbocation is formed with two benzyl group fragments in the stabilisation of which both phenylene rings participate. In the analogous carbocation which is formed from compound (II) there is one benzyl fragment and only one phenylene ring participates in its stabilisation. In addition there are seven resonance forms possible for the $[M-H]^+$ ion for compound (I) and four for compound (II).

The $[M-2H]^+$ ions (I) and (II) have the structures of anthracene and phenanthrene ions respectively.[4]

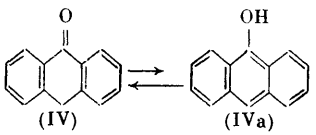
There are low intensity peaks for $[M-CH_3]^+$, $[M-C_2H_4]^+$, $[C_7H_5]^+$ and $[C_6H_4]^+$ ions in the mass spectrum of compound (I) and others the formation of which is linked with the isomerisation of M^+ and the fission of bonds in the central ring.



(I) (II) (III)

Detection of the toxic hexachloro-9,10-dihydroanthracenes (III) with chlorine atoms at various positions in the phenylene rings was effected by gas chromatography-mass spectrometry (GC-MS). Two of the most intense peaks with *m/z* 388 and 390 were used out of the multiplet of peaks of their molecular ions.[5]

9(10H)-Anthracenone, anthrone (IV), is characterised by a tautomeric equilibrium with 9-hydroxyanthracene, anthrol (IVa). The keto form is thermodynamically the more favourable and anthrone predominates in the gas phase.

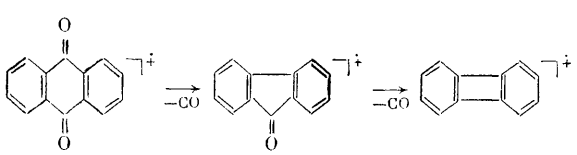


(IV) (IVa)

It was established that the enthalpy of formation of anthrone is 3 kcal mol^{-1} less than for anthrol and the enthalpy of formation of M^+ for the keto form is 77 kcal mol^{-1} greater than that of M^+ of the enol form.[6] Consequently the main decomposition of M^+ for compound (IV) is linked not with ejection of CO (as is characteristic of cyclic ketones) and the formation of a fluorene cation radical but with loss of HCO. However this process does not occur in practice in the case of 10,10-diaryl-9-anthrones.[7]

Much work has been devoted to the mass spectrometric study of anthraquinone (V) and its derivatives.[2] The main routes for the decomposition of anthraquinone on EI are determined by the sequential elimination of two CO groups, which was established by ^{18}O-labelled analogues,[8] with the formation of ions of fluorenone and biphenylene (Scheme 1).

Scheme 1



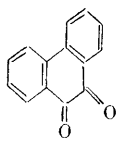
M^+, (V) $[M-CO]^+$ $[M-2CO]^+$

This fragmentation scheme for anthraquinone has become classical and is cited in many monographs and original papers.[1-3] The individual steps of this reaction sequence have been separated in the various field free regions of a reversed geometry double focussing mass spectrometer.[8] It was established that different amounts of energy are liberated in the formation of $[M-CO]^+$ ions depending on where they are generated, either in the ion source or in a field free region. But this in its turn means that $[M-CO]^+$ ions formed in these two regions have different structures. The structure of the ion in the second case is unknown. The $[M-CO]^+$ ions generated in the ion source most probably have the structure of the fluorenone ion since the mass spectrum of the latter is very similar to the spectrum of anthraquinone below the peak with *m/z* 180, which corresponds to the $[M-CO]^+$ ion. Attempts to detect all of the two-step reaction

$$M^+ \rightarrow [M-CO]^+ \rightarrow [M-2CO]^+$$

in the first field free region proved to be unsuccessful, which indicates the low rate of the second stage.

9,10-Phenanthrenequinone (VI) is decomposed on EI by an analogous scheme. Ejection of the first molecule of CO is predominant which is explained by the ease of the initial fission of the C–C bond between the α-diketo groups.[9]

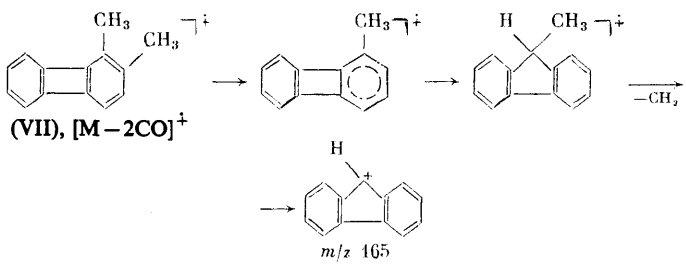


(VI)

It must be mentioned that anthracene is readily oxidised to anthraquinone on chemical ionisation in a mixture of $O_2/N_2/CO_2$ gases. Only the M^+ peak of anthraquinone was present in the negative ion mass spectrum recorded in this manner.[10]

In the case of 1(2)-methyl- and 1,2-methyl-9,10-anthraquinones (VII) a complex skeletal rearrangement occurs in the $[M-2CO]^+$ ions with the formation of a fluorene cation (Scheme 2).[11]

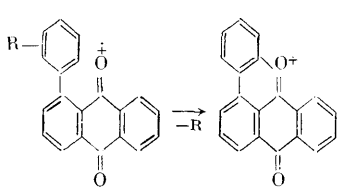
Scheme 2



(VII), $[M-2CO]^+$ *m/z* 165

The presence of a carbonyl group in anthraquinones has a special influence on fragmentation at the expense of substituents in the aromatic ring. In the spectra of 1-aryl derivatives of anthraquinone (VIII) containing an *ortho* substituent there was a main peak with *m/z* 283 caused by elimination of this substituent from M^+ (Scheme 3).[1]

Scheme 3



M^+, (VIII), R = H, *o*-CH_3, *o*-OCH_3, *o*-NO_2 *m/z* 283

This type of dissociation on ionisation has been investigated in detail[12] in a study of *o*, *m* and *p* isomers in a series of 1-aryl-anthraquinones (VIII, R = CH_3, OCH_3, F, Cl, Br, and NO_2). A substituent in the *ortho* position of the aryl group is readily eliminated by the process shown in Scheme 3. The same substituent in the *meta* or *para* position leaves with difficulty. In this case a hydrogen atom is readily lost from the *ortho* position (Table 1).

The main routes of fragmentation of 1- and 2-chloroanthraquinones and also of 1,5- and 1,8-dichloroanthraquinones on EI are linked with the loss of two molecules of CO from M^+. The $[M-CO]^+$ ions also exist as two structures in all these cases.[8]

After the ejection of two CO groups monohydroxyanthraquinones eliminate a third CO molecule and HCO.[13] Using [9,10-di-^{18}O]-1-hydroxy-9,10-anthraquinone as an example it was established[8] that the M^+ of this compound gives up $C^{16}O$ and $C^{18}O$ in the ratio 1:4, i.e. the elimination of CO from the carbonyl groups is preferred to elimination from the hydroxyl group. The $[M-C^{18}O]^+$ ions give up

$C^{16}O$ and $C^{18}O$ with a proability ratio of 1:5. The ejection of a second CO molecule from $[M-C^{18}O]^+$ ions is similar to that which occurs on decompositon of [9-^{18}O]-1-hydroxy-9-fluorenone.

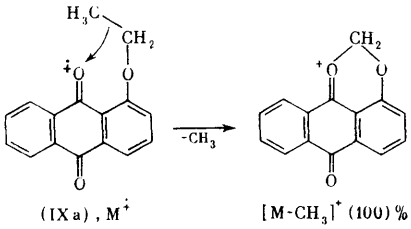
Table 1. Intensities ($\%\sum_{60}$) of peaks of characteristic ions in the mass spectra of compounds (VIII).

R	M^+	$[M-H]^+$	$[M-R]^+$	R	M^+	$[M-H]^+$	$[M-R]^+$
o-CH_3	6.5	1.5	36.5	*o*-Cl	0	0.2	43.0
m-CH_3	8.0	11.3	15.4	*m*-Cl	14.1	23.9	12.2
p-CH_3	8.6	12.2	8.3	*p*-Cl	16.4	26.5	9.4
o-OCH_3	3.0	0.3	36.5	*o*-Br	0	0.02	35.9
m-OCH_3	14.4	13.1	15.4	*m*-Br	9.5	13.9	14.8
p-OCH_3	10.4	9.7	8.3	*p*-Br	13.9	19.6	10.6
o-F	12.8	14.0	15.0	*o*-NO_2	0.02	0.09	39.6
m-F	15.8	27.4	2.8	*m*-NO_2	5.8	6.8	7.4
p-F	18.6	33.3	2.2	*p*-NO_2	2.3	2.6	3.5

The ease of formation of $[M-OH]^+$ ions in the case of dihydroxanthraquinones depends on the disposition of the hydroxyl groups.[13] The corresponding peaks were much more intense if the OH groups were in different rings. It was noted[13] that anthraquinones containing an OH group at positions 2, 3, 6, or 7 were more inclined to eject an OH radical from M^+ than were the 1, 4, 5 or 8 isomers for which the formation of an intramolecular hydrogen bond is possible.

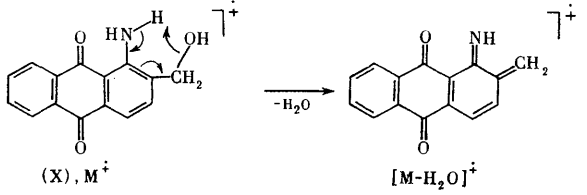
Marked differences were observed between the spectra of 1- and 2-methoxyanthraquinones.[13] Peaks for $[M-OH]^+$ and $[M-H_2O]^+$ were present only in the first case. The generation of the second ion is caused by the *peri* disposition of the CH_3O and CO groups providing migration of two H atoms to the carbonyl group. The principal differences between the mass spectra of the higher 1- and 2-alkoxyanthraquinones are explained by the *peri*-effect.[14] With the aid of 1- (IXa) and 2-ethoxyanthraquinones (IXb) labelled with deuterium in the ethyl group it was shown that the *peri* effect determines the loss of a CH_3 radical from compound (IXa) (Scheme 4), while in the case of compound (IXb) fragmentation of the ethoxy group is linked only with ejection of C_2H_4.

Scheme 4



In the general case substituted anthraquinones decompose on EI like the corresponding derivatives of aromatic compounds although the character of the fragmentation is determined by the nature of the substituent.[15] The double elimination of CO from M^+ typical of anthraquinones is, as a rule, completely suppressed but the CO molecules may be ejected from the fragment ions formed on elimination of substituents. For example the main decomposition of 1-amino-2-hydroxymethylanthraquinone (X) is linked with the elimination of a molecule of water (Scheme 5) and the elimination of CO is effected from the dehydrated ion.[16]

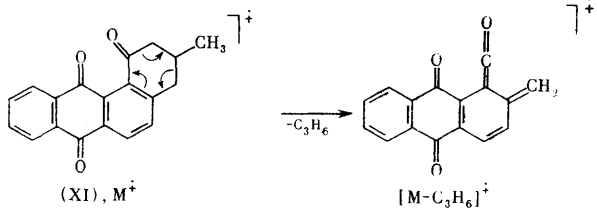
Scheme 5



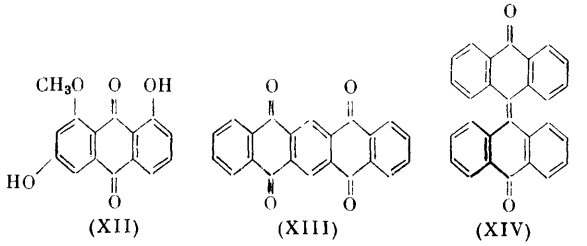
The decomposition of 1-arylamino- and 1,4-di(arylamino)anthraquinones on EI is linked with expulsion of the ArNH group from position 1. The resulting ions $[ArNH_2]^+$, $[ArNH]^+$ and $[M-ArN]^+$ may decompose further and the latter is capable of eliminating CO twice.[17]

The presence of an additional annelated ring on the anthraquinone molecule may introduce specificity into the character of the decomposition. For example in the case of the methyl ester of ochromycinone (XI) in addition to decarbonylation of M^+ there is also elimination of a C_3H_6 particle probably by a retrodiene decomposition (Scheme 6). Later OH, CO and HCO may be lost from the $[M-C_3H_6]^+$ ion.[18]

Scheme 6



An anthraquinone fragment is often encountered in natural compounds such as anthraquinone antibiotics in whose structure determination mass spectrometry was used.[19–25] For example on analysis of the mass spectrum, in which $[HOC_6H_3CO]^+$, (*m/z* 120, 12%) and $[HO(CH_3O)C_6H_3CO]^+$ (*m/z* = 150, 2%) ions were detected, the pigment isolated from the bacterium *Xenorhabdus luminescens* was assigned the structure 1,6-dihydroxy-8-methoxyanthraquinone (XII) and not 1,3-dihydroxy-8-methoxyanthraquinone.[26]



Fragmentation on EI of more complex anthraquinones of the type of pentacene-5,7,12,14-diquinone (XIII)[27] and 9,9′-dianthraquinone (XIV)[2,28] is also linked with repeated expulsion of a molecule of CO from M^+ and also of HCO at some stage.

III. Analogues of 9,10-dihydroanthracene with a heteroatom at position 9(10)

The mass spectral characeristics of heteroanalogues of 9,10-dihydroanthracene containing only one heteroatom (N, O, S, Si, P, etc.) in the central ring are considered in this section. Both general and specific routes of decomposition on EI are characteristic of compounds of this series depending on the nature of the heteroatom at position 9. One of the frequently encountered routes of fragmentation is the expulsion of the heteroatom from position 9 or the carbon atom with substituents from position 10. In both cases contraction of the central ring occurs with the formation of fluorene structures or their 9-hetero analogues (Scheme 7). The presence in the molecule of substituents inclined towards independent fragmentation may suppress these processes or cause them to occur in the later stages of ion fragmentation resulting in loss of the substituent. Some compounds of the type under consideration (XV) for which the disappearance of position 9 and/or 10 occurs at the first fragmentation of M^+ are shown in Table 2.

Scheme 7

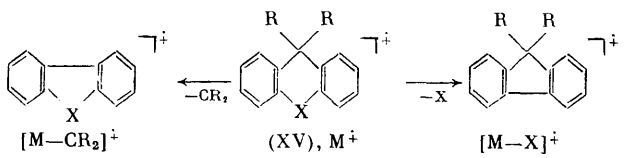


Table 2. Characteristic ions in the EI mass spectra of compounds (XV) (intensities are given in % maximal peak).

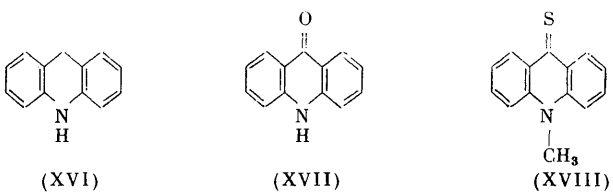
CR_2	X	Other substituents	$J_{[M-CR_2]^+}$	$J_{[M-CR_2]^+}/J_{M^+}$	$J_{[M-X]^+}$	$J_{[M-X]^+}/J_{M^+}$	Refs.
CO	O	–	50	0.50	–	–	[29]
CO	O	2,7-Cl_2	28	0.28	–	–	[29]
CO	O	2,7-F_2	40	0.40	–	–	[29]
CH_2	S	–	–	–	15	0.25	[30]
CO	S	–	38	0.38	–	–	[30]
CH_2	SO_2	–	–	–	25	0.31	[30, 31]
CO	SO_2	–	–	–	40	1.40	[30]
CO	NH	–	53	0.53	–	–	[32, 33]
CO	NH	1-CH_3	7	0.07	–	–	[34]
CO	NH	2-CH_3	8	0.08	–	–	[34]
CO	NH	4-CH_3	11	0.11	–	–	[34]
CO	NCH_3	–	11	0.11	–	–	[32]
CH_2	P(O)OH	–	–	–	62	0.75	[35]
CH_2	$P(O)OCH_3$	–	–	–	69	0.80	[35]
CO	P(O)OH	–	64	0.80	100	1.25	[35]
CO	$P(O)OCH_3$	–	30	1.15	23	0.97	[35]
CH_2	$SiClCH_3$	–	–	–	20	0.25	[36]
CH_2	SiF_2	–	–	–	18	0.18	[54]
CH_2	$Si(OCH_3)_2$	–	–	–	7	0.30	[54]

In one of the first studies on the mass spectrometric investigation of thioxanthene (XV, $CR_2 = CH_2$, X = S) and its 10,10-dideutero analogue it was established that their M^+ readily lose CH_2 and CD_2 (the corresponding peak has 60% intensity). This result was extremely unexpected since ejection of a carbene particle under EI conditions is energetically not favoured. In fact in more recent work[30,31,38] on the investigation of xanthene (XV, CR_2, CH_2, X = O), thioxanthene and their 10,10-dideutero analogues no peaks corresponding to ejection of $:CH_2$ and $:CD_2$ were detected. The elimination of CO from M^+ is a common process for carbonyl derivatives of these compounds.

In certain cases the process of forming $[M-X]^+$ ions is not a single step. This is a characteristic for example of phosphorus compounds [XV, $CR_2 = CH_2$, CO and X = P(O)OH or $P(O)OCH_3$] the molecular ions of which lose OH, OCH_3 and PO sequentially.[35]

After elimination of the heteroatom X from compounds (XV, $CR_2 = CH_2$) leading to a fluorene cation-radical, the fission of H is often a characteristic accompanied by the formation of a more stable fluorenyl cation.

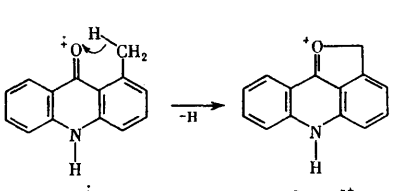
9,10-Dihydroacridines (acridanes). The mass spectrum of acridane (XVI) contains two peaks for M^+ (51%) and $[M-H]^+$ (100%) ions the intensities of which fell to 6–7% in the spectrum of 9-n-propylacridane where the base peak was the $[M-C_3H_7]^+$ ion. The character of the fragmentation is practically unchanged in the case of 4-ethyl- and 4-phenylacridanes, but in the case of 4-ethylacridane a noticeable peak for the $[M-1-28]^+$ ion appeared which is caused by the ejection of a molecule of ethylene from the C_2H_5 group as a result of a McLafferty rearrangement in the $[M-H]^+$ ion.[34]



(XVI) (XVII) (XVIII)

The mass spectral date of some acridones are given in Table 2. The molecular ion of acridone (XVII) may lose H and HCN after ejection of CO and the formation of a carbazole ion-radical.[32,33] Elimination of CS is a characteristic of 10-methylthioacridone (XVIII).[3] Competition between fragmentation of the side chain and ejection of CO was observed on fragmentation of substituted acridones (1-, 2-, 3-, and 10-methyl, 2-ethyl, 2-n-butyl, 4-isopropyl, 4-t-butyl, 1-isopropyl-4-methyl). In all cases apart from the methylacridones, β-fission (benzylic) dominates accompanied by loss of part of the alkyl substitutent.[33,39] It was proposed[34] that this process in the M^+ of 1-methylacridone is facilitated by the possibility of forming an oxonium ion (Scheme 8). In all these cases the ejection of CO occurs after the given reactions.

Scheme 8

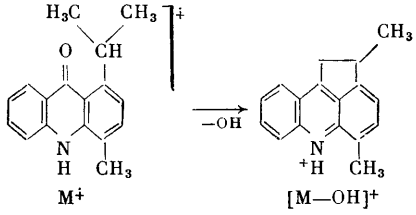


M^+ $[M-H]^+$

A special feature of the dissociation of 1-isopropyl-4-methylacridone on ionisation is the ready formation of the $[M-OH]^+$ ion, the peak of which reached 80%.[34] The composition of this ion was

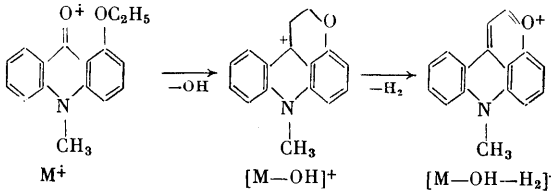
proved by high resolution mass spectrometry, and the one-step character of its formation by the presence of the appropriate metastable peak (Scheme 9).

Scheme 9



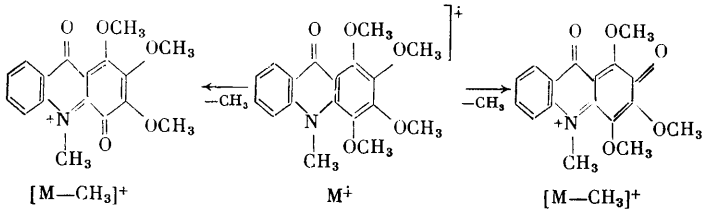
A series of specific fragmentation routes was discovered for alkoxy substituted acridones,[32] which in the general case decompose as alkylaryl ethers. Stepwise expulsion of OH and H_2 is a characteristic of 2-ethoxyacridone. It was proposed that the driving force of these reactions is the formation of cyclic oxonium ions (Scheme 10).[32,40]

Scheme 10



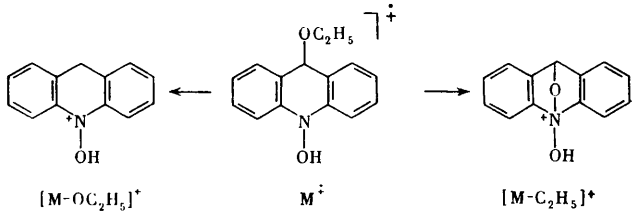
The form of the decomposition of 1,2,3,4-tetramethoxy-10-methylacridone is an example of the high regioselectivity of fragmentation. It was shown that deutero analogues that in this case the elimination of CH_3 occurs only from positions 2 and 4 in a 60:40 ratio. Such selectivity of fragmentation is caused by the possibility of forming well-stabilised ions (Scheme 11).

Scheme 11



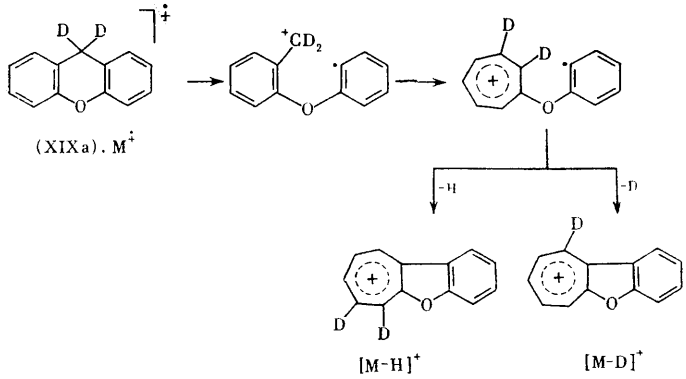
Like the 9-alkylacridanes, 9-ethoxy-10-hydroxyacridane loses the substituent from position 9 very readily on EI leading to the maximum peak in the mass spectrum. A less intense peak corresponds to loss of C_2H_5 from M^+ (Scheme 12).[41]

Scheme 12



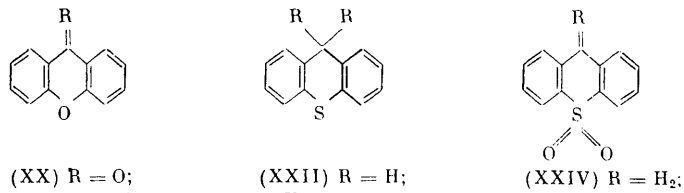
Xanthenes. The mass spectrum of unsubstituted xanthene (XIX) is very sparse and contains the base peak of the $[M-H]^+$ ion together with an M^+ peak (~45%).[30,42] In the spectrum of 9,9-deuterated xanthene (XIXa) in place of the expected peak for the $[M-D]^+$ ion a doublet was observed of peaks for $[M-H]^+$ and $[M-D]^+$ ions which were close in intensity.[31] Thus randomisation of H atoms occurs in the M^+ of xanthene even before decomposition, possibly according to the following scheme (Scheme 13).

Scheme 13



The mass spectra of complex derivatives of xanthene[43–45] and of tetrachloroxanthene[42] have been described in the literature. A series of papers is devoted to a detailed mass spectrometric investigation of xanthone (XX) and its dimethyl, hydroxy and methoxy derivatives.[29,46,47] The sequential elimination of two molecules of CO is a characteristic feature of the decomposition of the M^+ of xanthone (XX). It was shown[29] with an ^{18}O-labelled analogue that the first molecule of CO is wholly ejected from the carbonyl group. However it was discovered[8] that ejection of CO from M^+ in the second field free region of the reversed geometry mass spectrometer may also proceed with the participation of the ether oxygen in the first act of CO elimination. It must be noted that the molecular ion of thioxanthone (XXI) readily loses CS.[3]

A correlation was observed in the case of dihaloxanthones between elimination of CO and the halogen from M^+. In a series of fluorinated, chlorinated, brominated and iodinated derivatives it was shown that the stronger the C–Hal bond the higher became the intensity ratio $[M-CO]^+/[M-Hal]^+$.[29] The decomposition rule described has enabled ready detection of tetrachloroxanthone among environmental contaminants[42,48]



(XX) R = O;
(XXI) R = S

(XXII) R = H;
(XXIII) R = CH_3;
(XXV) R + R = O

(XXIV) R = H_2;
(XXVI) R = O

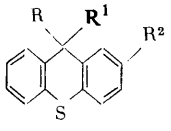
Thioxanthenes. Thioxanthene (XXII) is readily distinguished from xanthene by the character of the fragmentation involving ring fission since its M^+ loses S and HCS. However the peak of the $[M-H]^+$ ion is the base peak and exceeds the intensity of M^+ almost twofold in the mass spectrum of thioxanthene,[30] while in the spectrum of 9,9-D_2-thioxanthene the same doublet of peaks for $[M-H]^+$ and $[M-D]^+$ ions was observed as in the spectrum of deuteroxanthene. Thus the same mechanism for the fission of H occurs for thioxanthene as for xanthene (Scheme 13).[31] It must be

noted that in the mass spectrum of 9,9-dimethylthioxanthene (XXIII) the peak for the $[M-CH_3]^+$ ion possesses maximal intensity and may then lose S.[49]

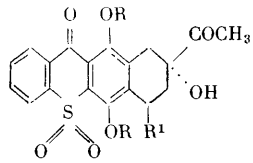
Decomposition of thioxanthene S,S-dioxide (XXIV) on EI proceeds by several parallel routes, viz. sequential elimination of 1) OH, CO and H, 2) SO and H and 3) SO_2 and H (the latter process leads to the maximal peak in the mass spectrum).[30] As was shown[31] with the aid of the 9,9-dideutero analogue of compound (XXIV) the H atom from position 9 participates in the expulsion of OH. At the same time $[M-SO_2]^+$ ions preferentially split off a H atom from the benzene ring and, to a lesser extent, from position 9.[31]

The main decomposition of the M^+ of thioxanthone (XXV) is linked with the sequential expulsion of CO and S, and also of CO, CS, and H.[30] In the case of thioxanthone S,S-dioxide (XXVI) the main reaction is the elimination of SO, seemingly as a result of isomerisation into the sulphonate form.[50]

On investigating chlorprothixene (XXVII) and its analogues (XXVIIa, b) by chemical ionisation (CH_4 as gas reagent) and negative ion recording, the unexpected formation of $[M+H]^-$ was detected in addition to the normal $[M-H]^-$ ion.[51] The generation of the former is caused by the presence of an S atom in the molecule. The strong formation of $[M+H]^-$ ions was also noted in a study of sulphur-containing anthracycline compounds (XXVIII) by secondary ion mass spectrometry (Cs^+, 12 and 23 keV) and negative ion recording.[52]



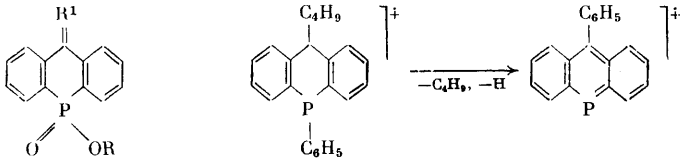
(XXVII) R + R^1 = $CHCH_2CH_2N(CH_3)_2$; R^2 = Cl;
(XXVIIa) R + R^1 = $CHCH_2CH_2N(CH_3)_2$, R^2 = H;
(XXVIIb) R = $CH_2CH_2CH_2N(CH_3)_2$, R^1 = H, R^2 = Cl



(XXVIII) R = H, CH_3, R^1 = H, OCH_3

9,10-Dihydro-9-phosphanthracenes. The individual routes for the fragmentation of these compounds are given above in Table 1. The molecular ion of compound (XXIX) is able to lose H_2O and then PO with the formation of the fluorenyl cation. The latter is also formed from the M^+ of ester (XXIXa) by the stepwise expulsion of CH_3 and PO_2H or $HOCH_3$ and PO.[35] The molecular ion of ketone (XXX) may sequentially lose CO and OH or PO_2H and CO. The seqential elimination of CH_2O and PO is a characteristic of the methoxy derivative (XXXa).[35]

Scheme 14



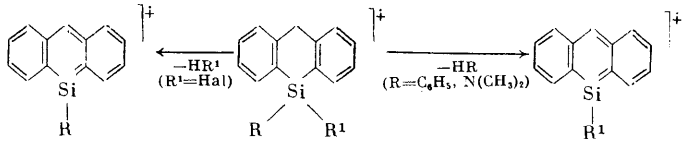
(XXIX) R = H, R^1 = H_2; (XXXI), M^+
(XXIXa) R = CH_3, R^1 = H_2;
(XXX) R = H, R^1 = O;
(XXXa) R = CH_3, R^1 = O.

The stepwise elimination of C_4H_9 and H (Scheme 14) is observed for 9-phenyl-10-t-butyl-9,10-dihydro-9-phosphanthracene (XXXI), in addition to expulsion of C_4H_8 as a result of a McLafferty rearrangement. It was proposed that transannular 1,4-migration of the phenyl group occurs in this process.[53]

9,10-Dihydro-9-silanthracenes. In the simplest compounds of this series (XXXII) the character of the fragmentation on EI depends on the nature of the substituent at the silicon atom. The molecular ion of 9,10-dihydro-9-silanthrene (XXXII, R = R_1 = H) decomposes by the sequential elimination of three H atoms with the formation of a fluorenyl cation. Derivatives containing alkyl groups on the silicon atom undergo fragmention like alkylsilanes. For example the weakly stable M^+ of 9,9-diethyl-9-sila-9,10-dihydroanthracene (XXXII, R = R^1 = C_2H_5) sequentially loses C_2H_5 (causing the base peak) and C_2H_4.[54]

A new fragmention route was detected for compounds (XXXII) with halogen substituents at the silicon atom such as (R = CH_3, R^1 = Cl),[36] (R = R^1 = Cl) and (R = H, R^1 = Cl),[54,55] (R = R^1 = F) and [R = $N(CH_3)_2$, R^1 = Cl][54] and (R = C_6H_5, R^1 = Cl or Br).[56–58] The molecular ions of such compounds readily lose hydrogen halide with the formation of silanthracene cation-radical which, in the case of compounds containing halogen and phenyl or a dimethylamino group, may also arise as a result of parallel expulsion of molecules of C_6H_6 and $(CH_3)_2NH$ respectively (Scheme 15). Both these ions are able to lose SiR and SiR^1 which leads to a fluorenyl cation (*m/z* 165).

Scheme 15



(XXXII), M^+

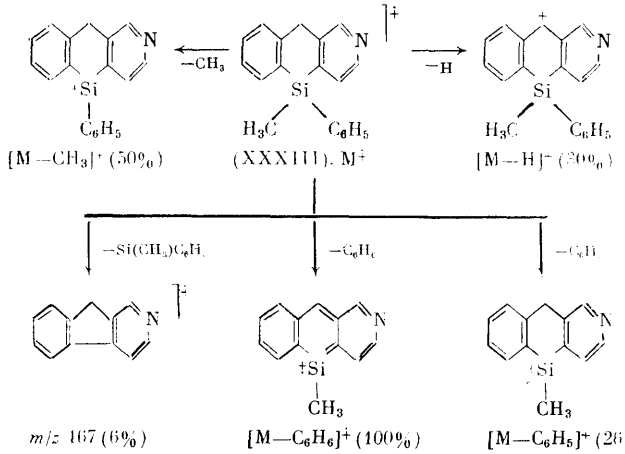
Elimination from M^+ of the substituent from the silicon atom together with an additional H atom from position 10 is also observed in the case of other types of substituent such as in compounds (R = R^1 = OCH_3) and [R = R^1 = $N(CH_3)_2$].[54] In the first case CH_3OH is readily lost (then CH_3 or CH_2O) and in the second, initially $(CH_3)_2NH$ [$N(CH_3)_2$ to a lesser extent] and then $N(CH_3)_2$.

Similar routes for fragmentation by EI also occur in the case of 10-methyl-10-phenyl-9,10-dihydro-10-sil-2-azanthracene (XXXIII). Two processes compete, viz. elimination from M^+ of a CH_3 radical and of a molecule of C_6H_6.[59,60] It was shown that with the aid of 9,9-dideutero analogues of compound (XXXIII)[59] that elimination of a hydrogen atom and also of a molecule of C_6H_6 occurs solely with the participation of hydrogen from position 9. These and several other decomposition processes for compounds of the 10-sil-2-azanthracene series are shown in Scheme 16.

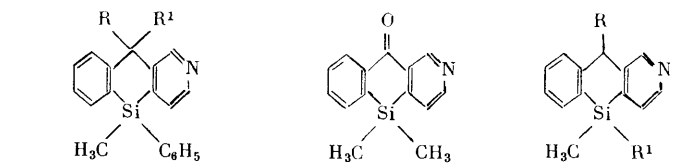
The character of the dissociation on ionisation of more complex analogues of compound (XXXIII) containing substituents or functional groups at position 9 is determined by the latter to a significant extent. Thus the presence of a carbonyl group in the molecule of 10-methyl-10-phenyl-10-sil-2-azanthrone (XXXIV) inhibits the expulsion of C_6H_6 mentioned above and the most intense peaks in the mass spectrum are the peaks for $[M-CH_3]^+$ (100%) and $[M-C_6H_5]^+$ ions. Expulsion of CO from M^+ for the compound in question is not important but a more significant reaction takes place accompanied by the elimination of H_2O,

$SiOCH_3$ and $Si(CH_3)C_6H_5$.[59] A series of specific fragmentation routes, facilitating the identification of regioisomers, was detected in the mass spectra of 4-, 5-,. 6-, 7- and 8-nitro-10,10-dimethyl-10-sil-2-azanthrones (XXXV).[61]

Scheme 16

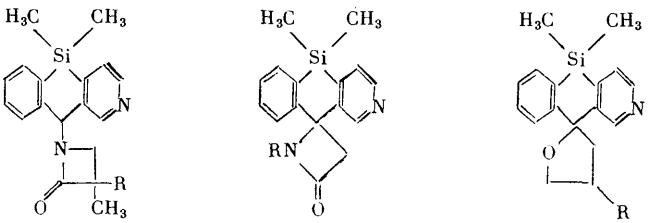


The tertiary alcohol (XXXVI) behaves specifically on EI. Its molecular ion is capable of losing two CH_3 radicals sequentially (contrary to the even-electron rule) with the formation of a silazanthracenyl ion.[59] Other decomposition routes are linked with the sequential elimination of CH_3 (maximum peak) and H_2O, CH_3 and C_6H_6. The fission of OH and H_2O from M^+ occurs weakly. The oxime obtained from ketone (XXXIV) is capable on EI of losing OCH_3, and also 1) CH_3 and H, 2) CH_3 and H_2O and 3) H, CH_3 and C_6H_5 sequentially.[59]



The main decomposition of substituted 9,10-dihydro-10-sil-2-azanthracenes (XXXVII) is caused by the loss of long alkyl substituents of the alkyl type from position 9 (loss of CH_2CH_2CN, $CH_2CH_2CH_2NH_2$ from M^+) or by the elimination of the substituent from the silicon atom (expulsion of CH_3 or C_6H_6). In the case of amines (R = NH_2) the intensity of the peak for $[M-H]^+$ ions is sharply increased and in contrast to the previous compounds significant peaks appear for $[M-SiR_2]^+$ ions. Decomposition at the expense of the amide substituent is characteristic of amides.

Compounds containing an azetidine substituent at position C(9) (XXXVIII) and also spiranes with azetidine (XXXIX) or tetrahydrofuran (XL) groups undergo fragmentation by fission of the four- and five-membered heterocycles respectively but a CH_3 radical is split away from the Si atom most frequently in the later stages of the decomposition.[63] For the derivatives (XXXVIII) for example the main process is elimination of the azetidine ring from M^+. Also typical is fission of the four-membered ring into two halves which occurs readily in $[M-CH_3]^+$ ions (formation of $[M-CH_3-CH_2CRCH_3]^+$ and $[M-CH_3-COCRCH_3]^+$ ions).

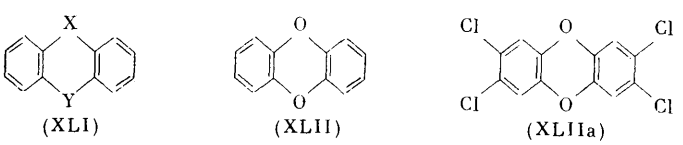


In spiro-compounds (XXXIX) fragmentation is caused mainly by the typical fission of the four-membered ring into two halves,[64] as a result of which $[M-RNCO]^+$ and $[M-CH_2CO]^+$ ions are formed and then lose a CH_3 radical. Ions with *m/z* 222 and 224, obtained by elimination of $RCHCH_2O$ and CH_2CRCH_3 from M^+, are diagnostically important in compounds of the (XL) series.

IV. Analogues of 9,10-dihydroanthracene with heteroatoms at positions 9 and 10

The character of the dissociation of the type of compound represented by general formula (XLI) on ionisation is determined by the nature of the substituents in the aromatic ring and on the heteroatoms at positions 9 and 10. In the simplest representatives of this series the primary decomposition of M^+ is expulsion of carbenoid particles X or Y, the ease of eliminating which increases with an increase in the stability of the latter. As in the previous section these typical routes for decomposition leading to a heterocyclic analogue of fluorene ion-radicals are demonstrated in the example of compounds in which it occurs most (Table 3).

Compounds of this series may contain the same or different heteroatoms at positions 9 and 10. In view of this further consideration will be given to their mass spectral characteristics.



1. Analogues of 9,10-dihydroanthracene with the same heteroatoms at positions 9 and 10

Dibenzo-*p*-dioxins. Unsubstituted dibenzo-*p*-dioxin (XLII) possesses a very stable M^+ which is not capable of losing the heteroatom with the formation of the dibenzofuran system. The M^+ expels only two molecules of CO or HCO and CO to a marked extent.[67,77] The fragmentation of 2-nitrodibenzo-*p*-dioxin is linked with elimination of CO, HCO, NO_2 and also NO_2 + CO and NO_2 + HCO.[77]

Much work has been carried out on the mass spectrometric investigation of polychlorinated dibenzo-*p*-dioxins, the detection and identification of which in the environment has become an important problem in recent years. The exception toxicity of some of the isomers reinforces the need to develop highly sensitive, selective and isomer-specific analytic methods. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (XLIIa) possesses such high toxicity that even standards of

this substance are not recommended to be held in analytical laboraties.

It has been shown using 2,7- and 1.6-dichloro-, 1,3,6-trichloro- and 1,2,3,4,6,7,8,9-octachlorodibenzo-*p*-dioxins and compound (XLIIa) as examples that their decomposition on EI is linked with the sequential elimination of CO and Cl. There are also marked peaks for $[M-2COCl]^+$ ions.[77,78] These features of the fragmentation are used for creating highly sensitive methods for the detection of compound (XLIIa) and its isomers chiefly using gas chromatography-mass spectrometry.[5,48,79–84] Mass spectrometry with chemical ionisation (gas-reactant O_2 or CH_4/NO_2) and negative ion recording possesses the greatest sensitivity and isomer specificity.[85–88] No less sensitive and specific is the method of tandem mass spectrometry (MS/MS) which was applied to M^+ and M^- ions generated from (XLIIa).[48,89] Decomposition of M^+, activated by collision with argon, leads to $[M-COCl]^+$ and $[M-2COCl]^+$ ions which characterise tetrachlorodibenzo-*p*-dioxins but do not permit their isomers to be distinguished. On activation by collision with argon, only $[M-Cl]^-$ and Cl^- ions are formed from M^-, which are not suitable for structural assignment. However with low energy collisions M^- ions form $[M-Cl+O]^-$, $[C_6H_{4-n}O_2Cl]_4^-$, $[M-HCl]^-$ and $[Cl]^-$ ions. With these, either directly or on the basis of peak intensity ratios, discrimination between 1,2,3,4-, 1,2,3,6-, 1,2,3,7- and 2,3,7,8-tetrachlorodibenzo-*p*-dioxins has been successful.[90]

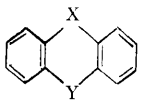
Table 3. Intensities of $[M-X]^+$ and $[M-Y]^+$ ions (as % maximal peak) in the mass spectra of compounds (XLI).

X	Y	$J_{[M-X]^+}$	$J_{[M-X]^+/J_{M^+}}$	$J_{[M-Y]^+}$	$J_{[M-Y]^+/J_{M^+}}$	Refs.
S	S	48	0.5	–	–	[65,66]
O	S	–	–	21	0.2	[67]
O	SO	–	–	100	1.2	[67]
O	Se	–	–	100	1.1	[67]
O	Te	–	–	100	1.3	[67]
O	AsCl	–	–	100	4.0	[68]
O	$SiCl_2$	–	–	100	1.1	[54,69]
O	$SnCl_2$	–	–	100	2.5	[70]
O	$SiHCH_3$	–	–	17	0.2	[54]
NH	S	–	–	53	0.5	[71]
NH	SO_2	–	–	12	0.1	[30]
NCH_3	SO	–	–	100	3.1	[72]
NH	AsCl	–	–	36	0.5	[73–75]
NH	$AsCH_3$	–	–	25	1.6	[73]
NC_2H_5	$SiHCH_3$	–	–	16	0.2	[54]
Se	Se	100	1.0	–	–	[76]*
NH	Te	–	–	100	1.1	[76]*
SiF_2	SiF_2	100	1.3	–	–	[54]
$SiCl_2$	$SiCl_2$	100	1.2	–	–	[54]

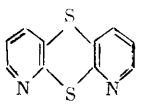
*Spectra were recorded on a laser microprobe mass spectrometer.

Some polybromo[91] and polybromochlorodibenzo-*p*-dioxins[92] have also been investigated by EI. It was shown that the M^+ of polybromo compounds lose Br, COBr, (Br + COBr) and (2Br + COBr). The formation of a large quantity of doubly charged ions was recorded.

Thianthrenes. The molecular ion of unsubstituted thianthrene (XLIII) is very stable and is capable of losing only S, CSH or S and CSH sequentially.[65,76] A similar type of fragmentation is also characteristic for diazathianthrene (XLIV).[66]



(XLIII) X = Y = S;
(XLV) X = S, Y = SO;
(XLVI) X = Y = SO;
(XLVII) X = S, Y = SO_2.

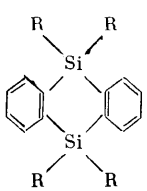


(XLIV)

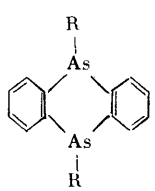
The sequential expulsion of S and H from M^+ was also observed for 2,3,7,8-, 1,4,6,9- and 1,3,7,9-tetramethylthianthrenes but elimination of CS and CSH was insignificant. The molecular ions of these compounds also lose CH_3 and then S.

The dissociation of the monosulphoxide (XLV)' and the disulphoxide (XLVI) of thianthrene on ionisation is fairly simple and is linked with the elimination of O and SO. In both cases the ion-radical of dibenzothiophene is formed in such processes and is generated from the M^+ of sulphone (XLVII) on expulsion of SO_2. SO is eliminated from the M^+ of (XLVII) as a result of skeletal rearrangment.[93]

Other compounds. The character of the fragmentation of 9,10-disila-9,10-dihydroanthracenes (XLVIII) depends on the nature of the substituents on the Si atoms.[54] The stable M^+ of the ancestor compound (R = H) may lose up to four H atoms, while seemingly $:SiH_2$ is lost from $[M-H]^+$ ions. The tetramethyl derivative (XLVIII, R = CH_3) has a weakly stable M^+ which readily loses CH_3 and then $:Si(CH_3)_2$. Decomposition of the tetramethoxy derivative (XLVIII, R = OCH_3) on EI is more complex. In this case the peaks for $[M-HSi(OCH_3)_2]^+$ and $[M-HSi(OCH_3)_2-CH_2O]^+$ ions are the most intense. In the case of the tetrahalogen compounds (XLVIII, R = F, Cl) the process of expelling dihalodisilyene from M^+ is clearly expressed and continues in the case of fluoride by elimination of H_2SiF_2 and of chloride by loss of a Cl atom.



(XLVIII)



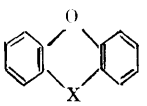
(XLIX) R = CH_3;
(L) R = Cl.

A specific character was observed for the fragmentation of derivatives of dihydroarsanthracenes (XLIX) and (L).[94] The molecular ion of the methyl derivative (XLIX) readily loses CH_3 and then As, CH_3 and As sequentially. In the case of the dichloro compound (L) the ions $[M-Cl]^+ \rightarrow [M-2Cl]^+ \rightarrow [M-2Cl-As]^+ \rightarrow [M-2Cl-2As]^+$ were formed sequentially from M^+ (the peak for the $[M-2Cl-As]^+$ ion possesses maximal intensity).

2. Analogues of 9,10-dihydroanthracene with different heteroatoms in positions 9 and 10

Phenoxathiins. The molecular ion of phenoxathiin (LI) is very stable and is capable of expelling CO, CHO and S and CHO sequentially.[67] 2,3,7,8-Tetramethylphenoxathiin is also stable on EI and the most marked decomposition of its M^+ is linked with the

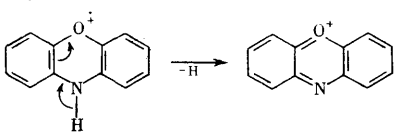
elimination of CH_3 and S or CH_3.[65] The main decomposition of its S-oxide (LII) is linked with ejection of SO, the M^+ loses an O atom to an insignificant extent. Sulphone (LIII) loses SOC in preference to SO_2 in the first stage of the decomposition.[93]



(LI) X = S;
(LII) X = SO;
(LIII) X = SO_2.

Phenoxazines. Phenoxazine (LIV) possesses a very stable M^+ the noticeable decomposition of which begins with fission of H (Scheme 17), after which CO is lost.[95,96] Nitro substituted phenoxazines lose a NO_2 group, 4,6-dinitro derivatives and a molecule of HNO_2 from the M^+.

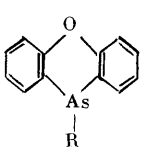
Scheme 17



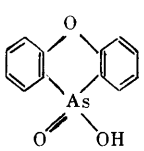
(LIV), M^+ $[M-H]^+$

In the latter case $[M-OH]^+$ ions are also formed with the participation of a hydrogen atom from the NH group.[95]

Phenoxarsines. Peaks for M^+ were recorded in the mass spectra of a large series of phenoxarsines (LV) and (LVI) which decomposed with the formation of $[M-R]^+$ and $[M-AsR]^+$ independent of the nature of the substituent R in the case of the compounds (LV) (the latter ions corresponding to dibenzofuran may be formed both in one step or several)[68,97]



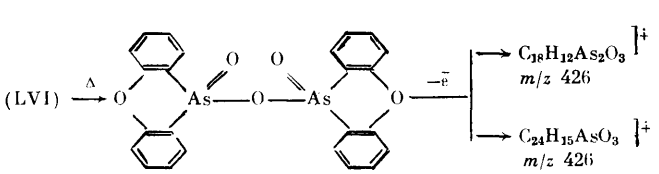
(LV) R = Cl, *p*-ClC_6H_4, 2-$C_6H_5OC_6H_4$, *p*-ClC_6H_4O.



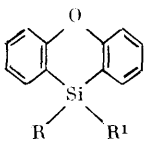
(LVI)

An interesting temperature dependence was observed for the mass spectrum of compound (LVI). At an ion source temperature below 350 °C it decomposed in a similar manner to compound (LV) with the formation of M^+ and $[M-HAsO_2]^+$ (*m/z* 243) ions. However at 390 °C condensation of two molecules occurred with elimination of water and a peak of M^+ with *m/z* 534 was present in the recorded mass spectrum and also a peak with *m/z* 426 corresponding to $[M-C_6H_4O_2]^+$ and $[M-AsO_2H]^+$ ions which decomposed further to ions with *m/z* 243 (Scheme 18).

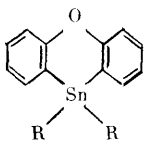
Scheme 18



Phenoxasilines and phenoxastannines. Decomposition on EI of 10,10-dimethyl- (LVII) and 10,10-diphenylphenoxasilines (LVIII) occurs mainly by expulsion of CH_3 and C_6H_5.[49,98] Fission of H and CH_3 from M^+ also leads to the most intense peak in the spectrum of their 10-methyl analogue (LIX).[54] However in the latter case $HSiH_3$ is lost from M^+ to a noticeable extent and such a process is not a characteristic of the first two compounds (here the formation of $[SiRR^1]^+$ ions is marked). A large number of rearrangement processes occurs on fragmentation of compounds (LVII) and (LVIII), in particular expulsion of SiO from $(M-R-R^1]^+$ ions or CH_2O, SiH_2O and SiHO from $[M-R]^+$ ions. The main and only fragmentation process for dichloro compound (LX) is ejection of $:SiCl_2$ from M^+.[54]



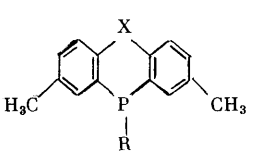
(LVII) R = R^1 = CH_3;
(LVIII) R = R^1 = C_6H_5;
(LIX) R = H, R^1 = CH_3;
(LX) R = R^1 = Cl.



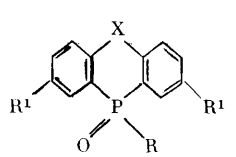
(LXI)

The nature of the substituent on the tin atom appreciably influences the fragmentation of the phenoxastannines (LXI) although the formation of $[M-R]^+$ ions is natural for all of them.[49,99,100] After elimination of radical R in the case of compounds (LXI, R = C_2H_5 and C_4H_9), olefin (R−H) is readily lost and the resulting ion then eliminates C_6H_4 two times. The methyl and phenyl derivatives (LXI, R = CH_3 and C_6H_5), after expulsion of R, lose fragments C_6H_4O, $C_{12}H_8O$ or C_6H_4. Fission of $SnCl_2$ is the main fragmentation route for the M^+ of dichloro compound (LXI, R = Cl).

Phenoxaphosphines and phenothiaphosphines. Phenoxaphosphines (LXII) and phenothiaphosphines (LXIII) are similar in their character of dissociation on ionisation.[101−104] Loss of RHP is a characteristic of their M^+.



(LXII) X = O, R = C_6H_5;
(LXIII) X = S, R = C_6H_5,
p-$CH_3C_6H_4$

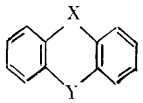


(LXIV) X = S, R = OH, OCH_3, R^1 = CH_3;
(LXV) X = SO_2, R = CH_3, C_6H_5,
p-$CH_3C_6H_4$, R^1 = F, Cl, CH_3.

The oxides of derivatives (LXIV) form very stable M^+ which may lose PO_2H and SH (when R = OH). The loss of SH is insignificant for the corresponding esters (R = OCH_3) but OCH_3 is readily eliminated and then S or PO. The peaks for M^+ and $[M-CH_3]^+$ ions possess the greatest intensity in the mass spectra of compounds (LXV). In all cases noticeable peaks were encountered for $[M-HPOR]^+$ ions.[102,103]

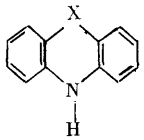
Phenoselenine (LXVI) and phenotellurine (LXVII) are fairly stable on EI and the sole primary route for their decomposition is expulsion of Se and Te respectively.[67] The resulting dibenzofuran

ions lose CO and CHO. A similar decomposition is characteristic of their sulphur analogues (LXVIII).[105]



(LXVI) X = O, Y = Se;
(LXVII) X = O, Y = Te;
(LXVIII) X = S, Y = Se, Te

Phenothiazines. This series of compounds is of interest since it includes a large number of pharmacologically active compounds, particularly tranquilisers. Unsubstituted phenothiazine (LXIX) possesses a very stable M^+, the most noticeable decomposition of which is caused by elimination of H, S or SH.[30,71] Its *S*-oxide (LXX) and *S,S*-dioxide (LXXI) differ fairly strongly in fragmentation character.[30] The former is intensively decomposed with the formation of $[M-O]^+$, $[M-OH]^+$, $[M-CO]^+$, $[M-CO-H]^+$ (base peak) and $[M-SO]^+$ ions and the second has a very stable M^+ which loses OH, CO, SO and H, SO and CO or SO_2.



(LXIX) X = S;
(LXX) X = SO;
(LXXI) X = SO_2

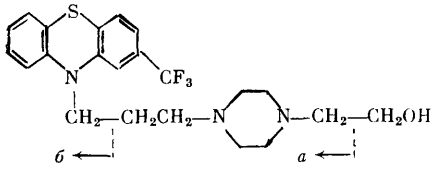


(LXXII) R = H;
(LXXIII) R = Cl.

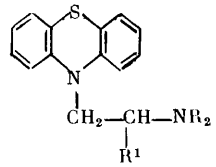
The main peaks in the mass spectra of the large series of physiologically active compounds of the phenothiazine series, among which are promazine (LXXII) and chlorpromazine (LXXIII),[71,72,106] are caused by ions formed on breaking the α-C−C bond relative to the nitrogen of the side chain, e.g. $CH_2=\overset{+}{N}(CH_3)_2$ (*m/z* 58) for (LXXII) and (LXXIII). The groups $HN(CH_3)_2$ or $H_2N(CH_3)_2$ may be lost from M^+ and also the substituent from the exocyclic nitrogen atom with migration of H atom to the heterocyclic ion. In the case of methoxyphenothiazines decomposition begins with expulsion of a CH_3 group and continues with loss of CO and S. Fragmentation of phenothiazine *S*-oxides with *N*-alkyl groups is complicated due to decomposition involving the sulphoxide group.[106,107]

The fragmentation regularities recorded for phenthiazine are used for the determination of chlorpromazine (LXXIII) metabolites in man.[108]

The GC−MS method (EI) in combination with silylation is used for the quantitative determination of the tranquiliser fluorphenazine (LXXIV) in plasma at the 50 pq ml^{-1} level.[109] It is proposed to carry out the determination with ions *a* and *b*.



(LXXIV)



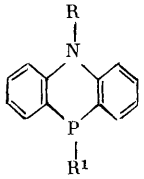
(LXXV) R = R^1 = CH_3;
(LXXVI) R = C_2H_5, R^1 = CH_3;
(LXXVII) R = C_2H_5, R^1 = H.

The metabolites of promazine (LXXII), which are volatile with difficulty, have been investigated with combinations of microliquid chromatography and mass spectrometry to provide mass spectra by chemical ionisation. Previously, using (LXXIII), 2-hydroxy- and acetopromazine as examples, it was shown that such mass spectra contain practically only peaks for $[M+H]^+$ ions.[110]

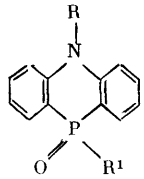
Mass spectra were obtained for a large series of phenothiazines under conditions of chemical ionisation (gas reagent was NH_3, CH_4/N_2O) recording negative ions.[111] For the majority of these compounds among which are (LXXII), (LXXIII), promethazine (LXXV), propiomazine, prochlorperazine, ethopropazine (LXXVI) and diethazine (LXXVII), the presence of peaks for $[M-H]^-$ ions in such spectra is characteristic.

The peaks for $[M-CH_2CH_2CH_2N(CH_3)_2]^-$ ions were the base peaks in the spectra of compounds of the type of (LXXII) and (LXXIII) with three C atoms between the nitrogen atoms. In the case of compounds of type (LXXV)−(LXXVII), containing two C atoms between the nitrogen atoms, the base peaks in the spectra corresponded most frequently to $[M-H_2NR_2]^-$ ions although peaks for $[M-CH_2CHR^1NR_2]^-$ ions were also present.

9,10-Dihydrophenophosphazines. The EI mass spectra of 9,10-dihydrophenophosphazines (LXXVIII) have stable M^+ which decompose by loss of R^1 and then R, since $[M-R^1]^+$ ions are the base peaks even at low electron energies. In the case of the 10-oxide derivative (LXXIX) the stability of M^+ is increased but the most noticeable dissociation processes are caused by the elimination of R^1 and PO.[74,112]



(LXXVIII)

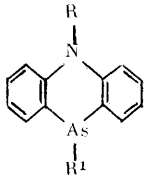


(LXXIX)

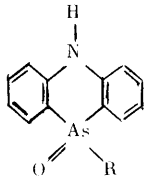
The adiabatic ionisation potentials of compounds (LXXVIII, R = CH_3, R^1 = CH_3, or C_6H_5) and (LXXIX, R = CH_3, R^1 = CH_3, or C_6H_5) were measured by photoionisation mass spectrometry. They were 7.03, 6.90, 7.50 and 7.40 eV respectively. Comparison of these values shows that the influence of the substituent is transmitted in the same way through both a trivalent and a pentavalent phosphorus atom.[113]

9,10-Dihydrophenarsazines. The EI mass spectra of substituted 9,10-dihydrophenarsazines (LXXX) contain M^+ peaks which readily lose the R^1 radical with the formation of the base ion and the latter ejects an As atom.[73−75,114] In some cases the one-step nature of the $M^+ \rightarrow [M-AsR^1]^+$ transition was demonstrated with metastable ions. In the case of (LXXX, R = H, R^1 = SCN) the formation was recorded of $[M-HSCN]^+$ ions which later eliminate As.[114]

The mass spectra of compounds (LXXXI, R = CH_3, C_6H_5, 2-ClC_6H_4) [74] and (LXXXI, R = OH) [114] contain M^+ peaks but the base peaks were of $[M-R]^+$ ions in the first case and $M-H_2O]^+$ ions in the second.



(LXXX) R = H, CH_3, C_6H_5; R^1 = Cl, OCH_3, CH_3, C_6H_5, 2-ClC_6H_4



(LXXXI)

* * *

The main influence of the fragmentation on the EI of derivatives and heterocyclic analogues of 9,10-dihydroanthracene therefore proved to be the nature of the heteroatom, the character of the substitution at positions 9 and 10 and also the type of substituent in the phenylene rings. In the case of such derivatives of dihydroanthracene as anthraquinones and also its analogues containing heteroatoms of the type S, SO, SO_2, Se, Te and also substituted Si, P, and As atoms in positions 9 or 10, the principal be the elimination of particles of the carbene type from these positions with contraction of the central ring to a five-membered ring. The ease of this process increased with the increase in stability of the eliminated carbenoid particle. For example the elimination of dihalosilyene, and of AsCl, Te, Se and P(O)OH determines the main character of the decomposition of the corresponding analogues of 9,10-dihydroanthracene.

A specific route for the fragmentation of 9-alkyl- or aryl-substituted 9,10-dihydro-9-silanthracenes is the expulsion from M^+ of the corresponding alkane or arene. It is possible that silanthracene ions are formed containing a Si=C double bond having no analogue in the unionised state.

Fragmentation of substituents in the series being considered depends on their location in the molecule. If the substituting group is side-by-side with the heteroatom the '*peri*-effect' is decisive. Fission of substituents in the phenylene rings and also in the *meso* position or at the heteroatom occurs in a similar manner to the decomposition of the corresponding aromatic or heterocyclic derivatives.

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Translated from *Uspekhi Khimii* **60** 1005–1048 (1991) U.D.C. 547.412.722.5 + 547.538.2'539.1

Perfluoroalkyl(aryl)acetylenes

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ABSTRACT. Methods of preparing perfluoroalkyl(aryl)acetylenes, their physical properties, and chemical reactivity have been reviewed. Synthetic routes to aliphatic, alicyclic, aromatic and heterocyclic compounds from perfluoroalkyl(aryl)acetylenes have also been examined.

The bibliography contains 361 references.

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I. Introduction

The study of fluorine-containing compounds is a key aspect of modern laboratory and industrial chemistry. Such compounds are placed in prominent position in the economies of the developing nations, and their varied structural types and unique properties are evident in the synthesis of such materials as fluorinated polymers, Freons, herbicides, drugs and dyes. The physiological activity of fluorine-containing compounds is so broad that they are used both medicinally and as highly toxic agents.

An enormous amount of data is available on fluorine-containing compounds, which has been reviewed in many well-known monograph series as well as in the journal literature.[1–4]

The chemistry of perfluoroalkyl(aryl)acetylenes has developed only in the last 40 years. Only the literature up to 1977 has been adequately reviewed,[5–7] while coverage of more recent information has been rather fragmentary.[8–10] This new field of organic chemistry has not been reviewed as an isolated topic.

In the present article we have sought to cover this field of chemistry with particular reference to the last ten years, which, as yet, has not been adequately studied as a review topic in the literature. We have excluded those properties of perfluoroalkyl-(aryl)-substituted acetylenes, such as oxidation and hydrogenation, which have already been analysed in depth in earlier reviews, and concentrated only on recent developments in this area; this review also excludes routine functional group interconversions involving this structural type. Information on the physical properties of the individual perfluoroalkyl(aryl)acetylenes, of which more than 300 are known to date, can be obtained from those references where synthetic details are reported.

II. Methods of preparation

Most synthetic routes to perfluoroalkyl(aryl)acetylenes are based on perfluoroalkyl(aryl) iodides which in many countries are commercially available and frequently used. Direct fluorination methods have been used to a lesser extent.

There are two classical multi-step routes to perfluoroalkyl-acetylenes. The first step in these methods is the addition of perfluoroalkyl iodides to olefins or acetylenes. The final step in the first method is dehalogenation of an intermediate perfluoro-dibromoalkene, which is normally carried out with zinc in ethanol or dimethyl sulfoxide.[11–13]

$$R_FCH_2CH_2Hal \xrightarrow{KOH,\ C_2H_5OH} R_FCH{=}CH_2 \xrightarrow{Br_2,\ h\nu}$$

$$\longrightarrow R_FCHBrCH_2Br \xrightarrow{KOH,\ C_2H_5OH} R_FCBr{=}CH_2 \xrightarrow{Br_2,\ h\nu}$$

$$\longrightarrow R_FCBr_2CH_2Br \xrightarrow{KOH,\ C_2H_5OH} R_FCBr{=}CHBr \xrightarrow{Zn} R_FC{\equiv}CH,$$

$R_F = CF_3,\ C_4F_9,\ C_6F_{13},\ C_8F_{17}.$

In certain countries perfluoroalkylethylenes are currently commercially available. They may be converted to perfluoroalkyl-acetylenes by an alternative scheme.[14,15]

$$R_FCH{=}CH_2 \xrightarrow{Cl_2,\ h\nu} R_FCCl_2CCl_3 \longrightarrow \Big]\xrightarrow{Zn}$$

$$CCl_3CCl{=}CCl_2 \xrightarrow{SbF_3/SbF_5} CF_3CCl{=}CCl_2 \longrightarrow \Big]$$

$$\longrightarrow [R_FC{\equiv}CZnCl + (R_FC{\equiv}C)_2Zn] \xrightarrow{H_2O,\ H^+} R_FC{\equiv}CH,$$

$R_F = CF_3,\ C_4F_9,\ C_6F_{13},\ C_8F_{17}.$

The debromination with zinc may be accompanied by partial prototropic isomerisation.[16]

Debromination of 1,3,3,3-tetrafluoro-1,2-dibromopropene with zinc in dioxane or with copper at 260 °C affords perfluoro-propyne.[17–19]

Dehalogenation is also the final step in the synthesis of perfluoro-2-butyne and other symmetrically substituted perfluoroacetylenes.[20–24]

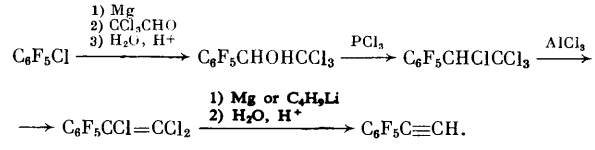
Trifluoromethylperfluoroalkoxyacetylenes have been prepared via elimination of BrCl with Zn/Cu couple in adiponitrile.[25]

$$F_3CC{\equiv}CCl \xrightarrow[H^+]{RCOF,\ AgF} \begin{matrix} F_3C & & OCF_2R \\ & C{=}C & \\ H & & Cl \end{matrix} \xrightarrow{Br_2}$$

$$\longrightarrow F_3CCHBrCClBrOCF_2R \xrightarrow{(C_2H_5)_3N} F_3CCBr{=}CClOCF_2R \xrightarrow{Zn/Cu}$$

$$\longrightarrow F_3CC{\equiv}COCF_2R,\ R = F,\ C_2F_5.$$

Dehalogenation is also a key step in the synthesis of pentafluorophenylacetylene.[26,27]

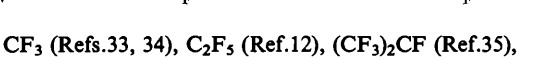


Chloropentafluorophenylacetylene is obtained if one equivalent of butyllithium is used in the last step instead of two equivalents.[27] A mixture of pentafluoro- and 2,3,5,6-tetrafluoro-phenylacetylene was obtained from the product formed by treatment of acetophenone with PCl_5.[28]

Reaction of pentafluorophenyllithium with alkenyl halides affords chloropentafluorophenylacetylenes (from CFCl=CFCl or CF_2=CHCl) and decafluorotolan (from CF_2=CFH or CF_2=CFBr). In this case, dehalogenation is accompanied by nucleophilic substitution of fluorine in the *p*-position, as a result of which tolan derivatives are formed with either one or two 2,3,5,6-tetrafluorophenyl rings.[29]

Treatment of pentafluorophenylcopper with iodotrifluoroethylene to give decafluorotolan is also accompanied by dehalogenation,[30] as well as by action of copper on pentafluorophenyltribromomethane at 570 °C (70% yield).[31]

Methods of preparing fluorine-containing alkynes by dehydrohalogenation of (a) (perfluoroalkyl)alkenyl halides, obtained normally by radical addition of perfluoroalkyl iodides to alkynes, or (b) dihalogenated perfluoroalkanes, obtained from the corresponding alkenes, are limited by the nature of the perfluoroalkyl (or perfluoroaryl) substituent.[32] Thus, in spite of the fact that the number of steps is normally smaller, such dehydrohalogenative methods are not always preferred to the dehalogenative routes described above. Anhydrous base or ethanolic base (with cooling) or trialkylamines have been used as dehalogenating agent.[13,33–35]



R_F=CF_3 (Refs.33, 34), C_2F_5 (Ref.12), $(CF_3)_2CF$ (Ref.35),

C_nF_{2n+1} (n=4, 6, 8) (Ref.13).

There was no increase in the yield of perfluoroalkylacetylenes with KF/18-crown-6-ether as dehydroiodinating agent.[36]

Dehydroiodination of 4,4,4-trifluoro-2-iodo-1-butene with alcoholic KOH gives a 1:2 mixture of the corresponding acetylene and allene.[37] Hexafluoro-2-butyne,[38,39] perfluoro-2,5-dimethyl-3-hexyne,[40] perfluoroalkylated acetylene-alcohols[41–43] and -thioethers,[44] and α-halogenoperfluoroalkylacetylenes[18,45] have all been prepared by dehydrohalogenation with alcoholic KOH or anhydrous base.

Perfluoroacetylenic tertiary alcohols, $R_2C(OH)C{\equiv}CR_F$ (R_F = C_4F_9, C_6F_{13}, C_8F_{17}), have been prepared by dehydroiodination of the corresponding iodides and converted to the corresponding perfluoroalkylacetylenes by Favorskii cleavage.[42,46,47]

Aryltrifluoromethylacetylenes[48] have been isolated in 65–78% yield by 2-step dehydrobromination of 3,3,3-trifluoro-1,2-dibromo-1-arylpropanes, and *bis*(trifluoromethyl)trifluoropropynylamine has been prepared by 2-step dehydrobromination of *N,N-bis*(trifluoromethyl)-3,3,3-trifluoro-1,2-dibromopropylamine.[49]

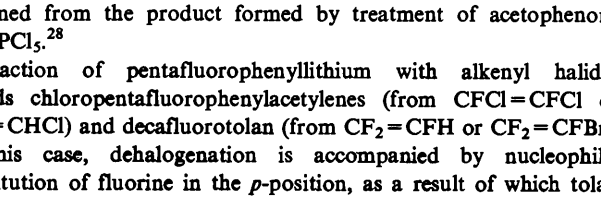
Aryltrifluoromethylacetylenes with a variety of substituents in the benzene ring have been synthesised under mild conditions. The dehydrochlorination in the second step has been carried out with $NaNH_2$ in *tert*-butanol/benzene at room temperature.[50,51]



R=X-C_6H_4, X=4-Cl, 2-Cl, 4-OCH_3, 4-NH_2, 4-C_6H_5; 3-pyridyl, 1-naphthyl and others.

In certain cases, dehydrohalogenation is accompanied by decarboxylation. Treatment of perfluoroalkylacetyl chlorides with strong base leads to perfluoroalkylacetylenes.[52]

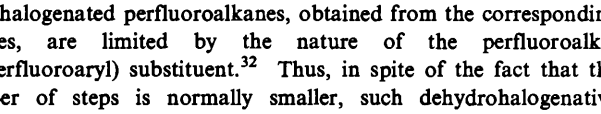
In an alternative synthesis, treatment of perfluorocarboxylic acid chlorides with triethyl phosphite leads to perfluoroalkylacetylenes with the same number of carbon atoms (60–66% yield).[53]



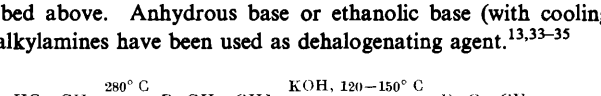
R_F = C_2F_5, C_6F_{13}, C_8F_{17}, $HCF_2(CF_2)_8$.

Aldol-type adducts are formed if the dephosphonylation is carried out in the presence of aldehydes[53] or their trimethylsilyl enol ethers.[54]

A new route to perfluoroalkylacetylenes is based on radical addition of perfluoroalkyl iodides to trimethylethynylsilanes in the presence of *tert*-butyl peroxide at 120 °C, followed by dehydroiodination and desilylation with potassium *tert*-butoxide at –20 °C. The yield exceeds 90%.[55]



Non-conjugated perfluorodiacetylenes are obtained by this method if the starting material is a diiodoperfluoroalkane:[55]

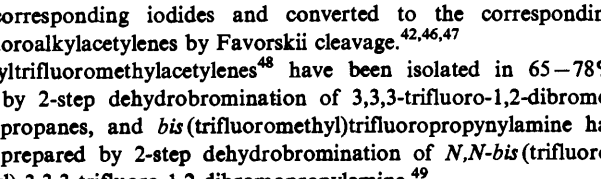


n = 2, 4, 6, 8, 10, 12.

The same products are obtainable from *bis*(trimethylsilyl)acetylene.

Organometallic compounds have also been widely used in the synthesis of perfluoroalkyl(aryl)acetylenes. There are two possible routes: one based on perfluoroalkyl(aryl) halides with intermediate formation of organometallic compounds, and the other based on alkylation of non-fluorinated acetylides with perfluoroalkyl(aryl) halides. Substituted and functionalised perfluoroalkyl(aryl)acetylenes are often obtained from perfluoroalkyl(aryl)acetylides. Such routes differ in the choice of the starting metal and the conditions. Organo-magnesium or -lithium compounds are normally used, although in certain cases the best results are obtained with organocopper, -zinc or -tin compounds.

Thus, perfluoroalkylacetylenes are prepared in up to 70% yield by the following scheme:[56,57]



R_F=C_4F_9, C_6F_{13}; R=C_2H_5, C_4H_9, C_8H_{17}, C_6H_5, *o*-$CH_3C_6H_4$, $CH_2CH{=}CH_2$.

The somewhat unexpected initial stages of this reaction, as proposed by the authors, was confirmed by the ultimate formation of $R_FCF=CHF$ on hydrolytic work-up.

Perfluorotolan was obtained in 56% yield by reaction of pentafluorophenylmagnesium bromide with diiodoacetylene in the presence of $CoCl_2$.[58]

Treatment of α-halogenoacetylenes with perfluoroalkyl(aryl)-copper reagents affords the corresponding perfluoroalkyl(aryl)-acetylenes.[59–61]

The interaction of hexafluorobenzene with lithium or magnesium acetylides proceeds with replacement of one or two fluorine atoms to give a mixture of perfluorophenylacetylenes.[61–63] Such reactions are facilitated by the addition of cerium and ytterbium salts.[63] *p-Bis*-(ethynyl)tetrafluorobenzene, for example, is obtained as follows:[61]

$$(C_2H_5)_3SiC\equiv CH \xrightarrow{C_6F_6} p\text{-}(C_2H_5)_3SiC\equiv CC_6F_4C\equiv CSi(C_2H_5)_3 \xrightarrow[H_2O/CH_3OH]{NaOH}$$

$$\rightarrow p\text{-}HC\equiv CC_6F_4C\equiv CH.$$

The same product is formed by treatment of trimethylsilylacetylene with bromo(iodo)pentafluorobenzene in the presence of Pd(0) and Cu(I).[64]

$PdCl_2-CuI$ may be used effectively in the reaction of iodoperfluorobenzene with terminal acetylenes.[65,66]

$$p\text{-}RC_6F_4X + HC\equiv CR' \xrightarrow{PdCl_2[(C_6H_5)_3P]_2,\ CuI} p\text{-}RC_6F_4C\equiv CR'$$

X = I, Br; R = F, OCH_3, $N(CH_3)_2$ etc.;
R' = C_6H_4X', X' = H, *p*-CO_2CH_3, *p*-NO_2;
$Si(C_2H_5)_3$; $(CH_2)_nCH_3$, $n=2-5$, etc.

Treatment of pentafluorochlorobenzene with lithium alkyl- or phenylacetylides affords the corresponding *p*-chlorotetrafluorophenylacetylenes.[67] Thus, reaction takes place by preferential replacement of fluorine not chlorine.

Coupling of lithium and magnesium acetylides may proceed with perfluoroalkyl(phenyl)iodonium triflates in place of perfluoroalkyl halides.[68] The highest yield was recorded for n = 8.

$$RC\equiv CM \xrightarrow[-78 \text{ to } -30\ ^\circ C,\ THF]{R_FI(C_6H_5)OSO_2CF_3} RC\equiv CR_F,\ M = Li,\ MgX;\ R_F = C_nF_{2n+1},$$

n = 2, 3, 6, 8; R = C_6H_5, C_6H_{13-n}.

The interaction of pentafluoroiodobenzene and 4-substituted tetrafluoroiodobenzenes with cuprous 3-(tetrahydropyran-2-yloxy)-prop-1-ynide in pyridine affords the corresponding fluorophenyl-substituted propargyl alcohols which are converted to the corresponding terminal acetylene derivatives on oxidation with NiO_2.[69]

$$p\text{-}RC_6F_4I + CuC\equiv CCH_2-O-\text{(THP)} \longrightarrow$$

$$\rightarrow p\text{-}RC_6F_4C\equiv CCH_2OH \rightarrow p\text{-}RC_6F_4C\equiv CH,$$

R = F, H, CH_3, CF_3, OCH_3, NH_2, $N(CH_3)_2$.

Reaction of perfluoroalkyl iodides with trimethylstannylacetylenes proceeds on UV irradiation in the presence of azodiisobutyronitrile or transition metal complexes to give perfluoroalkylacetylenes.[70–73]

$$R_FI + (CH_3)_3SnC\equiv CR \rightarrow R_FC\equiv CR,$$

R_F = CF_3, C_3F_7, $CF(CF_3)_2$, C_4F_9, C_6F_{13};
R = $C(CH_3)_3$, C_6H_{13}, C_6H_5, $Sn(CH_3)_3$, $C\equiv CSn(CH_3)_3$.

Iotsich reagents prepared from perfluoroalkyl(aryl)acetylenes have been used in the synthesis of allyltrifluoromethylacetylenes,[74] propargyltrifluoromethylacetylenes,[75,76] pentafluorophenyl-*tert*-butylacetylene,[77] acetylenic alcohols[78,79] and α-halogenoacetylenes,[80] as well as a number of elementoorganic compounds.[77,81–85] for example:

$$R_FC\equiv CMgX + R_nEX \rightarrow R_FC\equiv CER_n,$$

R_F = CF_3, C_6F_5; E = Si, Ge, Sn, As; R = CH_3, C_2H_5, C_3H_7, C_4H_9.

Lithium perfluoroalkylacetylides are more effective than the corresponding magnesium acetylides in certain cases.[86–89] Thus, lithium perfluoroalkylacetylides have been used for the preparation of a number of primary, secondary and tertiary acetylenic[27,42,86,87] and non-conjugated diacetylenic alcohols,[87] as well as certain perfluoroalkyl(aryl)acetylenic acids or esters[27,88,89,90] and the corresponding phosphine and arsine derivatives.[91]

Zinc perfluoroalkylacetylides[15,92] may also be used for the synthesis of perfluoroalkyl compounds, notably aryltrifluoromethylacetylenes,[92] α-halogenotrifluoromethylacetylenes,[25,93] vinylperfluoroalkylacetylenes,[94] and *bis*(trifluoromethyl)diacetylenes.[93]

Perfluoroalkyl(aryl)alkynylstannanes have been used to prepare perfluoroalkyl(aryl)alkynyl-silanes and -germanes in >90% yield.[95–97]

$$R_FC\equiv CSnR_3 + R'_3EX \xrightarrow[HMPT]{80\ ^\circ C} R_FC\equiv CER'_3 - R_3SnX,$$

E = Si, Ge; X = Cl, Br.

Reaction does not take place in the absence of solvent.[98] Specific solvating effects are responsible for polarisation of the E–X and Sn–C bonds in the starting materials.[96,99,100]

A similar reaction has been used for the replacement of one acetylenic stannyl group by another (trans-stannylation),[101,103] and for the synthesis of α-halogenoacetylenes.[104]

Trifluoromethylacetylene was prepared as long ago as 1959 by treatment of propiolic acid with SF_4 (60% yield).[105] Hexafluoro-2-butyne was obtained similarly by treatment of acetylenedicarboxylic acid with SF_4.[106] However extension of this method to other perfluoroalkylacetylenes is limited since the corresponding acetylenic acids are not readily available.

The intramolecular Wittig reaction, which is a well-known route to a variety of acetylenes,[107,108] has been applied to the synthesis of perfluoroalkyl(aryl)acetylenes as well as a number of functionalised derivatives: aryltrifluoromethylacetylenes,[109,110] perfluoroalkylpentafluorophenylacetylenes,[111] *bis*(pentafluorophenyl)acetylene,[112] aryloxyperfluoroalkylacetylenes,[113] arylthiotrifluoromethylacetylenes,[114] α-thienylperfluoroalkylacetylene,[115] perfluoroalkylacetylenic aldehydes and ketones,[116,117] esters,[118] thioesters,[119] and nitriles,[120] perfluoroalkylacetylenic acids and perfluoroalkylacetylenic phosphonates.[121] This is illustrated by the synthesis of thioester derivatives:[119]

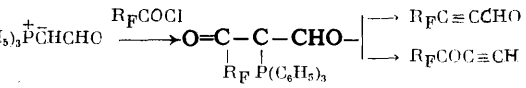
$$(C_6H_5)_3P + BrCH_2CSCH_3 \longrightarrow [(C_6H_5)_3\overset{+}{P}CH_2CSCH_3]\,Br^- \xrightarrow{NaOH}$$

$$\rightarrow (C_6H_5)_3\overset{+}{P}\overset{-}{C}HCSCH_3 \xrightarrow{R_FCOCl} (C_6H_5)_3\overset{+}{P}-C(-O-C(=O)-R_F)=C(-SCH_3)-C\equiv CR_F \xrightarrow[-(C_6H_5)_3PO]{180-220\ ^\circ C}$$

$$\rightarrow R_FC\equiv CC(=O)SCH_3$$

R_F = C_2F_5, C_3F_7, C_7F_{15} etc.

On hydrolysis of C-perfluoroacylformylmethylenetriphenylphosphoranes, the corresponding aldehydes and ketones are obtained in approximately equal amounts. In this case, the reaction proceeds in two directions as a result of charge delocalisation.[116]



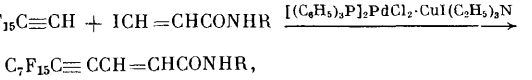
$R_F = CF_3$, C_2F_5, n-C_3H_7.

Perfluoroalkyl(aryl)acetylenes are also formed on hydrolysis of perfluoroalkyl(aryl)-substituted triazines[122] and pyridazines.[123,124] The latter are obtained by a multistep route from readily available tetrafluoropyridazine.[125] Yields are not high by this route, but it is interesting in that a variety of perfluoroalkyl groups can be introduced from accessible starting materials.

There is also reference in the literature to the formation of perfluoroalkylacetylenes by pyrolytic processes. For example, hexafluoro-2-butyne is obtained in high yield by pyrolysis of perfluorocyclobutene in a flow system over CsF or KF at 510–590 °C.[126] Perfluoroalkynes are formed by pyrolysis of various sodium perfluoroalkenoates,[127,128] as well as by pyrolysis or photolysis of certain sulphur-containing three- and five-membered heterocyclics.[129]

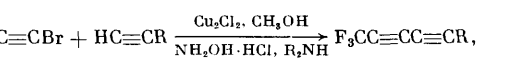
Trifluoromethylarylacetylenes may also be prepared by replacement of halogen by fluorine in trihalogenomethylacetylenes.[130]

Catalysts play an important role in the conversion of terminal acetylene derivatives to acetylenes containing two conjugated or non-conjugated multiple bonds. Conjugated enynes were thus obtained in the presence of a palladium catalyst:[47]



$R = CH_2CH(CH_3)_2$.

In recent years the Cadiot-Chodkiewicz reaction has been generally applied to the synthesis of conjugated trifluoromethyldiynes, as illustrated in the following variant:[131,133]



$$R = CH(CH_3)_2,\ C(CH_3)_3,\ C(OH)(CH_3)_2.$$

The yield (around 35%) is lower than in the preparation of simple, non-fluorinated, diynes since the resulting fluorinated diyne reacts to some extent with the nucleophiles (amines, methanol) which are present in the medium. Attempts to conduct this reaction under different conditions, notably by using alkylbromoacetylenes and trifluoropropynes, have been unsuccessful.

The first member of this class of perfluoroalkyldiyne—hexafluoro-2,4-hexadiyne—has been prepared by oxidative dimerisation of zinctrifluoromethylacetylide with $CuCl_2$ in dimethylformamide.[93]

A number of *bis*(perfluoroaryl)-1,3-butadiynes (including *p*-substituted derivatives) has been obtained by oxidative dimerisation in the presence of $CuCl_2$ or NiO_2.[61,66,69,134]

III. Characteristic physical properties

Many of the physical properties of perfluoroalkyl(aryl)acetylenes are typical of fluorine-containing compounds in general. By comparison with non-fluorinated acetylenes having the same number of carbon atoms, the boiling points and refractive indices are lower and the density is somewhat higher.[16,17,24,74,91,93,131–133]

The stereochemistry of certain perfluoroalkyl(aryl)acetylenes has been determined by gas-phase electron diffraction, microwave spectroscopy[135–145] and X-ray analysis.[146] The calculated C–C and C≡C bond lengths are in no way anomalous by comparison with those of simple alkynes.

The high polarity of unsymmetrically substituted perfluoroalkyl-(aryl)acetylenes is a result of the high electron-accepting property of the perfluoroalkyl and perfluoroaryl groups.[77,104,132,133,147–149] Perfluoroalkyldicetylenes have an unusually high polarity by comparison with non-fluorinated analogues (~3.8 D).[132,133,149]

The UV spectra of several perfluoroalkyl(aryl)acetylenes have been recorded.[29,58,62,93,112,150,151]

By comparing the IR spectra of perfluoroalkyl(aryl)acetylenes with those of non-fluorinated analogues, it is notable that the triple bond absorption in the former compounds is very high as a consequence of the high polarity.[17,25,35,48,55,61,74,93,123,131–133,143,151–158] The value of this absorption is shifted some 20–40 cm^{-1} into the short-wavelength region. By comparing the IR spectra of α-halogenotrifluoromethylacetylenes, the absorption of the triple bond is shifted into the long-wavelength region on passing from chlorine to iodine. The force constants for these compounds have been calculated.[156,157] The Δν(OH) shift values for phenol on complex formation with the triple bond of $Me_3MC{\equiv}CC_6H_5$ and $Me_3MC{\equiv}CC_6F_5$ increase in each case in the order M = C, Si, Ge, Sn, although the spectral shift in the spectra of the latter compounds is approximately half.[159]

Microwave[5,135,143,160] and infrared[143,155–157] spectral data have also been obtained for a number of trifluoromethylacetylenes.

In the ^{19}F NMR spectra the signals of the ^{19}F atoms in the trifluoromethyl group depend on the position of fluorine in the molecule. In the spectra of trifluoroalkanes, the signals are in the region 2–6 p.p.m.; for trifluoromethylethylenes they are in the region 10–15 p.p.m., and for trifluoromethylacetylenes in the region 25–29 p.p.m. (using CF_3COOH as standard).[161] Thus in acetylene derivatives the fluorine atom is least shielded.[5,15,17,18,35,74,93,123,131–133,143] The change in the chemical shift of the fluorine nucleus in the α-position relative to the triple bond is around 1.8 p.p.m. and is dependent on the polarity of the solvent.[162,163]

By comparing the ^{19}F NMR spectra of stannanes substituted with one to four $C{\equiv}C{-}C_6F_5$ groups, the chemical shift of the ^{19}F nucleus decreases with increase in the number of $C{\equiv}C{-}C_6F_5$ groups with a corresponding increase in the coupling constant from 2.4 to 3.5 Hz. This is in accord with the distribution of the electron density in the benzene ring.[84,164]

In the ^1H NMR spectra the signals of the hydrogen atom at the acetylene terminus are almost identical with those of non-fluorinated analogues. The signals from the protons of the CH_3 and CH_2 groups in the α-position relative to the triple bond are split (~4 Hz) as a result of remote interaction of the fluorine atoms through the triple bond; for the protons of the methine group in the spectra of 1,1,1-trifluoro-6-methyl-2,4-heptadiyne the value is ~1.2 Hz.[5,35,74,75,132,165]

In studying the chemistry of perfluoroalkyl(aryl)acetylenes, particular attention has been paid to their ^{13}C NMR spectra since the position of the signals from the carbon atoms is an indication of the distribution of electron-density in the molecule. The shielding of the carbon atoms of the triple bond is quite the reverse when a trifluoromethyl group is appended, by comparison with the shielding in the non-fluorinated analogue. This is an indication of an increase

in the polarisation of the triple bond in perfluorinated acetylenes.[149,165] Replacement of hydrogen in 3,3,3-trifluoropropyne by chlorine significantly affects the distribution of electron density. In unsymmetrical diynes the polarisation of a non-trifluoromethylated triple bond is the same as in the corresponding non-fluorinated diyne.[149]

The values of the spin-spin coupling constants for the C–F bond in the spectra of trifluoromethylacetylenes are as follows: $J_{CF}(CF_3)$ 256.9 Hz, $J_{C(1)F}$ 53–55 Hz, $J_{C(2)F}$ 6.5–7 Hz.[17,18,149,165,166]

The ^{13}C chemical shifts and spin-spin coupling constants have also been determined for perfluoropentylacetylene[167] and β-substituted trimethylethynyl-stannanes and -silanes containing CF_3 and C_6F_5 groups.[168,169]

A study has also been made of the photo-electron spectra of a number of trifluoromethylacetylenes, $CF_3C{\equiv}CX$ (where X = H, CF_3, C≡CF, Br, I, CN, SF_5,[170–173] $C(CH_3)_3$, $Si(CH_3)_3$ and $Ge(CH_3)_3$,[150,174,175] and of the X-ray spectrum of hexafluoro-2-butyne (300–800 eV).[176]

Electron-impact mass spectra have been recorded for many perfluoroalkyl(aryl)acetylenes and perfluorinated diynes.[17,19,30,89,91,132,143,153,155,177–183] Characteristically, the intensity of the molecular ion is less than that of non-fluorinated alkynes and alkadiynes. In most spectra the $[M-CF_3]^+$ ion is the most intense. The $[M-F]^+$ ion is also characteristic. ΔHf(g.) values (found or calculated) for the ion $[CF_3C{\equiv}CE(CH_3)_2]^+$ (E = C, Si, Ge, Sn) have been derived from the energy of the $[M-CF_3]^+$ ion as recorded by photoionisation mass-spectrometry. It has been shown that the CF_3 group has a similar stabilising effect to the cyano group in the analogous cation.[182] The introduction of a CF_3 group into the molecule increases the π-orbital ionisation potential (9.59 eV for 2-butyne and 12.36 eV for hexafluoro-2-butyne).[183]

Studies have also been made of the mass spectrum of negative ions from hexafluorobutyne.[184,185]

Quantum chemical calculations are also available for perfluoroalkyl(aryl)acetylenes and perfluorinated diynes.[109,144,147,149,186–191] Although independently computed data for σ- and π-charge density are not entirely consistent from one study to another, the calculations do confirm the charge distribution as determined from the $\delta(C^{13})$ chemical shift values.[149]

For complexes formed between acetylene derivatives of the type $R_FC{\equiv}CSnMe_3$ (R_F = CF_3, C_6F_5) and electron-donating solvents the stability constants decrease in the order: hexamethylphosphoramide > methyl tetramethylphosphorodiamidate > dimethyl sulfoxide > pyridine > acetonitrile > acetone.[85,192,193]

IV. Chemical properties

Normally, a mechanistic criterion is used as the basis for the classification of the chemical conversions of organic compounds. However, with perfluoroalkyl(aryl)acetylenes, reaction mechanisms have only been established with certainty in a few cases. Thus, in the present article, we have based the classification on the most likely mechanism, taking account of the nature of the reagent and the reaction conditions.

The polarisation of the triple bond by the perfluoro-alkyl or -aryl group largely determines the reactivity of perfluoroalkyl(aryl)-acetylenes. These groups are strong electron acceptors, primarily as a consequence of their inductive effect. The effect of the CF_3 group is readily transmitted through double and triple bonds, the $CF_3C{\equiv}C$ group being a stronger electron acceptor than the $CF_3CH{=}CH$ group and significantly greater in this respect than the CF_3 group.[8] By comparing the orientation of addition of nucleophiles to the system $CF_3CH{=}CHX$ where X is also an electron-accepting group), the relative electron-accepting effect of the CF_3 group is in the order: 2 × CF_3 > COOH > CF_3.[194] A comparison of the electron-accepting effect of the CF_3 group with that of other groups has been made elsewhere.[195] The CH-acidity of terminal acetylenes substituted by perfluoroalkyl groups is clearly greater (by a factor of *ca.* 2) than that of non-fluorinated terminal acetylenes.[78]

1. Electrophilic addition

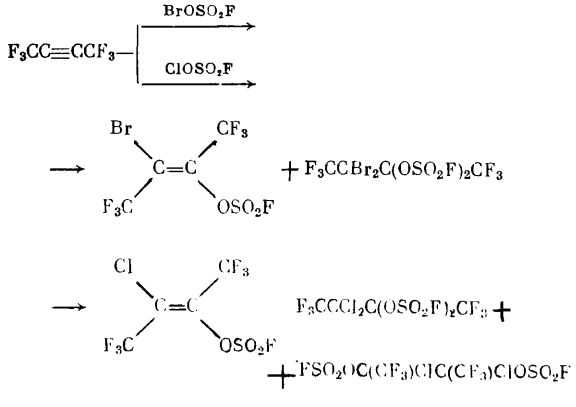
In their addition reactions, alkynes are less nucleophilic than alkenes,[196] and with perfluoroalkyl or perfluoroaryl substitution the nucleophilicity of the triple bond is even lower. Thus, electrophilic reagents do not readily react with perfluoroalkyl(aryl)acetylenes.

There are several reports on the interaction of perfluoroalkyl-(aryl)acetylenes with halogens in the absence of radical initiators or irradiation. However, strictly speaking, such reactions cannot be classified as electrophilic additions.[26,33,58,93,197]

Quite recently, information was published on the conjugate electrophilic addition of I_2 and mixed halides and pseudohalides—ClI, BrI, and ICN—to terminal perfluoroalkylacetylenes. Here, there is a sharp contrast with the results obtained on the interaction of other electrophiles to such compounds.[198] Electrophilic iodine attacks the terminal carbon atom. This fact is very important to the theory of addition to multiple bonds and can only be explained by a different mechanism of addition (via a carbenium or onium ion). Thus, in such polarised compounds hydrogen and halogen may attack different carbon atoms. There have been a few reports in the literature which substantiate this fact.[199]

Bromine adds to propargyltrifluoromethylacetylene at the mono-substituted acetylene group, while addition to the non-fluorinated analogue—propargylmethylacetylene takes place at the disubstituted acetylene group.[75] Allyltrifluoromethylacetylene and its homologues are brominated at the double bond (at –15 °C), as would be expected.[74]

Below –20 °C hexafluoro-2-butyne reacts with chlorine and bromine fluorosulphate to give the corresponding *trans*-monoadducts (in 38.8 and 34.9% yield) together with products formed as a result of addition of two molecules of the fluorosulphate: with $ClOSO_2F$ the di-adduct is a 3:2 mixture of regioisomers while that formed from two molecules of $BrOSO_2F$ is a single regioisomer:[200]



Trifluoromethylacetylene is more reactive towards hydrogen halides than trifluoromethylethylene,[78,201] just as non-fluorinated acetylenes react more smoothly than ethylenes. Trifluoromethyl-acetylene adds hydrogen halides under comparatively mild conditions

in accordance with the polarisation of the multiple bond, i.e. in the same manner as hydrogen halides add to the analogous perfluoromethylethylenes.[78,202]

The rate of addition of HBr and HI is significantly enhanced in the presence of aluminium halides as catalyst, under which conditions an electrophilic mechanism clearly obtains.

Hydrogen chloride adds to 1,1,1-trifluoro-2-butyne in the presence of $AlCl_3$ to give 1,1,1-trifluoro-2-chloro-2-butene.[16]

The addition of hydrogen halides to hexafluoro-2-butyne is considerably slower and requires (except with HF) a catalyst which promotes electrophilic addition, such as an aluminium halide.[24,202]

Hydrobromination of $CF_3C{\equiv}CN(CF_3)_2$ in the presence of $AlBr_3$ in the dark gives [*Z*]-2-bromo-3,3,3-trifluoroprop-1-enyl-*N*,*N*-*bis*-(trifluoromethyl)amine together with 7% of the regioisomer as an impurity.[197] The regioselectivity of the addition of HBr is explained by the fact that the amine forms with $AlBr_3$ a stable complex in which the polarisation of the triple bond is in the reverse direction by comparison with the uncomplexed amine.

Both geometrical isomers of $F_3CCBr{=}CHSF_5$ are formed by addition of $BrSF_5$ to 3,3,3-trifluoropropyne at 100 °C. However, the mechanism of this reaction has not been established.[44,203]

In the presence of a catalyst, substituted allyltrifluoromethylacetylenes add HBr only across the double bond, the regioselectivity of the reaction depending on the structure of substrate in such a way that the more stable carbonium ion is formed in the initial step.[204]

$$F_3CC{\equiv}CCH_2C(CH_3){=}CH_2 \xrightarrow{HBr} F_3CC{\equiv}CCH_2CBr(CH_3)_2,$$

$$F_3CC{\equiv}CCH_2CH{=}C(CH_3)_2 \xrightarrow{HBr} F_3CC{\equiv}CCH_2CH_2CBr(CH_3)_2$$

3,3,3-Trifluoropropyne is not hydrated with dilute H_2SO_4 at 100 °C. Trifluoroacetone is formed in low yield (19%) on treatment with $HgSO_4$ in water at 130 °C. Under the conditions of the Kucherov reaction (in the presence of $HgSO_4$ and H_2SO_4) a 1:2 mixture of the corresponding aldehyde and ketone is obtained at room temperature.[12] Under similar conditions 1,1,1-trifluorobutyne affords 4,4,4-trifluoro-2-butanone,[16] while perfluorohexylacetylene gives $C_6F_{13}COCH_3$.[205]

Hexafluoro-2-butyne is hydrated without a catalyst in sulfolane at 110 °C to give 1,1,1,4,4,4-hexafluorobutanone in high yield.[206]

Pentafluorophenylacetylene is hydrated very slowly under the Kucherov conditions with the formation of pentafluoroacetophenone (8% yield over 8 days).[26] *p*-amino-β,β,β-trifluoropropiophenone is obtained by hydrolysis of *p*-(trifluoropropynyl)phenyl isocyanate.[48]

Catalytic hydration can only be considered as an electrophilic process in a formal sense.

2. Reactions with nucleophilic reagents

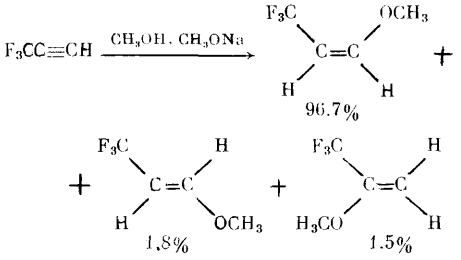
Nucleophilic addition is more characteristic of perfluoroalkylacetylenes since the R_F group significantly enhances the electrophilic character of the triple bond.

a) Addition of *O*-nucleophiles

Studies have been made of the addition of alcohols, phenol and organic acids of perfluoroalkylacetylenes. Non-fluorinated alkynes add such *O*-nucleophiles only in the presence of a catalyst on prolonged heating.[196] Perfluoroalkyl(aryl)acetylenes react with *O*-nucleophiles in the absence of catalyst on moderate heating or at room temperature in the presence of a catalyst.

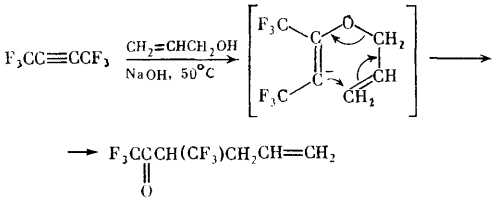
3,3,3-Trifluoropropyne does not add water either in the presence or absence of base. However, hexafluoro-2-butyne adds water in the presence of trimethylamine at room temperature with the predominant formation of *bis*(hexafluoro-2-butenyl) ether.[207]

Alcohols are added to 3,3,3-trifluoropropyne only in the presence of alkoxide or triethylamine at room temperature or lower to give the corresponding *Z*-propenyl ethers.[78,202,208]



In contrast to 3,3,3-trifluoropropyne, hexafluoro-2-butyne adds alcohols in the absence of catalyst at 95–100 °C. The proportion of (*Z*)- and (*E*)-enol ethers which are formed depends significantly on the nature of the solvent: without solvent the (*Z*)-isomers predominate, while in ether or sulfolane the (*E*)-isomers are principally formed (independent of the nature of the alcohol).[206] The (*Z*)-isomers are obtained almost exclusively on treatment with base, independent of the temperature and the nature of the solvent. On increasing the molecular weight of the alcohol, the proportion of (*E*)-isomer increases slightly.[206] There is a detailed discussion in the literature on the effect of the reaction conditions on the mechanism of this reaction.[206,208]

Allyl alcohol adds to hexafluoro-2-butyne with allyl rearrangement:[209]



Bis(pentafluorophenyl)actylene does not add methanol in the presence of NaOH: reaction proceeds by replacement of both *p*-fluoro atoms by an alkoxy group.[58] Such substitution by nucleophilic reagents is characteristic of perfluoroarylacetylenes.[66,69,190]

The addition of phenol to trifluoromethylacetylene in the presence of potassium *tert*-butoxide in alcoholic media at 25 °C (under kinetic control), or on heating at 150 °C (under thermodynamic control) leads to the exclusive formation of the corresponding (*Z*)-enol ether, as would be expected on the groups of polarisation of the triple bond.[210,211]

Acetic acids adds to hexafluoro-2-butyne in the same way as alcohols on heating at 60–100 °C (in the presence of sodium acetate as catalyst) to give the corresponding mono- and di-esters.[212] Dialkyl phosphites and thiophosphites also add to a variety of perfluoroalkylacetylenes at 50–100 °C:[213–214]

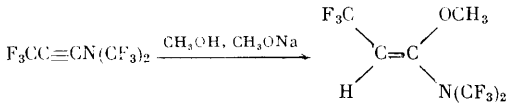
$$F_3CC{\equiv}CX \xrightarrow{(RO)_2PYH}$$

$$\longrightarrow F_3CCH{=}CXYP(OR)_2 \rightarrow F_3CCH{=}CXP(Y)(OR)_2,$$

X = H, Cl, Br, CF_3;

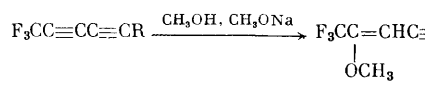
Y = O, S; R = C_2H_5, $CH(CH_3)_2$, CH_2CH_2Cl.

Methanol does not add to $CF_3C{\equiv}CN(CF_3)_2$ in neutral or acidic media. However, even at room temperature, treatent with alkoxide affords the corresponding (*Z*)-aminoacetal in 96% yield with 4% of the regioisomer.[197]



Stabilisation of the intermediate carbanion is facilitated by the inductive effect of the trifluoromethyl groups, as would be anticipated.

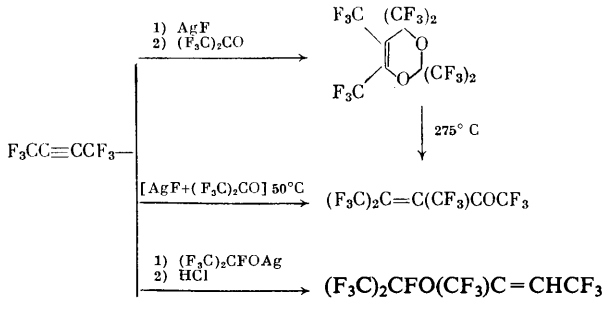
Recently, a study was made of the addition of methanol to isopropyltrifluoromethyldiacetylene in the presence of sodium methoxide at 55–60 °C.[132,133] In this case, the methoxy group is added to the acetylenic carbon substituted by the trifluoromethyl group, i.e. not in accordance with the polarisation of the system (see Section III). In a similar way, under still milder conditions (at room temperature with evolution of heat), alcohols add to trifluoromethyl-substituted diacetylenic alcohols.[133] The regioselectivity is the same as that observed for the addition of other nucleophiles to trifluoromethyldiacetylenes.



$$R = CH(CH_3)_2,\ C(OH)(CH_3)_2.$$

The regioselectivity of addition of alcohols to keto derivatives and to esters of trifluoroalkyl-substituted acetylenic acids is determined by the mesomeric effect of the carbonyl group.[80,118]

Typically, perfluoroalkylacetylenes react with perfluoro substituted carbonyl compounds—perfluoroanhydrides and perfluoroacetone—in the presence of metal fluorides (AgF). In the case of fluoroanhydrides, the anion $R_FCF_2O^-$ adds across the triple bond (see above).[25] Depending on the conditions, the reaction between hexafluoro-2-butyne and hexafluoroacetone in the presence of AgF (with intermediate formation of the anion $(CF_3)_2CFO^-$) leads to various products (see Ref. 6, Vol. 3, p. 124).



b) Addition of *S*-nucleophiles

The addition of *S*-nucleophiles to acetylenes is more characteristic than addition of *O*-nucleophiles. The rate of addition of *S*-nucleophiles to perfluoroalkylacetylenes is also greater than the rate of addition of *O*-nucleophiles.

Trifluoromethylacetylenes readily add thiols and thiophenols at room temperature (using sodium alkoxide or triethylamine as catalyst) as would be anticipated from the polarisation of the triple bond:[210,211215,216]

$$F_3CC{\equiv}CX \xrightarrow{RSH} F_3CCH{=}CX(SR),$$
$$X = H,\ C_2H_5,\ CF_3,\ Cl,\ Br,\ N(C_2H_5)_2;$$
$$R = C_2H_5,\ C_4H_9,\ HOC_2H_4,\ C_6H_5.$$

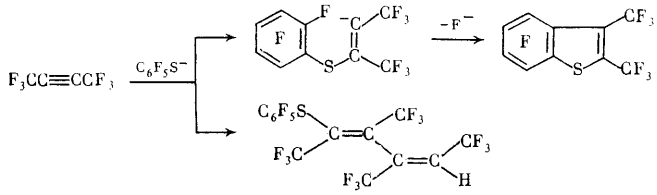
For the reaction 1-chloro-3,3,3-trifluoropropyne with thiols in the presence of alkoxide, 1,1-*bis*(alkylthio)-3,3,3-trifluoropropenes are formed as by-product.[215]

The addition of mercaptopurines in the presence of sodium methoxide leads exclusively to the formation of the corresponding (*Z*)-thioenolethers which rearrange to the (*E*)-isomers on UV-irradiation.[216]

The addition of alkyl mercaptans to allyltrifluoromethylacetylenes proceeds across the triple bond to give, initially, $CF_3CH{=}C(SR)CH_2CR{=}CR_2$ which isomerises to the corresponding 1-alkylthio-1,3-dienes, $CF_3CH_2C(SR){=}CHCR{=}CR_2$ under the conditions of the reaction.[217]

The addition of thiophenol to phenyltrifluoromethylacetylene under kinetic control (at 25 °C with sodium *tert*-butoxide as catalyst) leads to the (*Z*)-thioenolether, while a 23:64 mixture of (*Z*) and (*E*)-isomers is formed under thermodynamic control (at 150 °C). The geometry of the phenol and thiophenol adducts is different since with phenol the (*Z*)-isomer is stabilised by orbital interaction of the aryloxy group with the trifluoromethyl group.[211]

The reaction of lithium pentafluorophenylthiolate with hexafluoro-2-butyne at –70 °C gives a complex mixture of products, from which 4,5,6,7-tetrafluoro-2,3-*bis*(trifluoromethyl)benzo[*b*]thiophene and *trans,trans*-1-pentafluorphenylthio1,2,3,4-tetrakis(trifluoromethyl)butadiene have been isolated in 11% and 2% yield, respectively.[218]



Thiophosphites and esters of thio- and dithio-phosphoric acids add to trifluoromethylacetylene and hexafluoro-2-butyne in the same manner as mercaptans.[213,219]

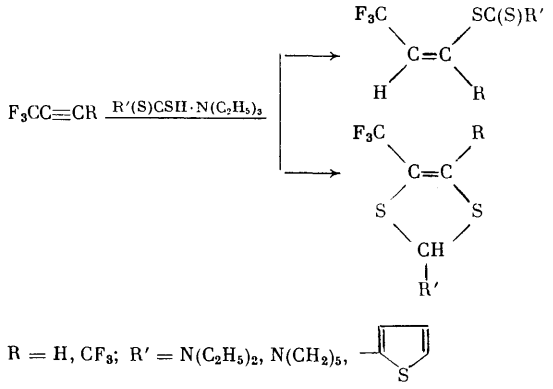
A study has also been made of the addition of methyl mercaptan to esters of perfluoroalkylacetylenic acids in the presence of NaOH. (Z)-Adducts are formed, and methyl mercaptan is liberated as a result of hydrolysis of the corresponding thioester.[220]

$$R_F = C_2F_5,\ C_3F_7,\ C_3F_7OCFCF_3,\ Cl(CF_2)_3,\ Cl(CF_2)_5.$$

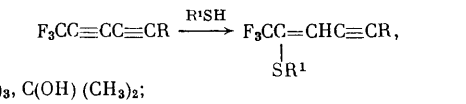
Thus, the orientation of addition, as in other related examples, is determined by the mesomeric effect of the carbonyl group.

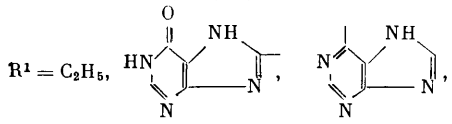
Trifluoromethylacetylenes and hexafluoro-2-butyne react with salts of dithiocarboxylic acids to give, depending on their structure, products arising by nucleophilic addition or 1,3-anionic cycloaddition.[221,222] Only the linear (*Z*)-adducts are obtained by addition of *N,N*-diethyl- and *N*-pentamethylene-dithiocarbamic acids salts,

while salts of 2-thienyldithiocarboxylic acid form 1,3-cycloadducts (see below) or a mixture of both linear and cyclic adducts.[221,222]



The nucleophilic addition of thiols and thioacids to trifluoromethyldiacetylenes has been studied during the last ten years. The reaction proceeds at room temperature with the same regioselectivity as the addition of alcohols, i.e. not in the same manner as the addition to perfluoroalkylacetylenes.[131–133,216,222] With diacetylenic alcohols it is necessary to perform the reaction in the cold (–20 °C), the product being formed in a matter of minutes.[133]





R^2(S)C; $R^2 = N(C_2H_5)_2$, $N(CH_2)_5$.

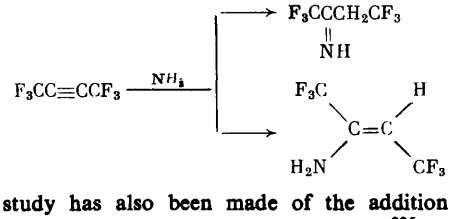
Molecular sulphur also serves as nucleophile in its addition to hexafluoro-2-butyne (at 110 °C in sulpholane) and to decafluorotolan (at 190 °C in benzene). The respective products are *tetrakis*-(trifluoromethyl)- and *tetrakis*(pentafluorophenyl)-thiophene.[58,206]

c) Addition of *N*-nucleophiles

The reaction of perfluoroalkylacetylenes with *N*-nucleophiles (ammonia, primary and secondary amines, and *N*-heterocyclics with an NH group) have been studied quite extensively, as well as the addition of secondary phosphines and arsines.

Trifluoromethylchloroacetylene reacts with ammonia at –78 °C to give 2,2,2-trifluoropropionitrile, while excess of ammonia at 50–60 °C yields malononitrile.[223]

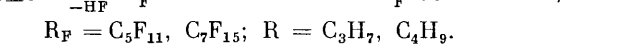
Ammonia adds to hexafluor-2-butyne in ether at 0 °C to give a 3:5 mixture of the corresponding imine and (*Z*)-enamine.[224]



A study has also been made of the addition of ammonia to trifluoromethyl-substituted acetylenic ketones.[225]

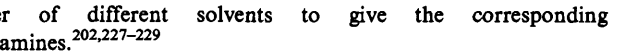
Ethylamine and aniline add to 3,3,3-trifluoropropyne at –70 °C to give a mixture of the corresponding imine and enamine.[210]

The addition of primary amines to other perfluoroalkylacetylenes at 0 °C is accompanied by dehydrofluorination. The enamines thus obtained are hydrolysed to the corresponding enaminoketones:[226]

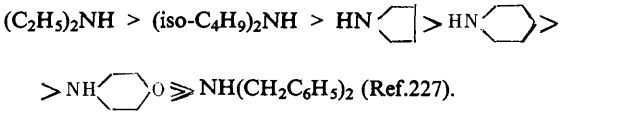


$R_F = C_5F_{11}$, C_7F_{15}; R = C_3H_7, C_4H_9.

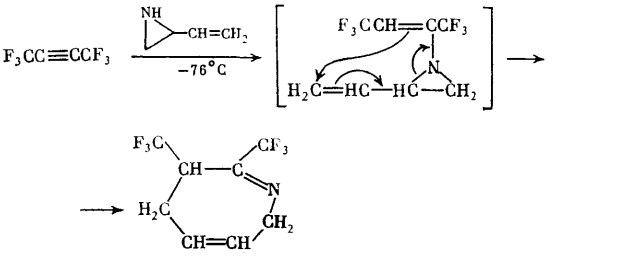
Secondary amines, such as aromatic nitrogen-containing heterocyclics—pyrazole, benzimidazole, pyrimidine, and purine—add to perfluoroalkylacetylenes at room temperature or on cooling in a number of different solvents to give the corresponding (*E*)-enamines.[202,227–229]



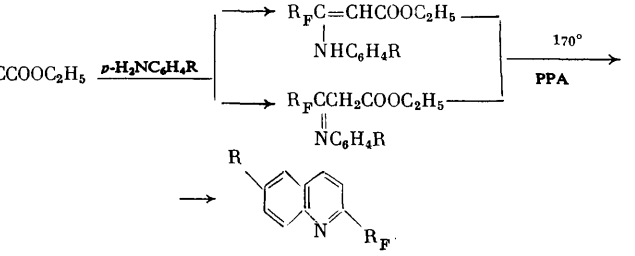
The rate of reaction is determined by the basicity of the amine and decreases in the order:[227]



The addition of vinylaziridine to hexafluoro-2-butyne is accompanied by opening of the 3-membered ring with the formation of a 7-membered ring.[230]



Primary aromatic amines add to perfluoroalkylacetylenecarboxylic acid esters at 40 °C (30 h) to give the expected mixture of enamine and imine. The regioselectivity of addition is the same as that resulting on addition of amines to non-fluorinated acetylenic esters.[88]



$R_F = C_4F_9$, C_6F_{13}, C_8F_{17}; R = H, OCH_3, Cl.

Secondary phosphines and arsines add to trifluoromethylacetylene and hexafluoro-2-butyne at 20 °C with the same regioselectivity as in the addition of amines. The product contains a mixture of (*Z*)- and (*E*)-isomers in varying proportion.[207,228,231]

There is an isolated example of the addition of dimethylamine to a mono-substituted perfluoroalkyldiacetylene. At –30 to –40 °C in ether, addition takes place only at the terminal triple bond, the

regioselectivity being in accord with the polarisation of the bond, as is the case with the addition of such secondary amines to perfluoroalkylacetylenes.[232]

$$C_3F_7C{\equiv}C-C{\equiv}CH \xrightarrow{(CH_3)_2NH} C_3F_7C{\equiv}CCH{-}CHN(CH_3)_2$$

However, in the case of di-substituted alkyl(trifluoromethyl)diacetylenes, secondary amines attack exclusively the carbon atom bearing the trifluoromethyl group, i.e. not in accord with the charge distribution in the compounds.[132,133]

$$F_3CC{\equiv}CC{\equiv}CR \xrightarrow{R_2'NH} F_3CC{=}CHC{\equiv}CR, \quad \begin{matrix} | \\ NR_2' \end{matrix}$$

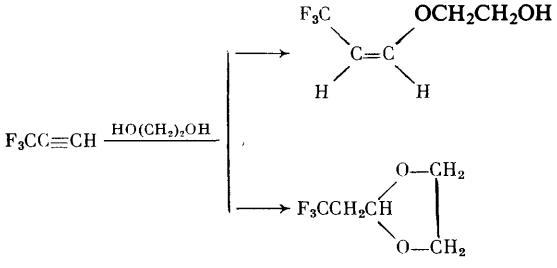
R = $CH(CH_3)_2$, $C(CH_3)_3$, $C(OH)(CH_3)_2$; R′ = CH_3, C_2H_5

Where the orientation of addition *O*-, *S*- and *N*-nucleophiles to trifluoromethyldiacetylenes is not in accord with the polarisation of such molecules, it is assumed that the regioselectivity is a function of increased stabilisation in the transition state (and intermediate) since it is only by such an orientation of addition that the entire conjugated system can participate and exert a stabilising effect.[149] If such shifts in electron density arise by a mesomeric effect, and not by an inductive effect, as is the case, for example, with diacetylenic acids[233] or phosphates,[149] the most stable transition state results by attack of the nucleophile at the terminal carbon atom furthest from the polarising group.[149]

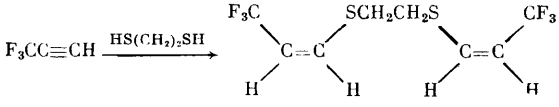
d) Addition of *O*, *S*- and *N*-dinucleophiles

The reactions of perfluoroalkylacetylenes with dinucleophiles is potentially interesting from the view-point of preparing perfluoroalkyl-substituted heterocyclics with high biological activity. Studies have been made of the reactions of perfluoroalkylacetylenes and perfluoroalkyldiacetylenes with compounds containing two hydroxyl groups, two sulfhydryl and two amino groups, as well as with compounds containing either a hydroxyl and a sulfhydryl group or a hydroxyl group and an amino group. The regioselectivity of these reactions is determined by the nature of the nucleophile.

Glycols react with trifluoromethylacetylene at –78 to 80 °C (in the presence of KOH) to give a 4:1 mixture of the corresponding (*Z*)-enolether and 1,3-dioxalane.[210]

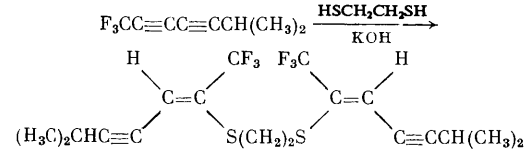


Under the same condition 1,2-dithiols react by a different pathway. (*Z,Z*)-1,2-*Bis*(vinylthio)ethanes are formed predominantly, together with small amounts of the corresponding dithiolane if the reaction is carried out in a non-polar solvent.[210]



The contrasting mode of addition of glycols and 1,2-dithiols to diacetylenes is because the activity of the triple bond of the second diyne molecule is significiantly greater than the activity of the double bond arising as a result of the initial addition of the 1,2-dithiol molecule.

Trifluoromethyldiacetylenes react with ethanedithiol, irrespective of the conditions, to give linear (*Z,Z*)-*bis*-adducts. However, the orientation of addition of ethanedithiol is the reverse of that observed with perfluoroalkylacetylenes.[165]



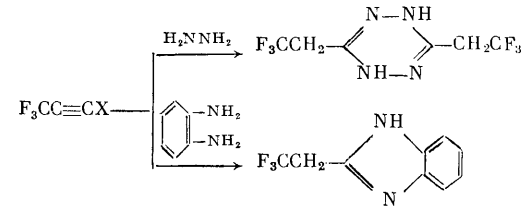
Monothioglycol adds to trifluoromethylacetylene to give only the corresponding thioenolether as a 7:1 mixture of (*Z*)- and (*F*)-isomers.[210]

The reactions of perfluoroalkylacetylenes with nitrogen-containing binucleophiles (e.g. hydrazine and its derivatives, ethylenediamine, phenylenediamine, guanidine and hydroxylamine) have been studied quite extensively.

Hydrazine reacts with trifluoromethylacetylene at –70 °C to give 3,3,3-trifluoropropanal hydrozone (as a 10:1 mixture of (*Z*)- and (*E*)-isomers), which is converted to the corresponding azine in the presence of an excess of trifluoromethylacetylene.[210]

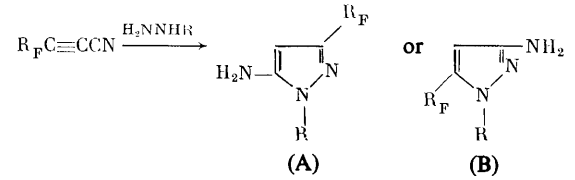
Treatment of hexafluoro-2-butyne with hydrazine affords 1,1,1,4,4,4-hexafluoro-2-butanone hydrazone.[224]

α-Halogenotrifluoromethylacetylenes interact with hydrazine at –60 °C with participation of both the triple bond and α-halogen to give 3,6-*bis*(2,2,2-trifluoroethyl)-1,4-dihydro-*s*-tetrazine. *o*-Phenylenediamine reacts in a similar way to give 2-(2,2,2-trifluoroethyl)benzimidazole.[234]



X = Cl, Br.

Perfluoroalkylacetylenes react with hydrazine, methylhydrazine and phenylhydrazine on heating in methanol according to the following scheme:[235,236]



(A) (B)

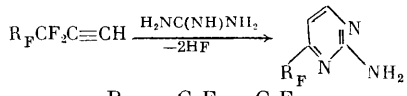
$R_F = C_7F_{15}$; R = H, CH_3 (A), C_6H_5 (B).

Ethylenediamine adds to trifluoromethylacetylene at –70 °C to give the corresponding imidazole exclusively. Total replacement of fluorine takes place at a higher temperature to give the hydrofluoride salt of ethylenediamine and tarring.[210]

The reaction of trifluoromethylacetylene with *o*-phenylenediamine proceeds at room temperature during 5 days to give the corresponding substituted benzimidazole as the main product. This is accompanied by small amounts of isomeric enamines,

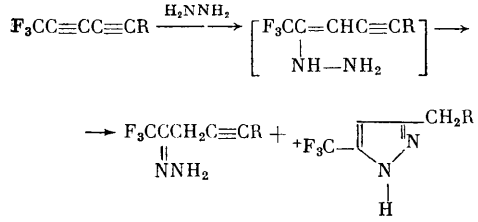
$CF_3CH=CHNHC_6H_4NH_2$ and $CF_3C(NHC_6H_4NH_2)=CH_2$, in 8:1 proportion.[210]

The addition of guanidine to perfluoroalkylacetylenes at 0 °C in THF/water leads to perfluoroalkylaminopyrimidines. The atoms of fluorine of the CF_2-group participate in the reaction.[237]



$R_F = C_5F_{11}$, C_7F_{15}.

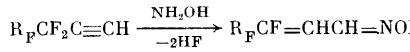
Trifluoromethyldiacetylenes react with hydrazine at −10 to −20 °C to give, initially, an enehydrazine which readily isomerises to the corresponding non-conjugated hydrazone or cyclises to a pyrazole derivative.[132,133]



The proportion of hydrazone and pyrazole depends on the nature of the radical, R, which affects the electrophilicity of the triple bond. The hydrazone:pyrazole ratio is 2:1 for R = Pr-*i*, and 1:10 for R = $Me_2C(OH)$.

The reaction of trifluoromethyldiacetylenes with ethylenediamine, the basicity of which is greater than that of hydrazine, proceeds in the absence of solvent at −60 °C with the formation of the corresponding trifluoromethyldiazepine exclusively. Both linear and cyclic products are formed in THF.[238]

The reaction of perfluoroalkylacetylenes with *N,O*-dinucleophiles has only been studied with hydroxylamine.[237] At 35 °C in ether/ethanol containing Et_3N, an oxime is formed during 20 h by elimination of HF.[237]

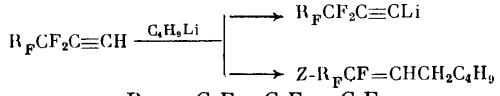


d) Addition of *C*-nucleophiles

Reactions with *C*-nucleophiles are not as well defined as those with *O*-, *S*- and *N*-nucleophiles since in the majority of cases there are no mechanistic details.

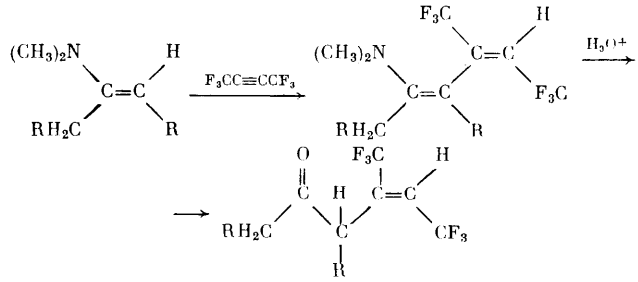
Alkyllithiums are normally selected for studies involving the interaction of unsaturated compounds with *C*-nucleophiles.

Treatment of terminally unsubstituted perfluoroalkylacetylenes with butyllithium in THF at −60 °C leads to replacement of the acidic hydrogen by lithium or addition to the triple bond to give an anomalous by-product:[89]



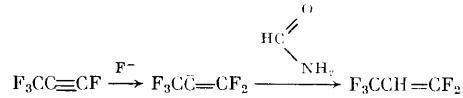
$R_F = C_3F_7$, C_5F_{11}, C_7F_{15}.

Certain enamines serve as *C*-nucleophiles in their reactions with perfluoroalkylacetylenes. Reaction is exothermic and proceeds by attack of the carbon atom at the β-position relative to nitrogen.[239]

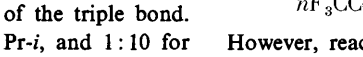


R, R = $(CH_2)_3$; R = CH_3.

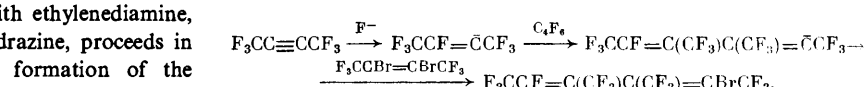
The fluoride ion of certain metallic fluorides (AgF, CsF, HgF_2) adds to perfluoroalkylacetylenes to give *C*-nucleophilic species. In the presence of a proton donor these are quenched to effect nucleophilic hydrofluorination, as shown below with perfluoropropyne.[18]



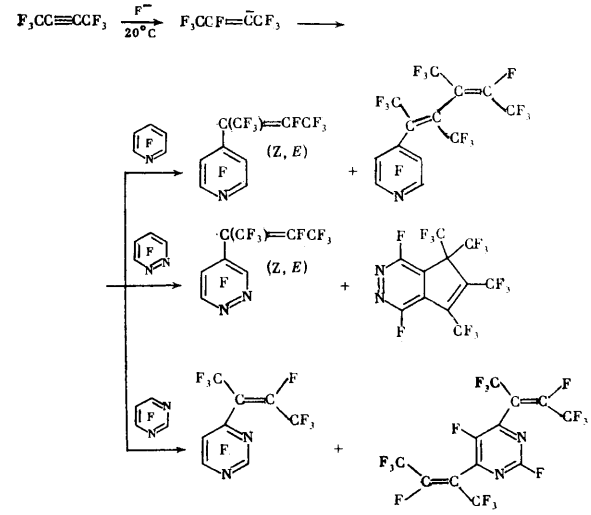
If there are no added reagents to intercept the formed carbanion, hexafluoro-2-butyne polymerises in sulpholane on treatment with CsF.[240–242]



However, reaction can be stopped at the stage of dimerisation if a suitable electrophile, e.g. $F_3CBr=CBrCF_3$, is present:[240,243]



The intermediate obtained by reaction of hexafluoro-2-butyne with fluoride ion is an extremely reactive nucleophile, which participates in nucleophilic substitution with a number of *N*-heterocyclics—perfluoro-pyridine, -pyridazine and -pyrimidine.[240,244]



Anionic telomerisation (n = 2,3) also takes place with perfluoropyridine, while in the case of perfluoro-pyridazine and -pyrimidine

an additional product arises as a result of nucleophilic attack at two electrophilic ring positions.

1-Chloro-3,3,3-trifluoropropyne reacts smoothly with perfluoroisobutylene in the presence of fluoride ion. The latter initiates the formation of perfluoro-*tert*-butyl anion which readily displaces chlorine.[245]

$$(F_3C)_2C{=}CF_2 \xrightarrow{F^-} (F_3C)_3C^- \xrightarrow[-Cl^-]{F_3CC\equiv CCl} F_3CC{\equiv}C\dot{C}(CF_3)_3.$$

The reaction of HCN with 3,3,3-trifluoropropyne in the presence of KCN and Cu_2Cl_2 at 110–120 °C possibly involves nucleophilic addition.[202]

$$F_3CC{\equiv}CH \xrightarrow{HCN} F_3CCH{=}CHCN \xrightarrow{10\%NaOH,\ H_2O} F_3CCH{=}CHCOONa.$$

3. Radical polymerisation and addition

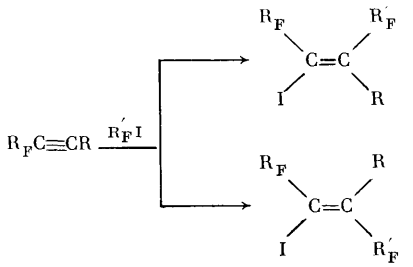
Various polymeric products—linear, cyclic (including benzene derivatives by trimerisation) and tetramers—are formed from perfluoroalkyl(aryl)acetylenes on photochemical activation, heating, or on treatment with peroxides or complex metal catalysts.[246–256]

UV-irradiation of hexafluoro-2-butyne affords tetramers of different structural type, amongst which perfluoro-octamethylcubane, perfluoro-octamethylsemibulvalene and perfluoro-octamethyloctatetraene have been identified.[252] It is thought that all of these products arise via UV-irradiation of the two geoisomeric forms of the simple tetramer, perfluoro-octamethylcyclo[4.2.0.0^{2,5}]-3,7-octadiene, or the dimer, perfluorotetramethylcyclobutadiene. It is possible that reaction proceeds via other cyclic systems.[243,252,253]

Certain linear fluoro-polymers and -copolymers with other monomers have been used as stable plastic materials, although they are not as useful as Teflon.[25] Polymers based on fluorine-containing diacetylenes have been used in the manufacture of heat-sensitive materials with improved surface characteristics. These have been applied domestically and scientifically in the design of electronic and optical probes.[256–268]

Examples of radical halogenation[24,34,38,48,259] and hydrobromination[197,202,260] of perfluoroalkylacetylenes have been reported. In the latter reaction, the regioselectivity of addition is the same as that of electrophilic hydrobromination.[197]

Perfluoroalkyl iodides add to perfluoroalkylacetylenes under photochemical or thermal activation as follows:[22,40,261–266]



$R_F = CF_3,\ C_3F_7,\ C_6F_{13},\ C_8F_{17};$
$R = H,\ CF_3;\ R'_F = CF_3,\ C_2F_5,\ C_3F_7,\ CF(CF_3)_2.$

Hydrolysis of the resulting perfluoroiodoalkenes in the presence of freshly precipitated copper leads to perfluoroallenes.[263] Iodotrichloromethane reacts with trifluoromethylacetylenes in the same way as iodotrifluoromethane.[266]

The addition of $I(CH_2)_2O(CF_2)_2SO_2F$ to 3,3,3-trifluoropropyne in the presence of benzoyl peroxide at 195 °C leads to a 3 : 1 mixture of the corresponding (*Z*)- and (*E*)-iodoethylenesulfonyl fluorides.[267]

In the photochemical reaction of perfluoropropyne with trichlorosilane, the Cl_3Si radical attacks primarily the C_2 atom, whereas in the reaction with trimethylsilane attack is predominantly at the C_1 atom. In the case of 3,3,3-trifluoropropyne, both radicals attack primarily the terminal carbon atom.[268]

Trifluoronitrosomethane interacts with 3,3,3-trifluoro-1-propynyl-*N,N-bis*(trifluoromethyl)amine at 95 °C to give a 97% yield of 1 : 1 adduct as follows:[269]

$$F_3CC{\equiv}CN(CF_3)_2 + F_3CN{=}O \longrightarrow \underset{96\%}{F_3CN{=}C(CF_3)CN(CF_3)_2} + \underset{4\%}{F_3CCC{=}NCF_3}$$
(O; O; $N(CF_3)_2$)

The stable *bis*(trifluoromethyl)nitroxyl adds to perfluoroalkylacetylenes at 85 °C with the formation predominantly of the corresponding perfluorinated carbonyl and dicarbonyl compounds.[270]

$$R_FC{\equiv}CR \xrightarrow{(F_3C)_2NO} R_FC{=}CR \longrightarrow R_FCOCOR + R_FCOC[ON(CF_3)_2]_2R$$
($(F_3C)_2NO$; $ON(CF_3)_2$)

$R_F = CF_3,\ C_6H_5;\ R = H,\ F,\ CF_3,\ C_6H_5.$

N-Chlorodimethylamine adds to hexafluoro-2-butyne by a radical mechanism.[207] Several products are obtained by radical addition of *N*-bromo-*bis*(trifluoromethyl)amine to 3,3,3-trifluoropropyne: (*Z*)-2-bromo-3,3,3-trifluoro-1-propenyl-*N,N-bis*-(trifluoromethyl)amine is the main product (52%), formed together with 21% of the corresponding (*E*)-isomer and a mixture of (*E*)- and (*Z*)-regioisomers in 3% and 11% yield, respectively.[197]

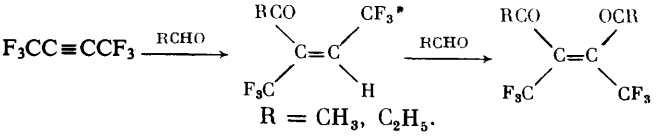
Perfluoroalkylacetylenes add perfluorohydrazine by a radical mechanism to give *N,N*-perfluorodiamines which rearrange on heating to imines:[271,272]

$$F_3CCCF(NF_2)R \text{ (NF)} \quad \text{and} \quad F_3CCF(NF_2)CR \text{ (NF)}$$

Hexfluoro-2-butyne reacts similarly with tetraphenyldiphosphine.[207]

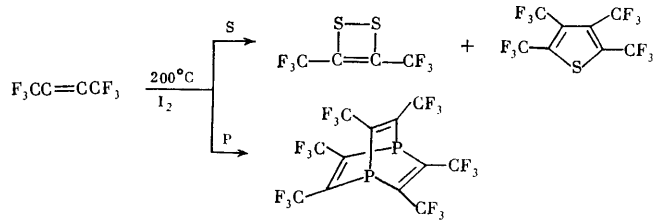
The reaction of 3,3,3-trifluoropropyne with atomic oxygen has also been studied.[273] Radical addition of methanol and 2,2,2-trifluoroethanol to hexafluoro-2-butyne under γ-irradiation affords *trans*-4,4,4-trifluoro-2-trifluoromethyl-2-buten-1-ol (12%) with the former alcohol and, with the latter, a 1 : 1 mixture of *cis*- and *trans*-1,1,1,5,5,5-hexafluoro-3-trifluoromethyl-3-penten-2-ol.[174]

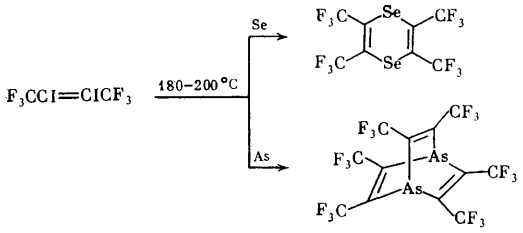
The radical addition of acetaldehyde and propionaldehyde to hexafluoro-2-butyne has also been studied (under γ-irradiation or in the presence of benzoyl peroxide). Reaction proceeds with the formation of adducts in 1 : 1 and 1 : 2 proportion.[274]



$R = CH_3,\ C_2H_5.$

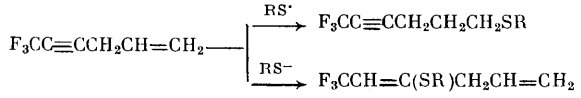
Sulphur and phosphorus react with hexafluoro-2-butyne in the presence of iodine to give heterocyclic compounds. Selenium and arsenic only form heterocyclic compounds with 2,3-diiodohexafluoro-2-butene.[259,275,276]





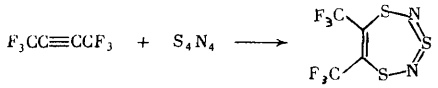
Hydrogen sulphide reacts with 3,3,3-trifluoropropyne and hexafluoro-2-butyne on irradiation to give stable enethiols, $F_3CCH=CHSH$ and $F_3CCH=C(SH)CF_3$.[277] On UV-irradiation of these same perfluoroalkyacetylenes with methyl mercaptan, 1:2 adducts of the type, $CF_3CH(SCH_3)CH_2SCH_3$, are formed.[278]

The addition of alkyl mercaptans to allyltrifluoromethylacetylene and its homologues in the presence of *tert*-butyl peroxide takes place across the double bond. The thiiyl radical thus attacks the terminal carbon atom, while nucleophilic addition of mercaptide anion takes place across the triple bond:[217]

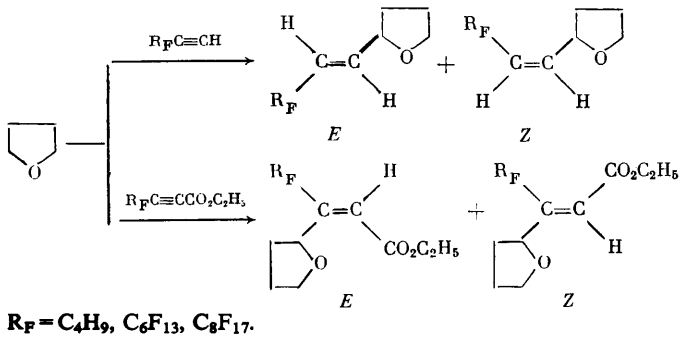


Dimethyl disulphide reacts with hexafluoro-2 butyne on UV-irradiation at 100 °C to give a high yield of 2,3-*bis*-(methylthio)hexafluoro-2-butene as a mixture of (*Z*)- and (*E*)-isomers.[279]

Hexafluoro-2-butyne condenses with tetrasulphur tetranitride to give *bis*(trifluoromethyl) derivatives of a trithiadiazepine. However, the mechanism of this reaction has not been established.[280]



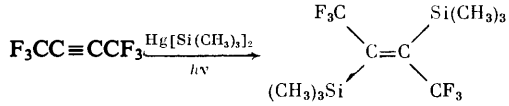
Perfluoroalkylacetylenes and esters of perfluoroalkylpropiolic acid add tetrahydrofuran (on heating) according to the following scheme:[281]



$R_F = C_4H_9$, C_6F_{13}, C_8F_{17}.

The regioselectivity of the reaction between tetrahydrofuran and perfluoroalkylpropiolic acid esters is a consequence of the mesomeric effect of the carboxyl group. In both cases, (*E*)-isomers are formed (80 and 70% yield, respectively).

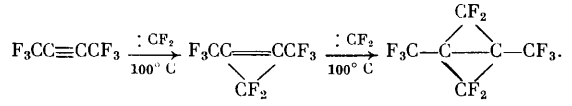
The possibility of silylating perfluoroalkylacetylenes has also been investigated. This is exemplified by the following scheme:[282]



Flash-photolysis of 3,3,3-trifluoropropyne is reported to give HF.[283]

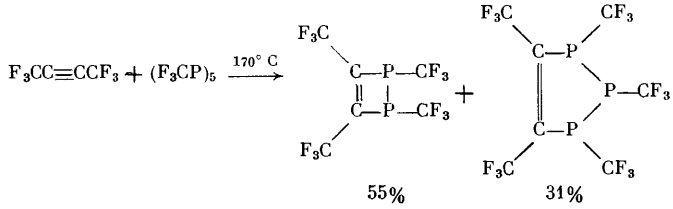
4. Reactions with carbenes and related compounds

Difluorocarbene, obtained by pyrolysis of $(CF_3)_3PF_2$ at 100 °C adds to hexafluoro-2-butyne in the gas phase as follows:[284]

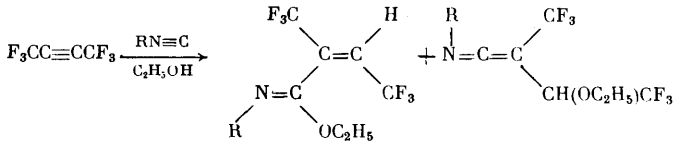


3,3,4,4-Tetrafluoro-3-trifluoromethyl-1-butyne, $CF_3C\equiv CH$ and $C_2F_5C\equiv CH$ react with difluorocarbene, obtained by heating $(CH_3)_3SnCF_3$ at 150 °C, to give the corresponding cyclopropenes in low yield.[35] Hexafluoro-2-butyne reacts with dichlorocarbene, generated by thermal decomposition of CCl_3SiF_3, to give a mixture of 3,3-dichloro*bis*(trifluoromethyl)- and 1,3-dichloro*bis*(trifluoromethyl)-cyclopropene.[285]

A mixture of four- and five-membered phosphorus-containing heterocyclics is obtained by reaction of hexafluoro-2-butyne with phosphenes.[286]

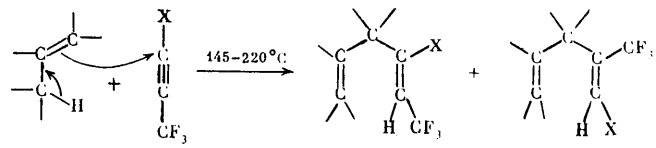


Treatment of hexafluoro-2-butyne with isonitriles in ethanol affords a mixture of iminoesters and ketenimines. The proportion of each depends on the nature of the isonitrile (see Ref. 6, Vol. 3, p. 121).



5. Condensation with alkenes

The high electrophilicity of the triple bond of perfluoroalkylacetylenes and the high nucleophilicity of the double bond of alkenes favour interaction between these compounds:[287]

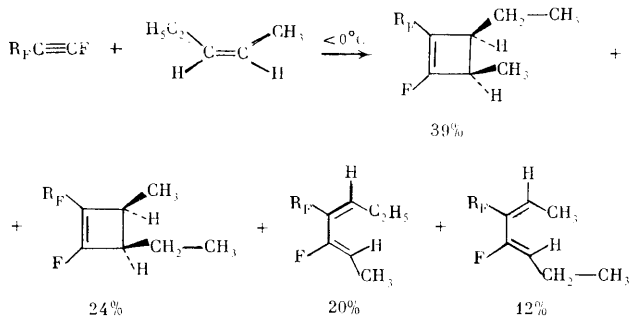


X = H, CF_3.

Thus, reaction of 3,3,3-trifluoropropyne with alkenes leads to a regioisomeric mixture of two non-conjugated 1,4-alkadienes. With substitution of the alkene at C_1 and C_2, several isomeric adducts may be formed.

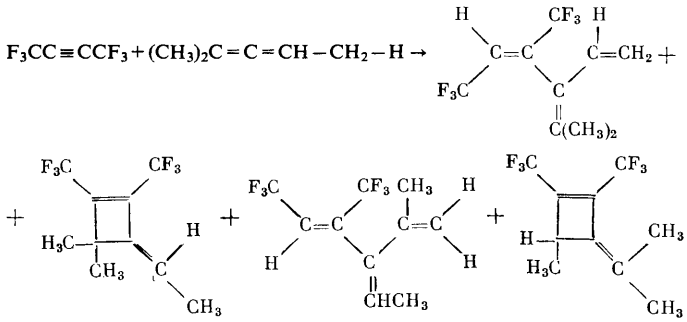
A 1:1 and 1:2 adduct are obtained by reaction of hexafluoro-2-butyne with isobutene.[287]

The interaction of perfluoro-3-methyl-1-butyne with the (*Z*)- and (*E*)-isomers of 2-pentene affords a [2+2]-cycloadduct together with lesser amounts of acyclic compounds formed as a result of ring cleavage of a σ-bond.[122]

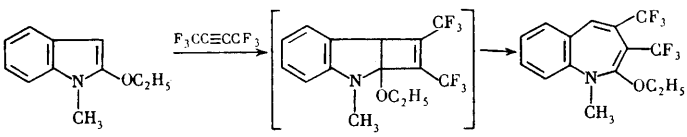


Phenylperfluorohexylacetylene reacts similarly with tetrafluoroethylene. Ring opening of the intermediate cycloadduct yields 1,1,4,4-tetrafluoro-2-perfluorohexyl-3-phenyl-1,3-butadiene.[32]

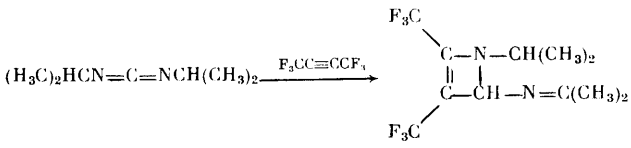
The direction of the related reaction of hexafluoro-2-butyne with allenes depends on the substitution of the latter.[288] Thus, reaction of 3-methyl-1,2-butadiene with hexafluoro-2-butyne affords only a [2+2]-cycloadduct,[289] while trimethylallene gives a mixture of products as follows:[290]



Hexafluoro-2-butyne condenses with *N*-methyl-2-ethoxyindole to give a 1-benzazepine via transannular cyclobutene ring opening.[291]



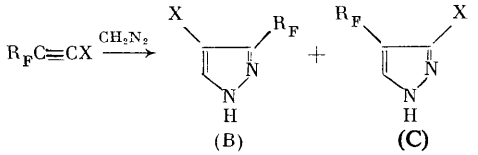
Heterocumulenes, such as diisopropylcarbodiimide, also participate in [2+2]-cycloaddition (see Ref. 6, Vol. 4, p. 121), e.g.



6. 1,3-Dipolar and anionic cycloaddition

Perfluoroalkyl(aryl)acetylenes have been widely used as active dipolarophiles in their reactions with such octet-stabilised dipoles as diazoalkanes, alkyl or aryl azides, nitrile oxides, nitrilimines, sydnones and nitrones. In this way a variety of perfluoroalkyl-substituted heterocyclics have been prepared, primarily with a view to studying the effect of perfluoroalkyl substitution on the biological activity of heterocyclics. Such 1,3-dipolar cycloadditions proceed under much milder conditions than the corresponding reactions with non-fluorinated acetylenes or perfluoroalkylethylenes.[1,6,196,201]

The reaction of perfluoroalkylacetylenes with diazomethane proceeds regioselectively at room temperature to give only one of the two possible cycloadducts. Isomer (B) is formed where X = H, and isomer (C) where X = COOEt. Thus, in the former, the perfluoroalkyl group determines the regioselectivity, while in the latter it is the carbethoxy group.[292,293]



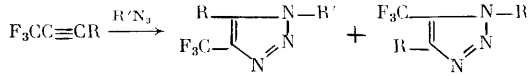
$R_F = CF_3, C_4H_9, C_6H_{13}, C_8H_{17}$; X = H, *n*-$CH_3OC_6H_4$, *n*-$NO_2C_6H_4$, $COOC_2H_5$.

Treatment of aryltrifluoromethylacetylenes with one equivalent of diazomethane gives a 19:1 mixture of the corresponding pyrazoles (B) and (C). Thus, condensation proceeds in accordance with the polarisation of the reactants. The regioselectivity of the reaction is not affected by electron-donating (e.g. OMe) or electron-accepting (e.g. NO_2) substituents in the benzene ring, but the yield of adduct is higher in the latter case.[109]

3,3,3-Trifluoropropyne react with trifluoromethyldiazomethane to give 3,5-*bis*(trifluoromethyl)pyrazole (and a trace of regioisomer in 6% yield), while hexafluoro-2-butyne affords 3,4,5-*tris*(trifluoromethyl)pyrazole.[294]

The addition of diphenyldiazomethane to perfluoropropyne proceeds non-selectively: a 1:1 mixture of isomeric pyrazoles is obtained.[295] The addition of diazocyclohexane,[296] tetraphenyldiazocyclopentadiene[297] and diazofluorene[298] to hexafluoro-2-butyne has also been studied.

Normally, organic azides interact with substituted acetylenes to give a mixture of regioisomeric triazoles. Activation of the triple bond by electron-accepting substituents facilitates this process.[299] Thus, the addition of aliphatic and aromatic azides to trifluoromethylacetylenes proceeds with the predominant formation of 4-trifluoromethyl-1,2,3-triazoles, the permitted R and R′ values being shown below.[109,300–302]



R = H, CF_3, C_6H_5, 4-$NO_2C_6H_4$, 4-$CH_3OC_6H_4$, Br, $CH(OH)_2C_2H_5$, $C{\equiv}CC(CH_3)_3$, $C \equiv CC(OH)(CH_3)_2$;
R′ = CH_3, C_6H_5, 4-$NO_2C_6H_4$, 4-$CH_3OC_6H_4$.

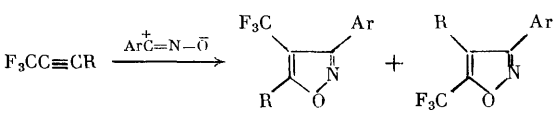
In exactly the same way, phenylperfluorohexyl-[32] and phenylpentafluorophenyl-acetylene[300] react with phenyl azide to give the corresponding 1-phenyl-4-perfluorohexyl- and 1-phenyl-4-pentafluorophenyl 1,2,3-triazoles.

Azides react similarly with non-fluorinated acetylenes.[299] Thus, in such additions, the regioselectivity is not determined by the distribution of electron-density in the substrate.

It is reported[93] that hexafluoro-2,4-hexadiyne readily reacts with two molecules of *p*-dimethylamino- and *p*-methoxy-phenyl azide to give a high yield of the corresponding *bis*(triazoles) with the trifluoromethyl groups in the 5- and 5′-positions. Here, the regioselectivity is different to that observed with the addition of azides to simple perfluoroalkylacetylene (see above), and the data requires corroboration.

Biologically active perfluoroalkyl(aryl)-substituted isoxazoles, which are normally difficult to prepare, are obtained by treatment of the corresponding perfluoroacetylenes with nitrile oxides.

In all reactions of trifluoromethylacetylenes with arylnitrile oxides, the regioselectivity is in accordance with the polarisation of the reactants and independent of the nature of the substituents either in the trifluoromethylacetylene or the benzene ring. The selectivity reaches 99% in certain cases:[50,165,303]



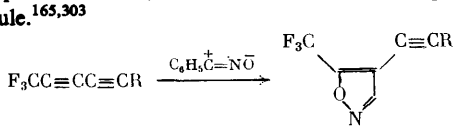
R = H, Br, CF_3, X—C_6H_4 (X = 2-Cl, 4-CH_3O, 4-NO_2, 4-NH_2); Ar = C_6H_5, 4-ClC_6H_4, 2,6-$Cl_2C_6H_3$, 3-pyridyl.

Non-fluorinated acetylenes take part in this reaction under harsher conditions, and the regioselectivity is in the opposite sense.[50] Thus, treatment of pentafluorophenylacetylene with benzonitrile oxide affords 3-phenyl-4-pentafluorophenylisoxazole,[304] while phenylacetylene gives 3,5-diphenylisoxazole.[305] If the reaction is conducted in the presence of triethylamine, there is partial replacement of the *p*-fluorine atom by the triethylammonio group.[304]

In the reaction of perfluoroacetylenecarboxylic acid ethyl esters with nitrile oxides, the regioselectivity is determined by the mesomeric effect of the carbethoxy group.[306]

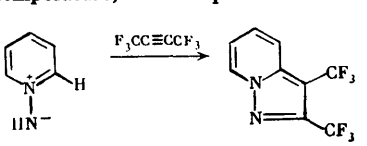
Quinoline and isoquinoline *N*-oxides react with hexafluoro-2-butyne in a more complex manner with intermediate formation of the expected ylids.[307]

Non-conjugated, methylene-bridged trifluoromethyldiacetylenes having a terminal triple bond react with nitrile oxides predominantly at the terminal bond, as is the case with non-fluorinated analogues. However, if the non-fluorinated triple bond is disubstituted, addition takes place predominantly at the acetylene group substituted by the trifluoromethyl group, as is normally the case.[165,308] This bond is also highly activated in conjugated trifluoromethyldiacetylenes. Thus, the regioselectivity of the reaction, as is the case with nucleophilic addition, is not in accord with the polarisation of the molecule.[165,303]

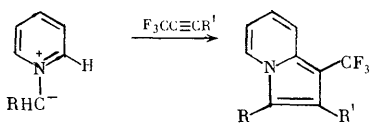


The kinetics of the reaction of 3,3,3-trifluoropropynyldiphenylphosphine with *C,N*-diphenyl- and *C*-acetyl-*N*-phenyl-nitrilimine has also been studied, although there was no product analysis.[309]

N-Nitrilimines (azomethine imides) based on pyridine, quinoline[310] and pyrazoline[311] interact smoothly with hexafluoro-2-butyne at room temperature, for example:[310]

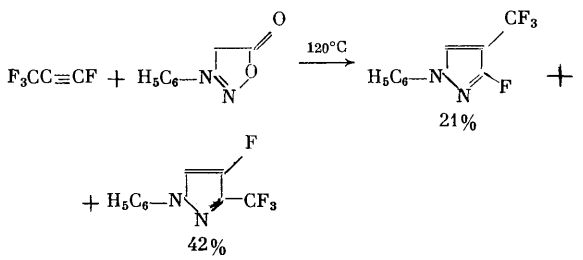


The reaction of trifluoromethylacetylenes with related ylids[312] and with *N*-(2,2,2-trifluoroethyl)pyridinium salts[313] proceeds in the same way, although by-products have also been isolated:



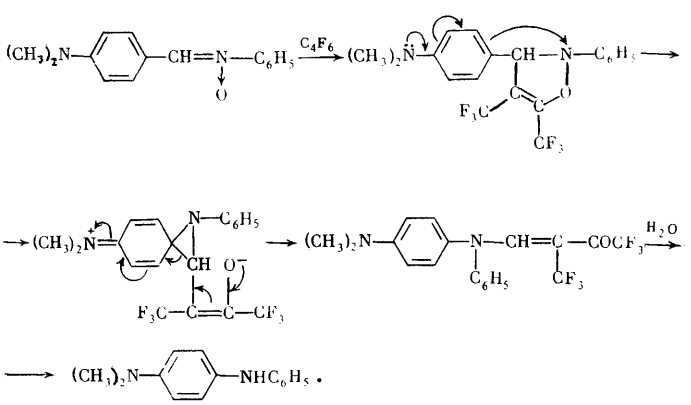
R = CF_3, COF_3; R′ = H, CF_3.

Perfluoropropyne reacts with *N*-phenylsydnone non-selectively:[302]

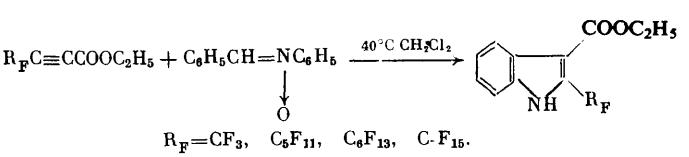


Hexafluoro-2-butyne affords 3,4-*bis*(trifluoromethyl)-1-phenylpyrazole with this same sydnone.[302]

The interaction of hexafluoro-2-butyne with phenyl-, *p*-anisyl-, *p*-nitrophenyl-, *p*-*N,N*-dimethylaminophenyl-nitrone has also been reported.[314] In all reactions, an isoxazoline is formed initially, but the ring is further transformed as reaction progresses. With the first three nitrones, re-cyclisation and hydrolysis takes place to give the corresponding 2,3-*bis*(trifluoromethyl)indole. *C*-(*p*-*N,N*-dimethylaminophenyl)-*N*-phenylnitrone condenses with hexafluoro-2-butyne as follows:[314]

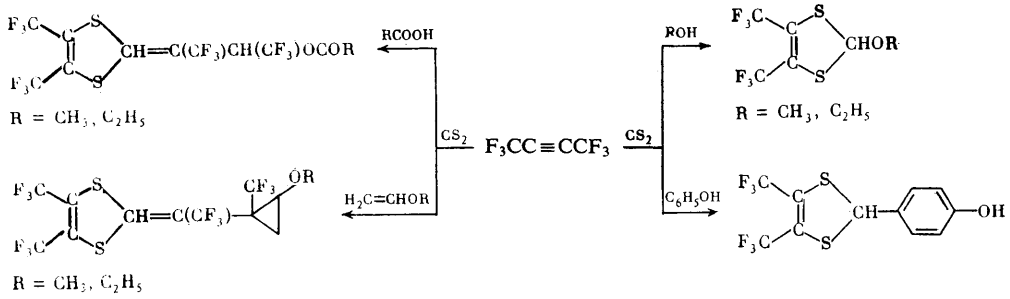


In the reaction of *C, N*-diphenylnitrone with perfluoroacetylenecarboxylic acid ethyl esters, the orientation of addition is determined largely (90%) by the carbethoxy group.[315]

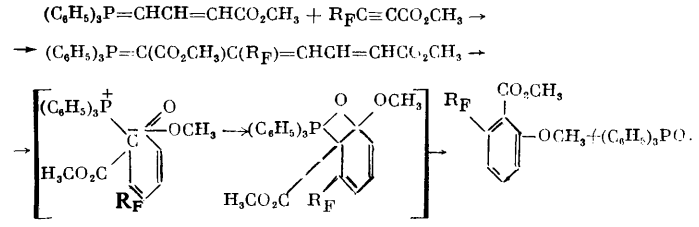


Anionic cycloaddition has only been studied with dithio-acids. Aminodithiocarbamates react with trifluoromethyl-acetylenes and -diacetylenes by nucleophilic addition (see above). 1,3-Anionic cycloaddition only takes place with 2-thienyldithiocarbamates.[221,222]

Hexafluoro-2-butyne and CS_2 participate in a variety of 1,3-anionic cycloadditions,[316–318] for example:



The reactions of perfluoroacetylenecarboxylic acid esters with phosphonium and arsonium ylids have been studied in recent years.[319–321] Thus, interaction of phosphorane (D) with methyl perfluoroalkylactylenecarboxylates takes place via intramolecular Wittig reaction to give the corresponding perfluoroalkyl-substituted *o*-methoxybenzoates:[319]



7. Diene synthesis

Alkynes and aryl-substituted acetylenes react as dienophiles with 1,3-alkadienes, but only under forcing conditions. Perfluorinated analogues, however, often react at room temperature. Under certain conditions they may even react with diene systems which are normally unreactive, such as aromatic hydrocarbons. Diene synthesis with perfluoroalkyl(aryl)acetylenes plays an important role in the preparation of mono- and poly-cyclic compounds, including heterocyclics substituted by perfluoro-alkyl and -aryl residues. Such products have potential biological activity, and the incorporation of polarising substituents is synthetically useful.

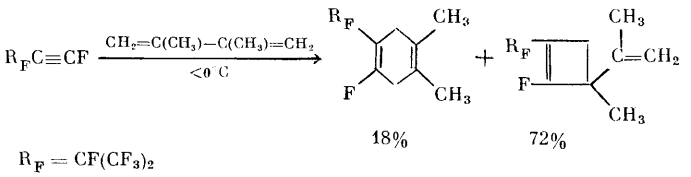
The interaction of 3,3,3-trifluoropropyne with 1,3-butadiene was first mentioned in 1956, but detailed experimental data was not presented.[5]

Recently it was shown that 3,3,3-trifluoropropyne reacts with cyclopentadiene even at room temperature, and with 1,3-butadiene and 2,3-dimethyl-1,3-butadiene on heating at 100 °C.[76] The reactions of 3,3,3-trifluoropropyne and hexafluoro-2-butyne with hexafluoro- and perfluoro-1,3-cyclohexadienes (at 200 °C) affords the expected cycloadduct together with products formed by dimerisation of the cycloalkadienes.[322,323] Bromo-3,3,3-trifluoropropyne interacts exothermically with cyclopentadiene at room temperature, while reaction with 1,3-butadiene and 2,3-dimethylbutadiene requires heating (100 °C). These thermal cycloadditions are accompanied by tarring and dehydrogenation to give aromatic compounds.[76]

Phenylperfluorohexylacetylene readily reacts with divinyl on heating.[32]

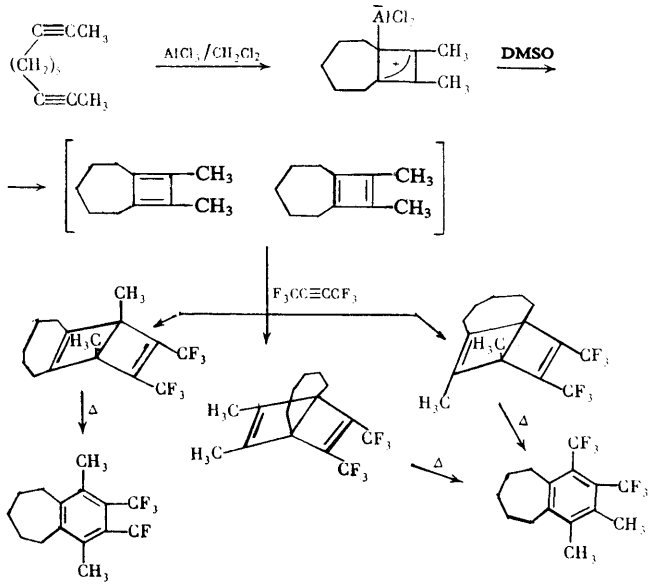
The most studied dienophile is hexafluoro-2-butyne. The latter reacts with 1,3-butadiene or 2,3-dimethyl-1,3-butadiene at room temperature or at temperatures in the region 28–100 °C.[324] The corresponding benzenoids are formed via dehydrogenation of the adducts at 700–800 °C. The major by-products are trifluoromethylbenzene and 2,3-*bis*(trifluoromethyl)-1,3-butadiene.[324]

With perfluoroacetylenes, however, [2+2]-cycloaddition prevails over [4+2]-cycloaddition,[122] as illustrated below.



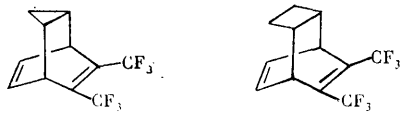
Reference has also been made to the reactions of hexafluoro-2-butyne with cyclic conjugated alkadienes having a four-, five-, six-, seven- or eight-membered ring.

Dimethylpentamethylenecyclobutadiene initially affords a 1:1 adduct which subsequently isomerises as follows:[325]



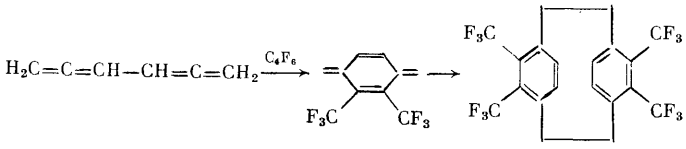
Reaction proceeds in the normal way with cyclopentadiene and variedly substituted cyclopropylfulvenes to give 2,3-*bis*(trifluoromethyl)bicyclo[2.2.1]hepta-2,5-diene[326,327] and the corresponding cyclopropyl derivatives, respectively.[328,329] With cycloheptatriene,[326] its 7-cyano derivative,[330] and with cyclooctatetraene (at 150 °C),[326]

transannular ring closure of the initial cycloadducts yields the following compounds:

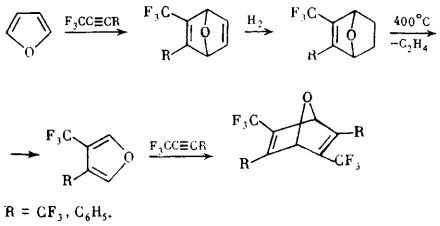


Bis(pentafluorophenyl)acetylene and pentafluorophenylacetylene react with tetraphenylcyclopentadiene to give, predominantly, hexaarylbenzenes.[112]

The adduct formed from hexafluoro-2-butyne and 1,2,3,5-hexatetradiene dimerises to give the corresponding paracyclophane:[331]

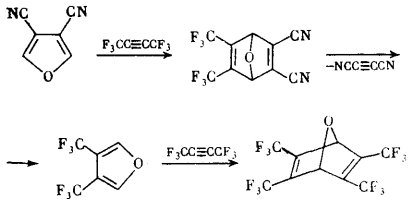


Perfluoroalkylacetylenes readily react with furan, pyrrole, triazine and substituted derivatives of these heterocyclics. At 100 °C in THF furan affords the expected [4+2]-adduct, which, after partial hydrogenation, eliminates ethylene on heating. The resulting 3,4-disubstituted furan then reacts with a second molecule of perfluoroalkylacetylene as follows:[110,332,333]



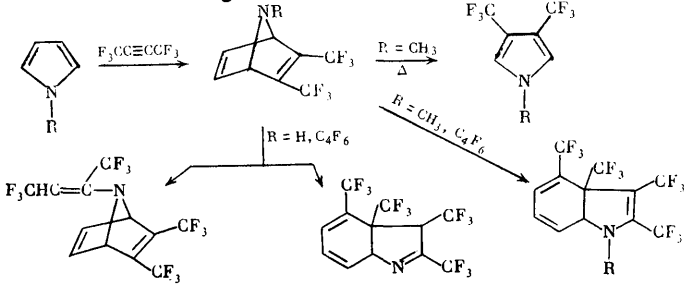
R = CF_3, C_6H_5.

In a similar way, cycloaddition of hexafluoro-2-butyne with 3,4-dicyanofuran is accompanied by elimination of dicyanoacetylene:[332]



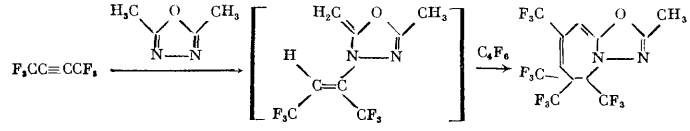
Novel and interesting cycloadducts have been obtained by reaction of furan with [α,α-*bis*(3,3,3-trifluoropropynyl)]benzyl benzoate and [1,1-*bis*(3,3,3-trifluoropropynyl)]ethyl acetate.[90]

Normally, pyrrole reacts with dienophiles by ene synthesis rather than [4+2]-cycloaddition. However, the latter prevails with hexafluoro-2-butyne, the initial cycloadduct reacting subsequently as shown in the following scheme:[334]

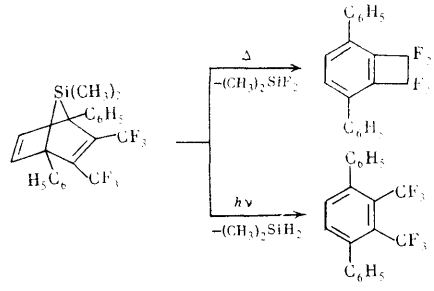


The products formed by heating hexafluoro-2-butyne with *N*-benzoyl-2,5-dialkylpyrroles at 300 °C eliminate acetylene to give the corresponding tetra-substituted *N*-benzoylpyrroles.[335]

Hexafluoro-2-butyne reacts with 2-phenyl-4,6-diaryl-1,2-dihydro-*s*-triazines to give the corresponding 4,5-*bis*-(trifluoromethyl)-2,6-diarlypyrimidines.[336] An unusual condensation of hexafluoro-2-butyne with 2,5-dimethyl-1,3,5-oxadiazole has also been reported:[337,338]

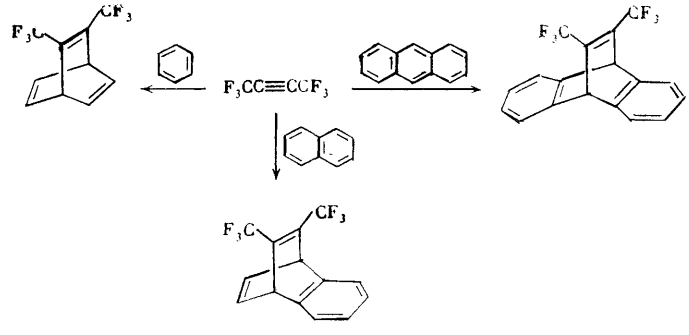


The structure of the product was established by X-ray analysis. The reaction of hexafluoro-2-butyne with five-membered and six-membered silacyclodienes proceeds in the first phase to give the expected [4+2]-adduct, which may be transformed on heating, as exemplified below:[339,340]



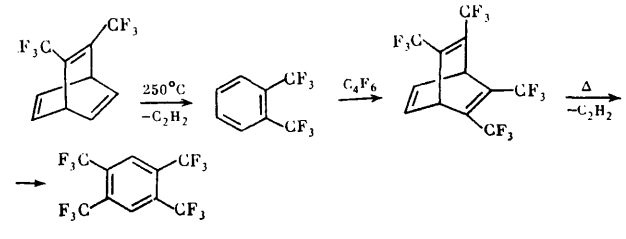
The reaction with germanium-containing analogues proceeds in the same way.[341]

Hexafluoro-2-butyne serves as an active dienophile towards aromatic hydrocarbons: benzene, toluene, xylene, 1,2,5-trimethylbenzene, durene, *p*-(polymethylene)benzenes, naphthalene and anthracene. The cycloaddition takes place at 150–200 °C.[342–344]



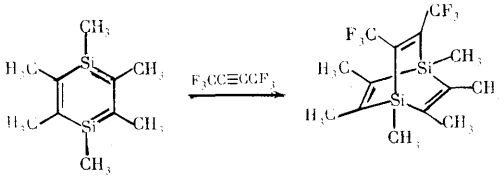
1,12-Dihydroeicosafluoro-6-dodecyne also reacts with aromatic hydrocarbons.[343]

On increasing the temperature, the adducts eliminate acetylene to give, for example, 1,2-*bis*- and 1,2,4,5-*tetrakis*-(trifluoromethyl)-benzene:[343]

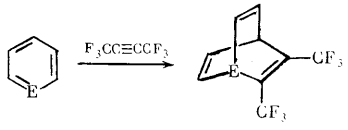


The reaction of hexafluoro-2-butyne with a number of six-membered heteroarenes has also been reported. Here, the conditions of the cycloaddition are dependent on the nature of the heteroatom.

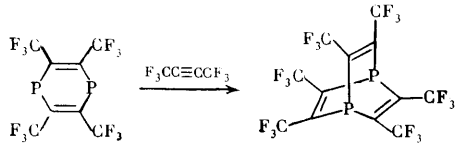
Hexamethyl-1,4-disilabenzene reacts with hexafluoro-2-butyne in the same way as benzene:[345]



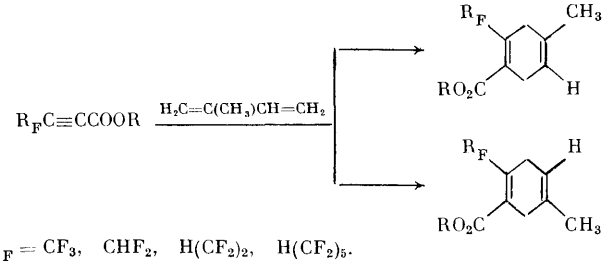
Hetero-analogues of benzene with a Group V element in the ring react under much milder conditions:[346–348]



E = P (at 100 °C); As (at room temp.); Sb, Bi (at 0 °C)



Diene syntheses with perfluoroacetylenecarboxylic acids and their esters as dienophile have been carried out with cyclopentadiene,[349] isoprene, 2,3-dimethylbutadiene and furan.[144] The carboxyl group determines the orientation of cycloaddition, as in other reactions with such acetylene derivatives. In the case of isoprene, the ratio of regioisomers is in the range 2.7 to 1.8, the ratio decreasing as the size of the substituent increases.[144] The resulting products have been used for the synthesis of substituted phthalic acids.[350]

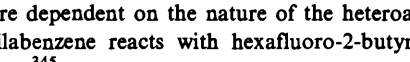


R_F = CF_3, CHF_2, $H(CF_2)_2$, $H(CF_2)_5$.

Diene synthesis with trifluoromethyl-substituted diacetylenes has been studied with two non-conjugated compounds—1,1,1-trifluoro- and 1,1,1-trifluoro-4,4-dimethyl-2,5-heptadiyne—and two conjugated compounds—1,1,1-trifluoro-6-methyl- and 1,1,1-trifluoro-6,6-dimethyl-2,4-heptadiyne.[76,151] There was no reaction between non-conjugated diynes and cyclopentadiene at room temperature. Only the triple bond substituted by the trifluoromethyl group is active at 100–150 °C. Dicyclopentadiene is formed as a by-product. Conjugated alkadiynes react with cyclopentadiene even at room temperature, again with participation of only the trifluoromethyl-substituted triple bond.[76,151]

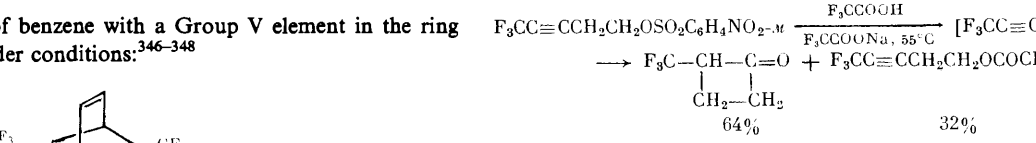
8. Molecular rearrangements

Trifluoromethyl-acetylenes,[16,202] -diacetylenes,[75] and allyltrifluoromethylacetylenes[217] undergo prototropic isomerisation in the presence of a catalytic amount of base. The triple bond is thus shifted away from the trifluoromethyl group:

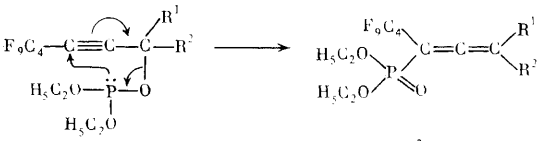


Perfluoropropyne isomerises to perfluoroallene on treatment with CsF.[17] The same isomerisation takes place during the preparation of other perfluoroacetylenes.[128]

β-Carbenium ions, formed from perfluoroalkylacetylenes, are converted to cyclobutane derivatives as a consequence of the high electron-accepting character of the perfluoroalkyl group.[86]



Acetylene-allene rearrangement takes place with certain functionalised perfluoroalkylacetylenes, for example:[351]



$R^1 = R^2 = CH_3$; $R^1 = CH_3$, $R^2 = C_2H_5$; $R^1 = R^2 = H$; $R^1 = H$, $R^2 = CH_3$.

9. Complex formation

As a result of the high electrophilicity of perfluoroalkyl(aryl)-acetylenes, the latter undergo complex formation with metals of the platinum sub-group (Pt, Pd, Ir, Ru, Rh, Os), the iron group (Fe, Co, Ni), and many other metals (Mo, W, V, Ti, Mn, Au). Group VIII complexes with hexafluoro-2-butyne have been studied most of all. The chemistry of these complexes has already been reviewed in detail,[5,6,352–354] and the volume of data in this field is too great to be incorporated in any way in this review.

Partial protection of multiple bonds by complexation with $Co_2(CO)_8$ has been widely applied in recent years as a device to increase the regioselectivity of reactions with such compounds.[355,356] However, complexes formed from trifluoromethyl- and pentafluorophenyl-substituted alkynes do not demetalate by the usual routes, and thus have a limited synthetic value.[357–361] However, such complexes may undergo certain reactions which the parent alkynes do not. For example, complexes formed with trifluoromethyl- and pentafluorophenyl-acetylenealcohols readily dehydrate to novel conjugated trifluoromethyl- and pentafluorophenyl-alkenynes, which are converted to the corresponding nitroalkenynes on treatment with $Fe(NO_3)_3.9H_2O$.[358–360] Dehydration of the trifluoromethylacetylene-alcohols is accompanied by partial dimerisation of the resulting enyne complex.[361]

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In this review, it has been noted that perfluoroalkyl(aryl)-acetylenes do not readily add halogens by an electrophilic mechanism. Such additions require radical conditions. In the addition of mixed halogens (IF, ICl) and pseudohalogens (e.g. ICN) to terminal perfluoroalkylacetylenes, the regioselectivity is not determined by the polarisation of the triple bond: attack by the cation proceeds at the terminal carbon atom. However, hydrogen halides add quite smoothly to perfluoroalkyl(aryl)acetylenes in the

presence or absence of catalysts normally used for electrophilic addition. Here, the regioselectivity of the process is in accord with polarisation factors.

Contrasting with the reactions of electrophilic reagents, nucleophiles add to perfluoroalkyl(aryl)acetylenes more readily than to alkynes, even at low temperatures. Here also, the regioselectivity is in accord with the polarisation of the triple bond.

Fluoride ion plays an important role in the reactions of perfluoroalkyl(aryl)acetylenes. The anions formed as a result of addition of fluoride ion (to reagent or substrate) participate readily in a variety of additions and cyclisations.

The addition of nucleophiles to trifluoromethyldiacetylenes does not proceed in a manner as would be anticipated with a strongly polarised conjugated system. The triple bond substituted by a trifluoromethyl group is more active than a non-perfluoroalkylated triple bond. Only by nucleophilic attack of the trifluoromethylated triple bond does a transition state develop with the participation of the entire conjugated system.

Perfluoroalkyl(aryl)acetylenes are highly active in pericyclic reactions. They participate in diene syntheses, even at room temperature, and take part in both 1,3-dipolar and anionic cycloaddition. The regioselectivity of the cycloaddition of perfluoroalkylacetylenes to unsymmetrically substituted dienophiles and dipolarophiles is in accord with polarisation factors, but with perfluoroalkyldiacetylenes mixtures of regioisomers are formed.

A special mention has been made of the usual reactions of perfluoroalkyl(aryl)acetylenes with non-metals—sulphur, selenium, phosphorus and arsenic—from which heterocyclic compounds have been isolated.

The study of addition reactions with perfluoroalkylacetylenes and perfluoroalkyldiacetylenes has made a significant contribution to the generalised theory of addition to unsaturated compounds: the regioselectivity of addition is not always in accord with polarisation factors, even where the triple bond is highly polarised, as has been seen in certain reactions with perfluoroalkylacetylenes and, especially, with diacetylenes.

Many of the properties of perfluoroalkyl(aryl)acetylenes have been widely utilised in organic synthesis, and there is much potential for even broader application. Undoubtedly, these compounds will play a more significant role in the next ten years in various fields of research as more and more is understood of the effect of perfluoroalkyl and perfluoroaryl substitution on chemical, physical and physiological properties.

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Translated from *Uspekhi Khimii* 60 1049–1076 (1991) U.D.C. 547.297 + 541.49 + 541.452

The structure of equimolar complexes of acyl halides with Lewis acids

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ABSTRACT. The results of studies on the structures of equimolar complexes of acyl halides with Lewis acids in the solid state and in solutions are surveyed. The methods for the identification of acylium salts and donor–acceptor complexes as well as the factors influencing the equilibrium between them are examined. Communications reporting the formation of complexes of other types in acyl halide–Lewis acid systems are reported and are discussed critically.

The bibliography includes 102 references.

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I. Introduction

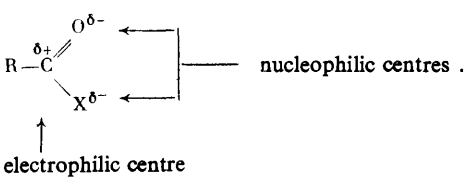
The discovery by Friedel and Crafts towards the end of the past century of the activating effect of aluminium chloride on acid halides initiated the fruitful application of the $RCOX-MX_n$ systems (RCOX = acyl halide, MX_n = Lewis acid) in organic synthesis. The continued interest in these systems is associated mainly with their use in the acylation of arenes, which is a classical method of synthesis of aromatic ketones.[1–4] The systems $RCOX.MX_n$ have also found applications in reactions with olefins, acetylenes, and other unsaturated compounds, which lead to saturated and unsaturated ketones, aliphatic haloketones, oxonium and pyrylium salts, etc.[2,5,6] The reactions of the complexes $RCOX.MX_n$ with unsaturated compounds have not lost their immediate interest, the region of their application is being expanded, and the study of their mechanisms is being continued at the present time.[5–16]

By virtue of studies on the $RCOX.MX_n$ systems, initiated as early as the beginning of the century and developed to the greatest extent in 1960's–1970's by Susz, Cook, Olah, Carpentier, Boer, Weiss, Corriu, and others, considerable advances have been achieved in the understanding of the mechanism of the interaction of acyl halides with Lewis acids and in the determination of the structures of the complexes formed under these conditions. However, even now many important problems concerning the structures of these complexes remain unsolved.

The structure of the complexes $RCOX.MX_n$ has been the subject of many reviews and chapters in monographs.[2,5,7,17,18] Unfortunately none of them is sufficiently complete and many unsolved problems and contradictory data have not been dealt with in the reviews quoted. Such reviews are lacking in the Soviet literature. Furthermore, during the last decade the interest in the complexes of acyl halides with Lewis acids has increased greatly because it has been found that the conversion of the complexes $RCOX.MX_n$ into the complexes $RCOX.2MX_n$ is accompanied by an abrupt increase in their reactivity. The complexes $RCOX.2MX_n$, which have been called aprotic organic superacids, have higher reactivities in reactions with alkanes and cycloalkanes than all the known systems based on AlX_3 (including $RCOX.MX_n$) and also, as a rule, the strongest protic superacids.[19] Taking the foregoing into account, we believe it useful to publish a review on this topic. The structure of aprotic organic superacids (the complexes $RCOX.2AlX_3$), the types of reactions of alkanes and cycloalkanes initiated by them, and also the nature of the superacid properties of these complexes will not be considered here. That range of problems merits an independent review.

II. Interaction of acyl halides with Lewis acids. The structures of the postulated complexes

Acyl halides are amphoteric and are capable of reacting as both Lewis acid and Lewis bases:



The electrophilic centre of the molecule is the carbonyl carbon atom, while the nucleophilic centres are the oxygen and halogen atoms, the greatest electron density being concentrated on the oxygen atom.[5,20]

In conformity with their nucleophilic nature, acyl halides react with a wide range of Lewis acids. The first well characterised complex having the composition $RCOX.MX_n$ was obtained in 1943 by Seel[21] in the reaction of AcF and BF_3. On the basis of the results of elemental analysis and conductimetric measurements, the ionic salt structure $CH_3CO^{\oplus}BF_4^{\ominus}$ was attributed to the complex. It was

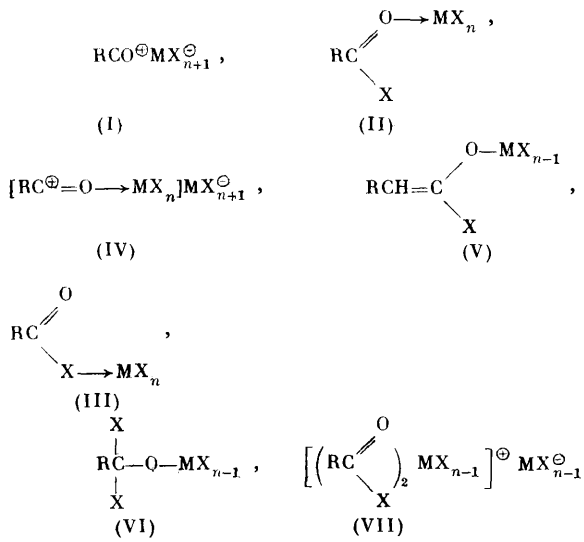
subsequently confirmed by other physicochemical methods. Certain 1:1 $RCOX.MX_n$ complexes and their constants are presented in Table 1.

Table 1. The properties of certain adducts $RCOX.MX_n$ (1:1).

Adduct	M.p., °C	Decomp. temp., °C	Refs.
$CH_3COCl \cdot AlCl_3$	65	–	[22]
$2\text{-}CH_3C_6H_4COCl \cdot AlCl_3$	55	–	[23]
$2,6\text{-}(CH_3)_2C_6H_3COCl \cdot AlCl_3$	82	–	[23]
$CH_3COCl \cdot GaCl_3$	86	–	[24]
$PhCOCl \cdot GaCl_3$	47	–	[24]
$CH_3COCl \cdot BCl_3$		–50	[24]
$CH_3COF \cdot BF_3$	–	20	[21]
$PhCOF \cdot BF_3$	–	–30	[25]
$CH_3COCl \cdot TiCl_4$	20	–	[26]
$C_3H_7COCl \cdot TiCl_4$	–4	–	[26]
$2\text{-}CH_3C_6H_4COCl \cdot TiCl_4$	70	–	[23]
$CH_3COF \cdot AsF_5$	175	–	[25]
$PhCOF \cdot AsF_5$	158	–	[25]
$CH_3COF \cdot PF_5$	–	30	[25]
$PhCOF \cdot PF_5$	–	–15	[25]
$CH_3COF \cdot SbF_5$	173	–	[25]
$PhCOF \cdot SbF_5$	150	–	[25]
$(CH_3)_3CCOF \cdot SbF_5$		20	[27]
$F_2CHCOF \cdot SbF_5$	–	50	[28]

The reactions of acyl halides with the halides of Group III–V elements (BF_3, BCl_3, $AlCl_3$, $AlBr_3$, $GaCl_3$, $GaBr_3$, $TiCl_4$, SbF_5, $SbCl_5$, AsF_5, PF_5, etc.), which lead, as a rule, to the equimolar adducts $RCOX.MX_n$, have been the most thoroughly investigated. The structures proposed for the adducts are presented in Scheme 1 below.[17]

Scheme 1



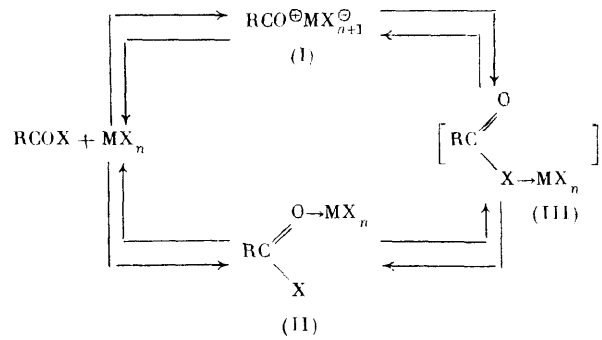
(I) (II) (IV) (V) (III) (VI) (VII)

It has now been shown by IR and NMR spectroscopy and also by X-ray diffraction that the stable 1:1 adducts $RCOX.MX_n$ exist in one of two forms: either as acylium salts (I) or as coordination complexes (II).[1,5–7,17,18] None of the postulated complexes (II)–(VII) has been detected in the study of a wide range of $RCOX.MX_n$ systems. In the study of the $FCH_2COF-SbF_5$ system by NMR, Olah[28] demonstrated in only one instance that three complexes coexist simultaneously in the system and attributed to them the structures of complexes (I), (II), and (III), (Scheme 2).[28] However, the final conclusion concerning the existence of type (III) complexes can apparently be reached only if its structure can be demonstrated by direct method.

The conversion of acyl halides by Lewis acids into the "Illary complexes" (V) has been postulated.[29,30] Susz and co-workers[31] investigated very carefully the possibility of the presence of the "Illary complex" in the $AcCl.AlCl_3$ system and showed that it is not formed at room temperature. Thus type (V) complexes as well as the other hypothetical complexes (IV), (VI), and (VII) could not be detected in any of the systems investigated.

The formation of the acylium salt (I) and of the coordination complex (II) corresponds to two possible pathways in the reactions of acyl halides with a Lewis acid. Attack on the first nucleophilic centre of the RCOX molecule (the halogen atom), accompanied by the heterolysis of the C–X bond, leads to the acylium salts (I), whilst attack on the second nucleophilic centre (the oxygen atom of the carbonyl group) leads to the formation of a donor–acceptor complex (II) as a result of the coordination of MX_n to the *n*-electron pair of the oxygen atom.

Scheme 2



The position of the equilibrium (I) ⇄ (II) depends on many factors: the strength of the Lewis acid MX_n, the nature of the groups R and X in RCOX, temperature, and (in solutions) also on the nature of the solvent (see Section VI).

All these factors determine whether or not the $RCOX.MX_n$ system exists exclusively as one of the complexes (I) or (II) or whether an equilibrium is established in which both structures contribute appreciably.

III. Acetylium cations. Quantum-chemical calculations

The simplest ionic products of the interaction of acyl halides with Lewis acids are acetylium salts containing the cation $CH_3CO^{\oplus}$, because the first member of the homologous series — the formylium cation $HCO^{\oplus}$ — could not be obtained as part of the composition of a stable compound.[32]

The cation having the empirical formula $C_2H_3O^{\oplus}$ can have a series of isomeric structures,[33–35] but only the cation $CH_3C^{\oplus}=O$ and the 1-hydroxyvinyl cation $CH_2=C^{\oplus}-OH$, which exist in the form of stable long-lived species, have been detected directly. Calculations

of the energies of the ions $C_2H_3O^{\oplus}$ by the *ab initio* method showed that the cation $CH_3C^{\oplus}=O$ corresponds to the minimum energy and that the ion $CH_2=C^{\oplus}-OH$ is the second as regards stability.[34,36]

The acetyl cation can be regarded as a hybrid of the three resonance structures (A'), (A"), and (A"'), which correspond to different locations of the positive charge (Scheme 3). In the carboxonium ion (A') the charge is concentrated on the oxygen atom, in the oxocarbenium ion (A") it is concentrated on the carbonyl carbon atom, while in the ion of the C-protonated ketene (A"') it is concentrated on the hydrogen atoms of the methyl group (hyperconjugation of the C–H β-bonds and the cationic centre):

Scheme 3

$$\underset{(A')}{CH_3C{\equiv}O^{\oplus}} \longleftrightarrow \underset{(A'')}{CH_3C^{\oplus}{=}O} \overset{H^{\oplus}}{\longleftrightarrow} \underset{(A''')}{CH_2{=}C{=}O}\ .$$

The foregoing is valid also for other ionic structures $RCO^{\oplus}$. The contribution of each resonance form to the real structure of the ion $RCO^{\oplus}$ depends to a large extent on the nature of the group R linked to the carbonyl and will be considered in Sections (IV.1) and (V.2).

IV The structure of equimolar complexes of acyl halides with Lewis acids according to X-ray diffraction data

1. The structure of acylium salts $RCO^{\oplus}MX^{\ominus}_{n+1}$

The existence of the ionic complexes (I) and the donor–acceptor complex (II) has been demonstrated by the direct X-ray diffraction method.[37–49] The first crystallographic determination of the structure of an acylium salt was achieved for acetylium hexafluoroantimonate by Boer.[45,46] Although the accuracy of this study, carried out by a photomethod, and the conclusions concerning the electron density distribution obtained on its basis are doubtful,[17] its principal result, indicating a truly ionic structure of the acylium salt, is incontrovertible.

Fig. 1 presents the structure of the acylium salt. Table 2 summarises the principal results of X-ray diffraction studies on ionic acylium salts (I).

As can be seen from Fig. 1 and Table 2, there is a chemical bond between the cation and the anion in the acylium salts. The C(2)–C(1)–O fragment has a linear structure corresponding to the *sp* hybridisation of the carbonyl carbon atom C(1). Thus the C(2)–C(1)–O angles are in all cases close to 180° and the C(1)–O bonds (~1.11 Å) are appreciably shorter than the $C_{sp^2}=O$ bond (1.20 Å for ketones and 1.17 Å for haloacyls[50,51]); the C(1)–O bonds in acylium cations are actually somewhat shorter than in the CO molecule (1.128 Å [45]) (Table 2).

The structure of the anionic fragment is close to a tetrahedron ($AlCl_4^{\ominus}$ and $GaCl_4^{\ominus}$) or an octahedron ($SbX_6^{\ominus}$) and the Al–Cl, Ga–Cl, and Sb–Cl bond length are close to the corresponding values for inorganic salts.

It follows from Table 2 that the C(1)–O bond lengths in various acylium salts are similar (~1.11 Å). On the other hand, the C(1)–C(2) bond length depends to a considerable extent on the nature of the group in which the C(2) atom is incorporated. For R = alkyl, the bond length is in the range 1.44–1.45 Å [the unduly short length quoted for the C(1)–C(2) bond in the compound $CH_3CO^{\oplus}SbF_6^{\ominus}$ is doubtful]. The closeness of these values to the $C_{sp^3}-C_{sp}$ bond length in the isoelectronic $CH_3C{\equiv}CH$ and $CH_3-C{\equiv}N$ molecules (1.46 Å [43,50]) does not provide grounds for the assertion that the resonance ketene form (A"') makes a contribution (see Scheme 3) to the structure of acylium salts in the crystal.[43,47,48] This conclusion is wholly confirmed by the ideal tetrahedral geometry at the C(2) atom.

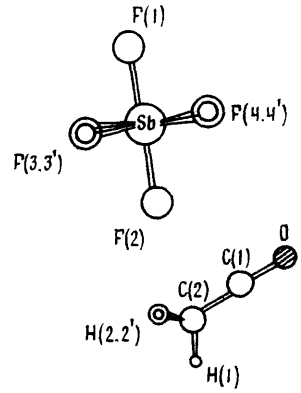
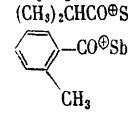
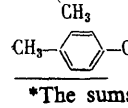


Figure 1. The structure of acetylium hexafluoroantimonate $CH_3CO^{\oplus}SbF_6^{\ominus}$.

Table 2. Geometrical parameters of the acylium salts $RCO^{\oplus}MX^{\ominus}_{n+1}$ (I) according to X-ray diffraction data.

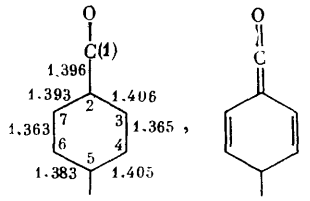
$RCO^{\oplus}MX^{\ominus}_{n+1}$	Bond lengths, Å		Minimum distances between non-bonded atoms*, Å			C(2)–C(1)–O angle, deg	Refs.
	C(1)–O	C(1)–C(2)	Cl–C(1)	Cl–O	Cl–C(2)H$_3$		
$CH_3CO^{\oplus}SbCl_6^{\ominus}$	1.109	1.452	3.34	3.58	3.55	180.0	[43,44]
$CH_3CO^{\oplus}AlCl_4^{\ominus}$	1.11 *	1.45 *	3.33	3.43	3.49	179.8	[43]
$CH_3CO^{\oplus}SbF_6^{\ominus}$	1.108	1.385				177.2	[45,46]
$CH_3CH_2CO^{\oplus}GaCl_4^{\ominus}$	1.099	1.435	3.42	3.43	3.51	177.7	[47]
$(CH_3)_2CHCO^{\oplus}SbCl_6^{\ominus}$	1.116	1.439	3.27	3.43	3.58	175.7	[47,48]
	1.111	1.387	3.31	3.42		178.7	[49]
	1.097	1.396	3.29	3.35		179.4	[41]

*The sums of the van der Waals radii are $r(C_{sp^2}-Cl)$ = 3.4 Å, $r(Cl-O)$ = 3.2 Å, and $r(C_{sp^3}-Cl)$ = 3.8 Å.

**Only the C(2)–O distance has been determined (2.56 Å). However, taking into account the constancy of the C(1)–O distances (1.11 Å), the C(2)–C(1) bond length was assumed to be 1.45 Å.[43]

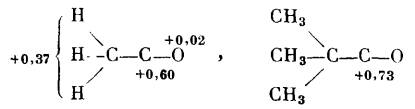
The structural data for the aryl cations $ArCO^{\oplus}$ leads to the opposite conclusion. It follows from Table 2 that in this case the C(1)–C(2) bond is somewhat shorter (~1.39 Å) than the $C_{sp^2}-C_{sp}$

bond in the isoelectronic PhC≡N (1.42 Å [50,51]). At the same time a shortening of the C(3)–C(4) and C(6)–C(7) bonds in benzene rings has been observed, which indicates a contribution by ketene-like structures:



X-Ray diffraction data also yield valuable information about the distribution of electron density in acylium cations. Thus comparison of the distances in the intramolecular contacts between non-bonded atoms shows that the C(1)–Cl and CH_3–Cl distances are almost always smaller than the sum of the corresponding van der Waals radii. On the other hand, the Cl–O distances exceed the sum of the van der Waals radii of Cl and O (Table 2). Thus structural data show that the positive charge in the cation $CH_3CO^{\oplus}$ is located mainly on the C(1) atom and the hydrogen atoms at C(2), which confirms the importance of the resonance forms (A″) and (A‴) [but not (A′)] in the crystal structures of acylium salts (see Scheme 3).

This conclusion agrees with the results of quantum-chemical calculations of the distribution of electron density in the cations $CH_3CO^{\oplus}$ and $(CH_3)_2CHCO^{\oplus}$ by the *ab initio* method,[33] whose results are presented below:



Calculation shows that the positive charge in the acylium cation is concentrated mainly on the carbon atom, while the oxygen atom is almost electrically neutral and the hydrogen atoms acquire an appreciable positive charge, shielding the C(2) atom.

It is noteworthy that the quantum-chemical calculations for the $RCO^{\oplus}$ structure (R = alkyl)[33] agree well with experimental bond lengths and angles quoted above (Table 2) for the $CH_3CO^{\oplus}$ cation. Another distribution of electron density in the $CH_3CO^{\oplus}$ ion, obtained on the basis of Boer's results,[45] appears less likely, since, according to these data, the charge on the hydrogen atoms (+0.07) in $CH_3CO^{\oplus}$ is close to the charge on the hydrogen atoms in ethane, which conflicts with the results of other studies indicating an appreciable deshielding of these atoms.

2. The structure of the donor–acceptor complexes RC(X)=O → MX_n

Fig. 2 illustrates the structure of the donor–acceptor complex and Table 3 lists the principal geometrical parameters of the type (II) complexes investigated.

X-Ray diffraction data demonstrate that the Lewis acid is coordinated to the electron pair of the oxygen atom. This is confirmed unambiguously by the presence of the M–O bonds. Thus the Al–O bond lengths in the type (II) complexes (1.820–1.847 Å) exceed only slightly the Al–O bond lengths in stable compounds such as aluminosilicates (1.79 Å). On the other hand, the Sb–O bonds (2.3–2.4 Å) in complexes (III) are significantly longer than, for example, in the complexes $Cl_3P{=}O \rightarrow SbCl_5$ (2.17 Å [52]) and $Me_3P{=}O \rightarrow SbCl_5$ (1.94 Å [53]), which indicates a lower stability of the complexes of acyl halides with acids such as $SbCl_5$ compared with $AlCl_3$.

Complex formation via the oxygen atom leads to the lengthening of the C(1)–O bond (1.21–1.24 Å) compared with the length 1.17 Å in the non-coordinated RCOX,[50] the C(1)–O bond lengths [as well as the C(1)–Cl bond lengths] in the adducts being distinguished by a marked constancy, which apparently indicates a similar strength of the C(1)–O bonds in type (II) complexes.

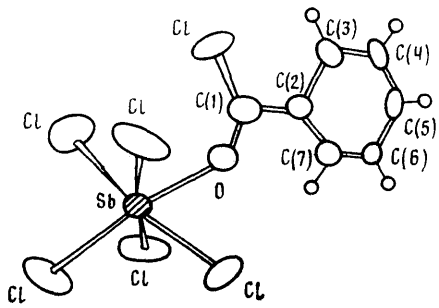


Figure 2. The structure of a type (II) coordination complex: $PhC(Cl){=}O \rightarrow SbCl_5$.

The C(1)–C(2) bond length in the CH_3CH_2–C(Cl)=O → $AlCl_3$ is close to the length of the classical C_{sp^3}–C_{sp^2} bond (1.49 Å [54]), while the Ar–C(1) bonds in ArC(X)=O → MX_n are appreciably shortened compared with C_{sp^2}–C_{sp^2} (1.47 Å [50]).

An important feature of the geometry of the donor–acceptor complexes is the appreciable increase of the M–O–C(1) angles (142–176°) compared with the value 120° characteristic of the sp^2-hybridised oxygen atom. Such a marked distortion of the angles has been attributed[41] to the steric effects observed in the packing of the crystal. On the other hand, the deformations of the angles at the carbonyl carbon atom C(1) are small. The $OAlCl_3$ and $OSbCl_5$ fragments have the geometries of a somewhat distorted tetrahedron and octahedron respectively.

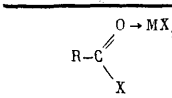
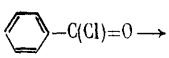
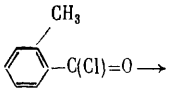
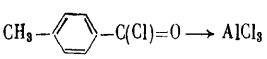
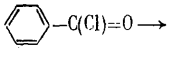
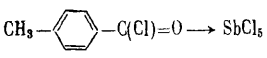
Thus the X-ray diffraction method yields valuable information about the structures of complexes (I) and (II) in the crystalline state.

V. Spectroscopic studies on the structures of the complexes RCOX.MX_n

1. ^{81}Br NQR study of the complex AcBr.$AlBr_3$

A single example of the application of the ^{81}Br NQR method to the study of the structures of complexes of the type RCOX.MX_n, namely AcBr.$AlBr_3$ at 77 K, has been described.[55] The spectrum of this complex lies in the same frequency range as that of the salt $KAlBr_4$.[56] Frequencies in the region corresponding to the vibrations of the C–Br bonds are not then observed at all, so that the presence of free AcBr and of the coordination complex $CH_3C(Br){=}O \rightarrow AlBr_3$ can be fully excluded. Thus at 77 K the complex AcBr.$AlBr_3$ consists of the ionic acetylium salt $Ac^{\oplus}AlBr_4^{\ominus}$. It follows from the multiplicity and relative intensities of the lines

Table 3. Geometrical parameters of the donor–acceptor complexes $RC(X)=O \rightarrow MX_n$ (II) according to X-ray diffraction data.

 (II)	Bond lengths*, Å			Angles, deg				Refs.
	M–O	C(1)–O	C(1)–C(2)	M–O–C(1)	O–C(1)–C(2)	O–C(1)–Cl	C(2)–C(1)–Cl	
$CH_3CH_2C(Cl)=O \longrightarrow AlCl_3$	1.847	1.221	1.488	141.6	124.5	119.1	116.1	[37]
	1.820	1.226	1.420					[38]
	1.824	1.235	1.442	146.2	124.3	117.0	118.7	[39]
	1.828	1.235	1.432	144.6	122.4	118.5	119.1	[39]
	2.317	1.236	1.453	145.9	121.0	121.1	117.9	[40]
	2.253	1.220	1.434	146.6	122.3	119.4	118.3	[41]
$(CH_2C(Cl)=O \longrightarrow SbCl_5)_2$	2.428	1.211	1.508	175.8	123.9	123.1	113.0	[42]

* The C–Cl bond lengths are similar for all the complexes, amounting to 1.71–1.72 Å.

that the unit cell contains two crystallographically independent $AlBr_4^{\ominus}$ anions. Above 77 K, the NQR spectrum cannot be observed, probably owing to the intense molecular movements in the crystal.

The same complex, obtained in an excess of CH_2Br_2, retains in the solid state its acylium structure, which differs, however, from the structure of the complex obtained in the absence of CH_2Br_2. The difference consists in the fact that, in the complex obtained in CH_2Br_2, the anion $AlBr_4^{\ominus}$ is additionally coordinated to the CH_2Br_2 molecule, i.e. the complex formed has the structure $Ac^{\oplus}[AlBr_4 \rightarrow CH_2Br_2]^{\ominus}$. Such interaction of the anion with a solvent molecule is manifested by a hypsochromic shift of the four lines corresponding to $AlBr_4^{\ominus}$ and by a decrease in the vibration frequency of the C–Br bond of methylene bromide.

However, the most extensive information about the structure of the complexes $RCOX.MX_n$ in the solid state and even more so in solution has been obtained by NMR and IR spectroscopy.

2. Identification of acylium salts by vibrational spectroscopy

As already mentioned, complex formation has an appreciable influence on the length of the C=O bond in RCOX, whose multiplicity increases in the acylium salts (I) and decreases in the donor–acceptor complexes (II). Accordingly, the formation of the acylium salt (I) is accompanied by a hypsochromic shift of the stretching vibration frequencies [ν(CO)] in RCOX, while the formation of complex (II) is accompanied by a bathochromic shift of this frequency.

Acylium salts can be clearly identified from the manifestation of an intense absorption in the frequency range 2200–2300 cm^{-1} corresponding to the stretching vibrations of the $[C=O]^{\oplus}$ bond (Table 4) and the vibrations of the M–X bonds in the anions $MX_4^{\ominus}$ or $MX_6^{\ominus}$.[1,5,7,17] This is accompanied by the disappearance of the stretching vibration frequencies of C=O [ν(CO) = 1750–1850 cm^{-1}] and C–X of the non-coordinated RCOX, while the stretching vibration frequencies of the C–H and C–C bonds are altered.

Although the appearance of a new high-frequency absorption undoubtedly indicates the formation of complexes (I), a complete interpretation of the absorption bands in the above region encountered serious difficulties for a long time. The point is that not one but two frequenices are very frequently observed in the range 2200–2300 cm^{-1} (Table 4).

In order to account for the presence of two frequencies, at ~2300 and ~2200 cm^{-1}, in the $AcCl.AlCl_3$ system, Cook[63,68] suggested that, apart from the acylium salt, complex (IV) is present (Scheme 1). In this complex the electron-deficient $CH_3CO^{\oplus}$ cation is additionally coordinated to the $AlCl_3$ molecule:

$$\underset{(I)}{CH_3CO^{\oplus}AlCl_4^{\ominus}} \quad \underset{(IV)}{[CH_3C^{\oplus}=O \rightarrow AlCl_3]Cl^{\ominus}}$$

$\nu(CO) = 2203\ cm^{-1}$, $\nu(CO) = 2307\ cm^{-1}$.

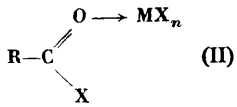
In contrast to Cassimatis's assignment,[62,66] Cook assigned to the $CH_3CO^{\oplus}$ cation the vibration with frequency ν(CO) = 2203 cm^{-1}, while frequency ν(CO) = 2307 cm^{-1} was assigned to complex (IV).[63,68]

Assuming that the formation of complex (IV), via the complex formation reaction between the electron-deficient species $CH_3CO^{\oplus}$ and the Lewis acid, is unlikely, Cassimatis[62,66] proposed the existence in equilibrium with the acetylium salt of its resonance hybrid, the cationic form (A‴) predominating:

$$\underset{2200\ cm^{-1}}{CH_3CO^{\oplus}} \rightleftarrows \underbrace{\{\underset{(A')}{CH_3C{\equiv}O^{\oplus}} \longleftrightarrow \underset{(A'')}{CH_3C^{\oplus}=O} \longleftrightarrow \underset{(A''')}{CH_2=C=O\overset{H^{\oplus}}{\}}}}_{2300\ cm^{-1}}.$$

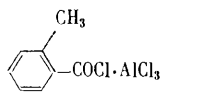
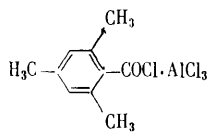
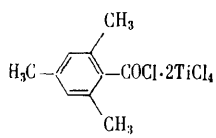
However, the hypothesis of the existence of two resonance structures as two individual complexes appears to be at least peculiar.

Table 4. Parameters of the IR spectra of certain



(II)

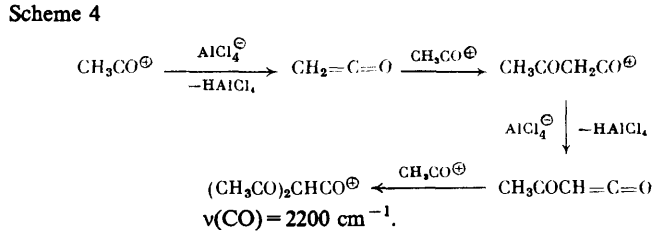
and $RCO^{\oplus}MX_{n+1}^{\ominus}$ (I) systems without a solvent.

$RCOX \cdot MX_n$	ν(CO), cm^{-1}		Refs.
	(II)	(I)	
$CH_3COF \cdot SbF_5$	1621 w; 1554 w	2294 s	[25]
$CH_3CH_2COF \cdot SbF_5$	1610 m	2290 s	[25, 57]
$(CH_3)_3CCOF \cdot SbF_5$	1570 m	2260 s	[27]
$PhCOF \cdot SbF_5$	1546 s; 1531 m	2212 s	[25, 57]
$PhCH_2COF \cdot SbF_5$	1599 m; 1516 m	2279 s	[27]
$SbF_5 \cdot FOC(CH_2)_3COF \cdot SbF_5$	—	2290 s	[58]
$CH_3COF \cdot AsF_5$	1620 w; 1558 w	2302 s	[25]
$CH_3COCl \cdot SbCl_5$	1709 m; 1587 w	2283 s	[25, 59]
$PhCOCl \cdot SbCl_5$	1656 s; 1575 s	2215 w	[25]
$CH_3COF \cdot BF_3$	1619 m; 1560 w	2299 s	[60, 61]
$CH_3COCl \cdot AlCl_3$	1639 m; 1560 w	2305 s	[31]
$CH_3COCl \cdot AlCl_3$	1633 s; 1560 s	2300 s; 2200 s	[62]
$CH_3COCl \cdot AlCl_3$	1637 s; 1567 s	2307 s; 2203 s	[39, 63, 64]
$PhCOCl \cdot AlCl_3$	1585 m; 1525 m	–	[23, 65]
	1602 m; 1525 m	2200 s	[23]
	1535 m	2190 s	[31]
$CH_3COBr \cdot AlBr_3$	1630 s; 1555 s	2300 s; 2200 w	[66]
$PhCOCl \cdot AlBr_3$	1540 s	—	[67]
$CH_3COCl \cdot GaCl_3$	1616 m; 1540 w	2300 s	[68]
$CH_3COCl \cdot TiCl_4$	1763 m*; 1620 s	–	[67, 69]
$PhCOCl \cdot TiCl_4$	1615 s; 1553 s	–	[23, 67]
	–	2170 s	[23, 67]

*This frequency is discussed in the text.

The controversial problem of the nature of the complex responsible for the appearance of the second absorption band in the range 2200–2300 cm^{-1} was successfully solved by Germain et al.[70,71] after it had been shown that, together with the acetylium salt $CH_3CO^{\oplus}AlCl_4^{\ominus}$ [ν(CO) = 2300 cm^{-1}], the product of the self-acylation of this salt—diacetylacetylium tetrachloroaluminate $(CH_3CO)_2CHCO^{\oplus}AlCl_4^{\ominus}$ [ν(CO) = 2200 cm^{-1}]—can be formed in the $AcCl-AlCl_3$ system. This process, which proceeds via the formation of the ketene form is illustrated in Scheme 4.

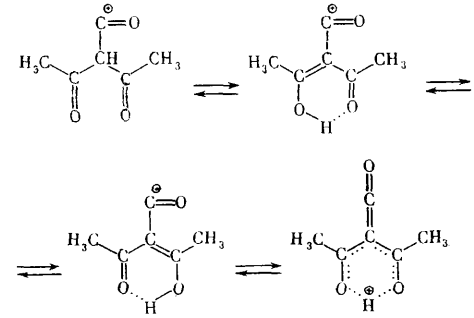
Scheme 4



ν(CO) = 2200 cm^{-1}.

The bathochromic shift of the absorption band of the $[C=O]^{\oplus}$ bond [ν(CO)] in the doubly acylated acylium salts relative to the corresponding bond in RCO^+ (R = alkyl) is quite reasonable if one takes into account the fact that in the given instance one should expect an appreciable contribution by the ketene-like limiting structure in which the $[C=O]^+$ bond has been lengthened:

Scheme 5



ν(CO) = 2200 cm^{-1}.

Both complexes, $CH_3CO^{\oplus}AlX_4^{\ominus}$ and $(CH_3CO)_2CHCO^{\oplus}AlX_4^{\ominus}$, were isolated in a pure form and were characterised. The self-acylation of the acetylium ion depends on the conditions under which the complexes are prepared, the nucleophilicity of the anion (thus self-acylation is not observed in the case of the weakly nucleophilic anion $SbF_6^{\ominus}$), and on the nature of R in $RCO^{\oplus}$ ($ArCO^{\oplus}$ does not form diacylated salts). The presence of the second frequency in the range 2200–2300 cm^{-1} is therefore not always observed (Table 4).

It follows from the foregoing that at the present time the IR spectra make it possible to detect reliably the formation of the ionic complexes (I). Table 5 lists the observed IR frequencies of the $CH_3CO^{\oplus}$ and $CD_3CO^{\oplus}$ ions and their assignments.[62]

Table 5. The assignments of the frequencies in the IR spectra of the cations $CH_3CO^{\oplus}$ and $CD_3CO^{\oplus}$.[62]

Frequency, cm^{-1}		Assignment
$CH_3CO^{\oplus}$	$CD_3CO^{\oplus}$	
2940 s	2209 s	ν(CH_3) (asym.)
2870 s	2049 s	ν(CH_3) (sym.)
2295 s	2297 s	ν(C=O)
1360 w	980 w	δ(CH_3) (asym.)
1319 s	1056 s	δ(CH_3) (sym.)
950 s	834 s	ν(C–C)
390 m	370 m	ν(C–C)

Analysis of the data in Table 4 shows that, with increase in the positive inductive effect of the group R in $RCO^{\oplus}$, which diminishes the charge on the carbonyl carbon atom, a bathochromic shift of the ν(CO) frequency is observed. For example, a bathochromic shift is

observed with increase in the number of methyl groups at the α-carbon atom:

	$(CH_3)_3CCO^{\oplus}$	$(CH_3)_2CHCO^{\oplus}$	$CH_3CH_2CO^{\oplus}$
ν(CO), cm^{-1}	2260	2270	2290

increase of the $+I$ effect of the group R

The factors promoting the stabilisation of the ketene form (A‴) also reduce the C–O bond order and hence lead to a bathochromic shift of the absorption band of this bond. Thus the lower frequencies [ν(CO) $\simeq$ 2200 cm^{-1}] for the cation $(CH_3CO)_2CHCO^{\oplus}$ or the cations $ArCO^{\oplus}$ compared with aliphatic acylium ions (Table 4) are due to the significantly greater contribution of the ketene structure.

3. Identification of donor–acceptor complexes by vibrational spectroscopy

As already mentioned, the formation of the $C=O\rightarrow MX_n$ donor–acceptor bond is accompanied by a bathochromic shift of the carbonyl group frequency (from 1750–1850 to 1560–1640 cm^{-1}).[1,5,7,17,18]

However, as can be seen from Table 4, not one but two frequencies are often observed in the range 1560–1640 cm^{-1}. The question of the assignment of these frequencies has been widely discussed in the literature but the situation is still not entirely clear. Different workers attribute different frequencies to the $\nu(C=O\rightarrow)$ vibration for the same complexes $RC(X)=O\rightarrow MX_n$: in the range 1560–1570 cm^{-1} according to Susz and Wuhrmann[31] and Cassimatis and Bonnin[62] or in the range 1620–1640 cm^{-1} according to the assignment by other workers.[43,63,64,68] Thus, in a study of the $AcCl.AlCl_3$ system in the solid state, Susz[31] observed in the IR spectrum, together with the intense frequency due to the acylium ion, a weak frequency at 1540 cm^{-1} and a very weak frequency at 1640 cm^{-1}. He suggested that the former refers to $\nu(C=O\rightarrow)$ for a type (II) donor–acceptor complex and the latter is caused by the formation of the product of the decomposition of the acylium salt—a type (V) "Illary complex" $CH_2=C(Cl)OAlCl_2$ and represents the stretching vibration frequency of the C=C bonds. However, the synthesis of the complex $AcCl.AlCl_3$ both at −15 °C and at 27 °C led to a product with the empirical formula $C_2H_3OAlCl_4$, i.e. the formation of an "Illary complex" was not confirmed and the problem of the assignment of the 1640 and 1560 cm^{-1} frequencies remained unsolved.

Another system investigated, namely $AcCl.TiCl_4$, did not contain acylium salts and the IR spectrum exhibited two absorption bands at 1620 and 1763 cm^{-1} which have undergone a bathochromic shift relative to ν(CO) for the non-coordinated carbonyl group in AcCl.[67,69]

Calculation of the force constants on the assumption that the 1620 cm^{-1} frequency is due to the $C=O\rightarrow TiCl_4$ coordinate bond led to more reasonable values than for the assignment of the 1763 cm^{-1} frequency to this bond.[69] The authors hypothesis that the 1763 cm^{-1} frequency is associated with the formation of a type (III) coordination complex via the chlorine atom appears to be unjustified, because the formation of such a complex should have been accompanied by a hypsochromic shift of the carbonyl frequency.

Susz[23,67] attributed the ν(CO) frequency in the range 1530 to 1560 cm^{-1} to the aromatic type (II) complexes $ArC(X)=O\rightarrow MX_n$ (MX_n = $AlCl_3$, $TiCl_4$, SbF_5), while in another study[72] frequencies in the range 1620–1630 cm^{-1} were assigned to ν(CO) for the weaker complexes $ArC(X)=O\rightarrow TiCl_4$ and it was noted that $SbCl_5$, being a stronger acceptor, induces a shift of the carbonyl frequency of the initial ArCOX by 210–220 cm^{-1}, while $TiCl_4$ gives rise to a shift of 140–150 cm^{-1}.

The identification of complexes (II) from the C–Hal bond vibrations presents an even greater difficulty. Furthermore, it is still not clear how ν(C–Cl) changes on coordination of MX_n to oxygen.

In most studies the appearance of a new ν(C–X) frequency on coordination of MX_n to oxygen is not reported at all. Cook[63] suggested that such coordination leads to the loosening of the C–Cl bond and to a pronounced bathochromic shift of this frequency to a region inaccessible to observation by IR spectroscopy. On the other hand, Jones and Wood[65] suggest that the force constant of the C–Cl bond increases on coordination of MX_n to oxygen and that ν(C–Cl) undergoes an appreciable hypsochromic shift. These workers attributed a value of 945 cm^{-1} to the ν(C–Cl) frequency in the spectrum of the complex $PhC(Cl)=O\rightarrow AlCl_3$ [for non-coordinated PhCOCl, ν(C–Cl) = 877 cm^{-1}].

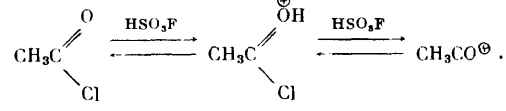
Cassimatis and Bonnin suggested[62] that the C–Cl bond in complexes (II) changes very insignificantly and attributed the low intensity vibration at 605 cm^{-1} to ν(C–Cl) for the complex $CH_3C(Cl)=O\rightarrow AlCl_3$ [ν(C–Cl) = 593 cm^{-1} for AcCl]. This second hypothesis that the C–Cl frequency changes only slightly (and that its intensity probably diminishes) appears more probable, since it agrees well with X-ray diffraction data indicating a small change in the C–Cl bond length on coordination to the oxygen atom.

Thus the disappearance of the frequency of the carbonyl group of the acyl halide and the appearance of a new frequency in the range 1530–1630 cm^{-1} indicate the formation of a donor–acceptor complex. However, a reliable assignment of the observed frequencies is as a rule extremely difficult.

One cannot rule out the possibility that, in the case of the acetyl complexes, the appearance of frequencies in the region 1530–1630 cm^{-1} of the IR spectrum may be due to the formation of the cation of protonated acetic acid $CH_3C(OH)_2^{\oplus}$ in the presence of traces of moisture.[73] This possibility is confirmed by the appearance of frequencies in the range 1550–1660 cm^{-1} after the addition of water to acylium salts.[58,74] The $RCOX.MX_n$ systems should therefore be studied in the complete absence of traces of moisture.

It is also necessary to take into account the fact that the salt optical components (especially NaCl and KBr glass) used to record IR spectra are not indifferent to the $RCOX.MX_n$ complexes. This probably explains the partial discrepancies between the IR spectra of the same systems in different publications and the at first sight paradoxical data showing that the crystals of individual complexes (I) exhibit in their IR spectra the presence, apart from their own frequencies, also of those complexes (II).[43]

This disadvantage in the study of the $RCOX.MX_n$ systems can be avoided by using Raman spectroscopy, which permits measurements in sealed glass tubes. Unfortunately Raman spectroscopy has not yet come to be widely used for the study of the $RCOX.MX_n$ complexes and similar systems. As examples of its employment, one may only quote isolated studies.[59,75] Thus, in a study of the spectra of solutions of AcCl in strong Brønsted acids (FSO_3H, $ClSO_3H$, etc.), Corriu et al.[75] showed that equilibrium involving the free AcCl, its protonated form, and the acetyl cation is observed in such systems:



The frequency ν(CO) of the cation $CH_3CO^{\oplus}$ in the Raman spectrum is 2309 cm^{-1}, while that of $CH_3C(Cl)=OH^{\oplus}$ is 1420 cm^{-1}, which indicates a stronger binding of the acyl halide to the proton compared with MX_n.

4. ^{1}H NMR study of the RCOX.MX_n systems

NMR spectroscopy has found extensive applications in the study of the RCOX.MX_n systems in solutions. This method makes it possible to identify complexes (I) and (II), to determine their content in the mixture, and to obtain information about the nature of the distribution of charges in complexes (I) and (II) in solutions of different kinds and about the interconversions between them.[1,5,7,17]

The ^{1}H NMR spectra of these systems were first described by Olah and co-workers.[25,27] The spectra of the AcF.SbF_5 systems in SO_2 or HF contain, apart from the signal due to the initial AcF (doublet with $J_{H-F} \simeq 7$ Hz), two new singlets located in a weaker field. The signal with δ_{CH_3} = 4.08 p.p.m. (singlet) has been assigned to the acetylium salt $CH_3CO^{\oplus}SbF_6^{\ominus}$ (I), while the singlet with the chemical shift δ_{CH_3} = 2.94 p.p.m. was assigned to the coordination complex $CH_3C(F)=O \rightarrow SbF_5$ (II).

The absence of splitting by the ^{19}F nucleus of the signal of the CH_3 group in complex (II), which is observed in the initial AcF, indicates, according to the authors,[25] the existence of the dynamic equilibrium

$$CH_3CO^{\oplus}SbF_6^{\ominus} \underset{SO_2}{\rightleftharpoons} CH_3C(F)=O\rightarrow SbF_5$$

(I) (II)

δ_{CH_3}=4.08 p.p.m., δ_{CH_3}=2.94 p.p.m.

The ^{1}H NMR spectroscopic data for complexes (I) and (II) are presented in Table 6. It follows from these results that the signals of the β-hydrogen atoms (here and henceforth this term is given to the hydrogen atoms attached to the carbon atom which is linked to the carbonyl group) in the salts $RCO^{\oplus}MX_{n+1}^{\ominus}$ (I) (R = alkyl, MX_{n+1} = $SbF_6^{\ominus}$, $BF_4^{\ominus}$, $SbCl_6^{\ominus}$, $AlCl_4^{\ominus}$, $SO_3F^{\ominus}$) lie in the range 4.0–4.5 p.p.m. relative to TMS (the chemical shift δ = 3.9 to 4.2 p.p.m. is characteristic of R = CH_3). The resonance of the β-protons in such a weak field indicates a high acidity and hence the location of the positive charge in the acylium salts in solution mainly on the carbonyl carbon atom, as has been observed for the crystalline state.[17] The chemical shifts of the β-protons in the range 2.9–3.6 p.p.m., i.e. in a higher field, are characteristic of complexes (II).

The chemical shifts of the β-protons in the salt $CH_3CO^{\oplus}SbF_6^{\ominus}$ in solution in CH_3NO_2 and $PhNO_2$ have been observed in a higher field than for the solutions in HF or SO_2. Furthermore, in solutions in CH_3NO_2 and $PhNO_2$ there is a sharp rise in the content of complexes (II).[11] In view of the very high regioselectivity of *para*-substitution on acylation of alkylbenzenes by the RCOX.SbF_5 systems (in nitromethane[11] or sulpholan[57]), it was concluded that there are no free ions in such solvents and only close ion pairs are present.

As regards the differences between the chemical shifts for acylium cations with different anions and in different solvents, it is not useful to discuss them because of the low accuracy of the chemical shifts quoted in the literature due to the difficulty of selecting an internal standard for such reactive complexes. As a rule, the ^{1}H NMR spectra quoted in the literature have been recorded using external standards.

In the identification of the donor–acceptor complexes (II) by the ^{1}H NMR method, there are serious complications. Thus it has been found that, in "super acid" media carboxylic acids also form two types of complexes: a protonated acid (δ_{CH_3} = 3.2 p.p.m.) and an acetylium salt (δ_{CH_3} = 4.35 p.p.m.), the chemical shift δ_{CH_3} for the protonated acid being close to those adopted for type (II) complexes (Table 6).

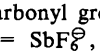
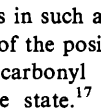
Scheme 6

$$CH_3C(=O)OH \underset{-60^\circ C}{\overset{H^{\oplus}}{\rightleftharpoons}} CH_3C(OH)_2^{\oplus} \underset{-30-0\ ^\circ C}{\overset{-H_2O}{\rightleftharpoons}} CH_3CO^{\oplus}$$

δ_{CH_3}=3.2 p.p.m., δ_{CH_3}=4.35 p.p.m.,

δ_{O-H}=12.4, 13.0 p.p.m.

Table 6. Parameters of the ^{1}H NMR spectra of the acylium salts and the coordination complexes (the chemical shifts are quoted relative to TMS).

RCOX.MX_n system	Solvent	δ, p.p.m.				Refs.
		$RCO^{\oplus}MX_{n+1}^{\ominus}$		$RC(=O\rightarrow MX_n)X$		
		β-H	γ-H	β-H	γ-H	
$CH_3COF\cdot SbF_5$	SO_2	4.1	–	2.9	–	[25]
$CH_3COF\cdot SbF_5$	CH_3NO_2	3.1	–	2.6 *1	–	[11]
$CH_3CH_2COF\cdot SbF_5$	SO_2	4.4	2.1	3.2	1.6	[25, 57]
$CH_3CH_2COF\cdot SbF_5$	HF	4.2	2.1	3.5	1.8	[25]
 $-COF\cdot SbF_5$	SO_2	4.5	2.6	Absent		[74]
$SbF_5\cdot COF(CH_2)_2COF\cdot SbF_5$	SO_2	4.6	3.7	3.7	4.6 *2	[58]
$SbF_5\cdot COF(CH_2)_3COF\cdot SbF_5$	SO_2	4.6	3.3	Absent		[58]
$(CH_3)_2CHCOF\cdot SbF_5$	SO_2	4.3	1.7	Absent *1		[27]
$PhCOF\cdot SbF_5$	SO_2	8.2–9.0		Absent		[25, 57]
	SO_2	7.3	8.9 8.6	Absent		[76]
$CH_3COF\cdot BF_3$	HF	4.2	–	3.0	–	[25]
$CH_3COCl\cdot AlCl_3$	CH_3NO_2	Absent		2.9 *1	–	[77]
$CH_3COCl\cdot SbCl_5$	$PhNO_2$	4.0	–	3.3 *1	–	[11]
$CH_3COCl\cdot AlCl_3$	$ClCH_2CH_2Cl$	Absent		3.4 *1	–	[77]
$CH_3COCl\cdot AlCl_3$	CH_2Cl_2	Absent		3.4	–	[78]
$CH_3COCl\cdot AlCl_3$	SO_2	4.2 *3	–	3.2	–	[79]
CH_3COOH	HSO_3F–SbF_5	4.4	–	3.2 *4	–	[80]

*1 The initial RCOX is also present in the solution.

*2 An ionic-coordination complex is formed.

*3 A different interpretation of the signals was given by Brownstein and Glavincevsky.[79]

*4 The protonated acid $CH_3C(OH)_2^{\oplus}$ is formed.

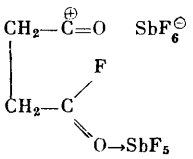
On this basis, Olah[7,58,80] revised his previous view concerning the presence of complexes (I) and (II) in the RCOF.SbF_5 systems in solutions in HF or SO_2 and assigned the ^{1}H NMR signal observed

in a strong field not to complex (II) but to the protonated acids $RC(OH)_2^{\oplus}$ formed as a result of the partial hydrolysis of ionic complexes (I). The fact that the addition of water to solutions of the $RCOF.SbF_5$ systems in SO_2 led to an increase in the high-field signal intensity and, conversely, that careful isolation from traces of moisture made it possible in certain instances to obtain for the first time solutions of the $RCOF.SbF_5$ systems in SO_2 containing only acylium salts $RCO^{\oplus}SbF_6^{\ominus}$ without any appreciable admixture of substances characterised by high-field signals (2.9–3.5 p.p.m.) constituted important evidence in support of the above hypothesis[57,58,74,76] (Table 6).

The presence or absence of signals due to the OH groups of the protonated acid $RC(OH)_2^{\oplus}$ (12–13 p.p.m. relative to TMS) (see Scheme 6) can apparently serve as an important criterion for the reliable assignment of the signals due to the CH_3 group observed in the region of ~3 p.p.m. Unfortunately, however, due attention has not been devoted to this problem in the literature concerned with the ^1H NMR spectroscopy of the $RCOX.MX_n$ systems.

Thus a reliable identification of the donor–acceptor complexes (II) in solutions by the ^1H NMR method is possible only under conditions where moisture is completely excluded.

The $RCOF.SbF_5$ systems in SO_2 (R = aryl, cycloalkyl, etc.) and $SbF_5.FCO(CH_2)_nCOF.SbF_5$ systems with $n \geqslant 3$ constitute as a rule ionic complexes (I) $RCO^{\oplus}SbF_6^{\ominus}$ and $SbF_6^{\ominus}{}^{\oplus}CO-(CH_2)_n-CO^{\oplus}SbF_6^{\ominus}$ [58] (Table 6). It is of interest that the latter complexes with $n = 2$ have the structure of ionic-coordination complexes in solution in SO_2.



The mutual influence of the oxocarbenium group is responsible for the change in structure from that of the diacylium salt ($n \geqslant 3$) to that of the ionic-coordination complex ($n = 2$). This also probably explains the failure of attempts to synthesise the complexes of SbF_5 with malonic acid difluoride ($n = 1$).

Since solvents such as SO_2 and HF are relatively unsuitable for catalytic reactions,[11] the structure of the $RCOX.MX_n$ system in organic media of low polarities is of special interest.

As shown above, the $RCOX.SbX_5$ (X = Cl, F) systems have been most thoroughly investigated by the NMR method in solvents such as SO_2, HF, CH_3NO_2, $PhNO_2$, and sulpholan, while in weakly polar solvents such as CH_2Cl_2, $C_2H_4Cl_2$, and $CHCl_3$ their investigation is hindered by the poor solubility and high oxidising capacity of antimony(V) derivatives. The NMR data for the structures of these systems in weakly polar solutions are therefore lacking in the literature. On the other hand, the $RCOX.AlX_3$ systems have been studied in both polar and weakly polar organic solvents.

The only solvent in which the ionic salts $RCO^{\oplus}AlCl_4^{\ominus}$ with R = Alk can apparently exist is SO_2. The $AcCl.AlCl_3$ systems in solution in SO_2 have been investigated,[71,79] but the results of these studies do not agree fully and have been given the opposite interpretation in the two investigations.

French investigators[71] concentrated attention on demonstrating the formation of the complex $(CH_3CO)_2CHCO^{\oplus}AlCl_4^{\ominus}$ in the $AcCl.AlCl_3$ system containing an excess of the acid chloride and there is no doubt that this does happen. The chemical shifts δ_{CH_3} = 3.0 and 3.97 p.p.m. are quoted for the salts $(CH_3CO)_2CHCO^{\oplus}AlCl_4^{\ominus}$ and $CH_3CO^{\oplus}AlCl_4^{\ominus}$ respectively in SO_2 (with MS as the external standard). Unfortunately the above workers concentrated attention on cationic species without presenting any data concerning complexes (II). Their second communication[79] reports the presence in the $AcCl.AlCl_3$ system of two complexes with δ = 4.18 and 3.20 p.p.m. This study will be discussed below [see Section (V)].

In all other solvents except $SO_2(C_6H_5NO_2$, CH_3NO_2,[77] CH_2Cl_2,[63,78] $C_2H_4Cl_2$,[77] etc.), the $CH_3COCl.AlCl_3$ system, having an ionic structure in the solid state, exists exclusively as the coordination complex (II). Apart from spectroscopic data, Wilinsky and Kurland[78] also describe chemical tests confirming the foregoing. Although this evidence is in our view not absolute, the conclusion that only complexes (II) are present is incontrovertible.

Thus one may conclude that, on the whole, conditions for the stabilisation of the ionic salts $RCO^{\oplus}MX_{n+1}^{\ominus}$ in weakly polar organic solvents have not so far been found for the $RCOX.MX_n$ (1:1) systems. As regards the complexes $RCOX.AlX_3$ (X = Cl, Br), the formation of the ionic salts $RCO^{\oplus}AlX_4^{\ominus}$ has not been observed for them also in more highly ionising media. We may note that the problem of the stabilisation of acylium salts in organic solvents has a direct bearing on the creation of highly reactive electrophiles.

5. ^{13}C NMR study of the $RCOX.MX_n$ systems

Important information about the composition of the $RCOX.MX_n$ systems in solutions and about the nature of complexes (I) and (II) has been obtained with the aid of ^{13}C NMR spectra.

Firstly, the characteristic chemical shifts $\delta_{\alpha-^{13}C}$ and especially $\delta_{^{13}CO}$ make it possible to identify very reliably complexes of types (I) and (II) in solutions, since the relative changes in the chemical shifts are small on passing from one solvent to another and on replacing an internal standard by an external one, which is an advantage of this method over ^1H NMR spectroscopy. Secondly, the ^{13}C NMR spectra yield additional important information about the structure and distribution of charges in the acyl cations $RCO^{\oplus}$.[7,81]

The ^{13}C NMR spectrum of a solution of the salt $CH_3{}^{13}CO^{\oplus}SbF_6^{\ominus}$ (53% isotope enrichment) in liquid HF was first described by Olah,[27] who erroneously attributed the signal of the carbonyl carbon atom $\delta_{^{13}CO}$ = 194 p.p.m. observed in the spectrum of this solution (quartet with $^2J_{C-C-H}$ = 6.3 Hz) to the $CH_3CO^{\oplus}$ ion. The signal with δ = 152 p.p.m. observed in a strong field, also present in the spectrum of this solution (however, this was reported only in a later communication[82]), was assigned by the authors to the product of the hydrolysis of the acylium salt $RC(OH)_2^{\oplus}$. In a study of the ^{13}C NMR spectra of acetic and benzoic acids in sulphuric acid and oleum at different concentrations, Masiel and Traficante[83,84] also observed two signals in the region of $\delta_{^{13}CO} \simeq$ 190 and 150 p.p.m. Despite Olah's assignment,[27] the signals observed in a weak field were assigned, in conformity with the data of Deno et al.,[85] to the protonated acid ions $RC(OH)_2^{\oplus}$. The logic of the studies of Masiel and Traficante[83,84] and the data of Deno et al.[85] concerning the formation of acylium ions from carboxylic acids in an $H_2SO_4-SO_3$ medium with a high acidity seemingly led to the conclusion that the $\delta_{^{13}CO} \simeq$ 150 p.p.m. signal, arising in the presence of a high content of SO_3 in the H_2SO_4 solution, should be attributed to acylium ions. However, Olah's incorrect assignment prevented the authors from arriving at this conclusion. They were forced to conclude that acylium ions could not be observed and the mysterious signal with $\delta_{^{13}CO} \simeq$ 150 p.p.m. remained unidentified.

The study by Traficante and Masiel[84] forced Olah to return to the problem of the identification of the acylium ion. For this purpose, a joint ^{13}C and ^1H NMR study of RCOOH solutions in the "super-

acid" HSO_3F-SbF_5 was undertaken.[80,82] It was shown clearly that at $T < -30$ °C the above solvent contains only the protonated acid ions $RC(OH)_2^{\oplus}$ characterised by $\delta_{C^1H_3} = 3.2$ p.p.m. and $\delta_{^{13}CO} = 190$ p.p.m. [for $CH_3C(OH)_2^{\oplus}$]. At a higher temperature, the acylium ions with $\delta_{C^1H_3} = 4.2$ p.p.m. and $\delta_{^{13}CO} = 148$ p.p.m. are in equilibrium with the above species. These data agree with Traficante's observations and demonstrate that the unassigned signals in the region of 150 p.p.m. should be attributed to the acylium ions $RCO^{\oplus}$.

The validity of the assignment of the 150 p.p.m. chemical shift to the carbonyl carbon atom of acylium iodide was later demonstrated by solid-phase ^{13}C NMR for the ionic salt $CH_3CO^{\oplus}AlBr_4^{\ominus}$.[86]

Table 7 presents the principal characteristics of the ^{13}C NMR spectra of certain acylium salts and coordination complexes. It shows that the ^{13}CO NMR signal of the $RCO^{\oplus}$ cations is usually observed in the range 145–157 p.p.m. The upfield shift of this signal relative to RCOF or RCOOH (this was the cause of the initial confusion as regards the assignment) is due to the change in the hybridisation of the carbonyl carbon from the sp^2- to the *sp*-hybridised state (see Section IV).

Table 7. Parameters of the ^{13}C NMR spectra of the acylium salts and the coordination complexes (the chemical shifts are quoted in p.p.m. relative to TMS).

System	Solvent	Assignment	^{13}C NMR spectroscopic data			Refs.
			δ_{CO}	$^1J_{CCH}$	$\delta_{\alpha\text{-}C}$	
CH_3COF			163		18	[28]
$CH_3COF \cdot SbF_5$	SO_2-SbF_5	$CH_3CO^{\oplus}$	148	9.3	5 *1	[81]
$CH_3COF \cdot SbF_5$	SO_2 *2	$CH_3CO^{\oplus}$	152		7	[27, 28]
		$CH_3C(F)=O \rightarrow SbF_5$	194	6.0		
CH_3COOH	HSO_3F-SbF_5	$CH_3CO^{\oplus}$	150	9.3		[82–84]
		$CH_3C(OH)_2^{\oplus}$	192	6.5		
$PhCOF \cdot SbF_5$	HF or SO_2	$PhCO^{\oplus}$	154	–	88 *3	
		$PhC(F)=O \rightarrow SbF_5$	182	–		[82, 87]
$CH_3-C_6H_4-COF \cdot SbF_5$	SO_2	$CH_3-C_6H_4-CO^{\oplus}$	157	–	83 *4	[87]
PhCOOH	Et_2O		173			[82]
PhCOOH	HSO_3F-SbF_5	$PhCO^{\oplus}$	154			[81–84]
		$PhC(OH)_2^{\oplus}$	183			

*1 $^1J_{CH} = 147$ Hz for the cation $CH_3CO^{\oplus}$.

*2 In solution in HF, the values of δ_{CO} for the acetylium cation and the coordination complex are respectively 151 and 193 p.p.m.

*3 The ^{13}C chemical shifts for the *ortho*-, *meta*-, and *para*-, carbon atoms of the aromatic ring are respectively 141, 133, and 149 p.p.m.

*4 The ^{13}C chemical shifts for the *ortho*-, *meta*-, and *para*-, carbon atoms of the aromatic ring are respectively 140, 134, and 166 p.p.m.

The ^{13}C NMR spectra also indicate a significant shielding of the α-carbon atoms of the acylium ions $RCO^{\oplus}$. Thus, for R = alkyl, $\delta_{\alpha-^{13}C} \simeq 0$ (relative to TMS) despite the presence of the neighbouring carbonium ion centre, which agrees with the calculation of electron density based on the results of X-ray diffraction analysis, also indicating a pronounced shielding of the α-carbon atom (see Section III).

Similar values of $\delta_{^{13}CO} \simeq 154-157$ p.p.m. and a similar tendency towards the shielding of the C(1) atom of the aryl group ($\delta = 80-90$ p.p.m.) are characteristic of the $ArCO^{\oplus}$ cations. The appreciable contribution of ketene-like forms to the $ArCO^{\oplus}$ structure is indicated by the chemical shift of the carbon atoms in the 2- and 4-positions in the aryl group (see the footnote to Table 7). Evidently the latter are appreciably deshielded and the maximum positive charge is located on the atom attached to the electron-donating group.[84]

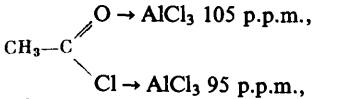
The formation of the type (II) complexes $RC(F)=O \rightarrow SbF_5$ (II) [or the protonated acids $RC(OH)_2^{\oplus}$] does not entail changes in hybridisation and the downfield shift of the signals observed in such cases ($\delta_{^{13}C-O\rightarrow} \simeq 190$ p.p.m.) is entirely logical and is associated with some displacement of electron density from the carbonyl group to the metal atom in MX_n.

The smaller positive charge on the carbonyl carbon atom in type (II) complexes induces a smaller deshielding (acidity) of the β-H atoms and hence a smaller shielding of the α-C atoms. As a result, the ^1H NMR signals of the β-protons in complexes (II) are located at a higher field (Table 6), while the signals of the corresponding α-^{13}C atoms are at a lower field compared with $RCO^{\oplus}$ ($\Delta\delta \simeq 20$ p.p.m.[81]).

6. Non-traditional types of treatment of the NMR spectra of the $RCOX.MX_n$ systems. Hypothesis of the existence of complexes other than $RCO^{\oplus}MX_{n+1}^{\ominus}$ and $RC(X) = O \rightarrow MN_x$

It follows from the foregoing that, in the course of the study of the complexes $RCOX.MX_n$, quite a few erroneous hypotheses were put forward and various contradictions arose, which have now been to a large extent resolved. In this Section we shall consider studies which reached conclusions different from those generally accepted or which we believe to be extremely doubtful on the basis of NMR spectra. Unfortunately, these investigations have not been assessed in the literature, with the exception of Olah's study[28] quoted in a review.[7]

Brownstein and Glavincevsky[79] investigated the complexes formed on interaction of AcCl with $AlCl_3$ in SO_2 by ^1H and ^{27}Al NMR at −24 to −54 °C. The reported composition of the system varies as a function of the reactant ratio. For the molar ratio $AcCl/AlCl_3 \geqslant 1$, a complex with $\delta_{^1H} = 4.18$ and $\delta_{^{27}Al} = 105$ p.p.m. is formed. The structure of a donor–acceptor complex (II) was assigned to it on the basis of the similarity of its ^{27}Al chemical shift to that observed by the same workers[88] for the complex $(CH_3)_2O \rightarrow AlCl_3$. The increase in the amount of $AlCl_3$ in the system to $AcCl:AlCl_3 = 1:(1.5-3)$ leads to the appearance in solution of yet another complex to which the authors[79] attribute the appearance of the second ^1H NMR signal with $\delta_{CH_3} = 3.2$ p.p.m. and the second signal in the ^{27}Al NMR spectrum with $\delta_{^{27}Al} = 95$ p.p.m. The structure of a donor–acceptor complex with additional coordination of one $AlCl_3$ molecule to the chlorine atom was assigned to this new complex:



3.2 p.p.m.

This conclusion is based on the closeness of the chemical shift of the new signal ($\delta_{^{27}Al} = 95$ p.p.m.) to the ^{27}Al chemical shift of the salt $Me_4N^{\oplus}AlCl_4^{\ominus}$.[88]

We believe that these conclusions[79] are erroneous. In our view, the additional coordination of an $AlCl_3$ molecule to the chlorine atom of the donor–acceptor complex (II) should lead to a downfield and not an upfield shift, of the kind observed by the above workers[79] for the signal due to the protons of the methyl group in the ^1H NMR spectrum. The appearance in the ^1H NMR spectrum of signals at a low field with increase in the acidity of the medium has in fact been observed by many workers (see, for example, Deno et al.[85]). A similar behaviour has been observed for the $AcX.nAlX_3$ systems in solution in CH_2X_2 with increase in the AlX_3 concentration.[86] We also think it unlikely that $AlCl_3$ should be coordinated to complex (II) and not to the free AcCl in the presence of free acid chloride in the system whose amount has been shown to be comparable,[79] even for an excess of $AlCl_3$, to the amount of complex (II). The fact that the assignments of the ^{27}Al spectra described by Brownstein and Glavincevsky[79] are actually the opposite of those put forward by other workers,[79,89–91] who assigned the chemical shift $\delta_{^{27}Al}$ = 93 p.p.m. (Δ = 300–500 Hz) to the coordinated $AlCl_3$ ($>C=O \rightarrow AlCl_3$) and the signal in the region of $\delta_{^{27}Al}$ = 102–107 p.p.m. (Δ = 10–30 Hz) to the anion $AlCl_4^{\ominus}$ is also somewhat perplexing.

Yet another study by the same workers[16] was devoted to the investigation of the $AcCl.SbCl_5$ system in solution in SO_2 by ^1H NMR. At −76 °C, the authors observed four signals with δ = 4.23, 3.02, 12.09, and 12.76 p.p.m. The first was attributed to a type (II) donor–acceptor complex, while the chemical shifts of 3.02, 12.09, and 12.76 p.p.m. were assigned to the salt $(CH_3CO)_2CHCO^{\oplus}SbCl_6^{\ominus}$. The authors assume that the last two signals correspond to the hydrogen atoms attached to a carbon or oxygen atom in the two tautomeric forms (see Scheme 5).

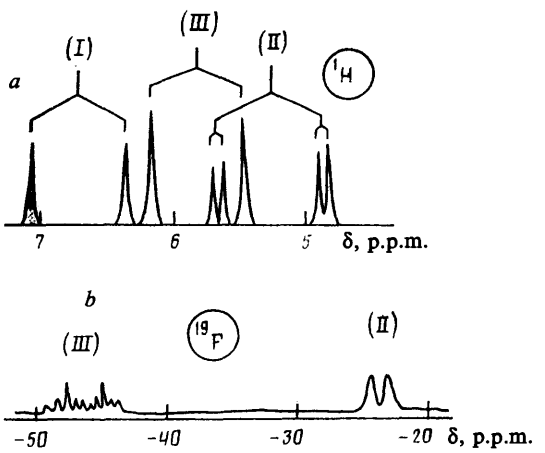
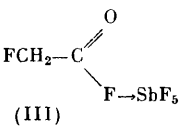


Figure 3. ^1H (*a*) and ^{19}F (*b*) NMR spectra of the $FCH_2COF.SbF_5$ system in SO_2 at −70 °C.

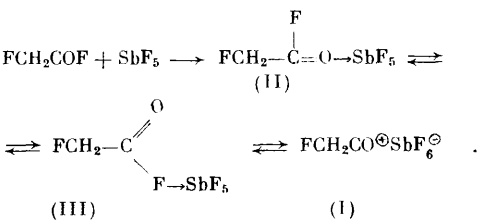
The validity of this interpretation[16] is open to serious doubt. Firstly, the observed ratios of the integral intensities (3 : 1 : 1) do not agree at all with the conclusion that $(CH_3CO)_2CHCO^{\oplus}SbCl_6^{\ominus}$ is present. Secondly, it had been shown earlier[92] that only a single signal with $\delta_{O...H}$ = 12.24 p.p.m., corresponding to the O-linked proton in the symmetrical ketene-like limiting structure, can be observed in a weak field in the ^1H NMR spectra of the salts $(CH_3CO)_2CHCO^{\oplus}MX_{n+1}^{\ominus}$ in solution in SO_2. On the other hand, the chemical shifts and the ratios of the intensities of the signals, attributed in the above study[16] to the diacetylacetylium salt, are fully consistent with the structure of the product of the hydrolysis of $CH_3CO^{\oplus}SbCl_6^{\ominus}$ — the protonated acid salt $CH_3C(OH)_2^{\oplus}SbCl_6^{\ominus}$.[74] The author's interpretation[16] of the ^1H NMR spectrum of a solution of the $CH_3COCl.SbCl_5$ system in SO_2 also appears erroneous.

In conclusion we shall consider Olah's study[28] in which the formation of a coordination complex via a halogen atom is reported:



(III)

In his study of FCH_2COF in the presence of an excess of SbF_5 in solution in SO_2 by the ^1H, ^{13}C, and ^{19}F NMR methods, Olah observed the presence of three complexes in equilibrium, to two of which the structure of the "classical" type (I) and (II) complexes was attributed, while the structure of the previously unknown complex (III) with the $RC(O)F \rightarrow SbF_5$ coordinate bond was assigned to the third complex (Fig. 3).



(III) (I)

Table 8. The assignments of the ^{13}C, ^{19}F, and ^1H NMR chemical shifts of the complexes $FCH_2CO^{\oplus}SbF_6^{\ominus}$ (I), $FCH_2C(F)=O \rightarrow SbF_5$ (II), and $FCH_2C(=O)-F \rightarrow SbF_5$ (III).

Compound	Chemical shift δ, p.p.m.				
	CH_2F			COF	
	^1H	^{19}F	^{13}C	^{13}C	^{19}F
FCH_2COF	5.0	229.4	75.4	159.7	−22.7
$FCH_2C(F)=O \rightarrow SbF_5$ (II)	5.3	229.0	75.9	162.1	−23.8
$FCH_2C(=O)-F \rightarrow SbF_5$ (III)	5.9	232.4	77.1	180.3	−46.6
$FCH_2CO^{\oplus}SbF_6^{\ominus}$ (I)	6.8	234.6	75.4	145.1	–

Table 8 and Fig. 3 present the characteristics of the NMR spectra of the $FCH_2COF \rightarrow SbF_5$ system in solution in SO_2 at −70 to −30 °C. According to the authors,[28] the NMR spectra agree with the presence of equilibria involving complexes (I), (II), and (III). The formation of a complex with structure (III) is indicated by the following data: the intermediate position of the signal due to the FCH_2 group in the ^1H NMR spectrum relative to the corresponding signals of complexes (I) and (II), the virtual absence of changes in the ^{13}C and ^{19}F NMR spectra of this group, which makes it possible to rule out the coordination of SbF_5 to the fluorine atom of the FCH_2 group, the appreciable deshielding of the carbon atoms and

especially the fluorine atom of the COF group, and also the characteristic multiplicity (doublet of quintets) of the signal in the ^{19}F NMR spectrum of this group (Fig. 3 and Table 8). The molar ratios of complexes (II), (III), and (I) depend on temperature and are respectively 20:50:30 at −70 °C and 27:38:35 at −30 °C. Direct structural evidence is apparently necessary for the final confirmation of the possibility of the existence of type (III) complexes.

Although the formation of stable type (III) complexes containing the Hal → MX_n coordinate bond cannot be regarded as rigorously demonstrated, complexes of this type have been postulated[7,28] as intermediates in the conversion of donor–acceptor complexes (II) into ionic salts (I).

VI. Factors influencing the equilibrium between ionic and coordination complexes

Evidently the knowledge of factors influencing the equilibrium (I) ⇄ (II) (especially in solutions) and hence the reactivity of the RCOX.MX_n systems is very important. Unfortunately, there have been no systematic studies on this problem.

We shall consider briefly the few literature data concerning the influence of the nature of the groups R and Hal in RCOHal, the strength of the Lewis acid MX_n, the nature of the solvent, and temperature on the structures of the complexes formed and the equilibrium between them.

1. The influence of the groups R and Hal in RCOHal and of the strength of the Lewis acid

This problem has been examined in a review.[5] It follows from experimental data that the capacity of the halide RCOHal for the formation of ionic complexes diminishes in the sequence

$$F > Cl > Br > I .$$

The tendency to form ionic salts in the RCOX.MX_n systems depends still more significantly on the strength of the Lewis acid (MX_n). Thus strong Lewis acids form predominantly ionic salts, while weaker ones give rise mainly to complexes (II). Unfortunately there is no universal series of the strengths of MX_n. One of the sequences taken from reviews[5,19] is presented below:

$$SbF_5 \simeq AsF_5 > BF_3 \simeq GaCl_3 \simeq SbCl_5 \geqslant AlCl_3 > PF_5 \simeq TiCl_4 > BCl_3 .$$

strength of Lewis acid

The quantitative influence of the acidity of the medium on the stability of the acylium salts formed in the RCOOH − H_2SO_4 − SO_3 systems has been investigated by French workers.[93] The results of studies by ^1H and ^{13}C NMR and IR spectroscopy agree fully with one another and with the studies of Deno et al.[85] and Traficante and Masiel,[83,84] indicating the presence in this system of equilibria between the free acid, its protonated form, and the acylium salt:

$$RCOOH \underset{}{\overset{H_2SO_4}{\rightleftharpoons}} R{-}C(OH)_2^{\oplus}\ HSO_4^{\ominus} \underset{-H_2O}{\overset{H_2SO_4-SO_3}{\rightleftharpoons}} RCO^{\oplus}HS_2O_7^{\ominus} ,$$

(A) (B)

(A)

^1H NMR: δ_{CH_3} = 2.8 p.p.m.,
^{13}C NMR: δ_{CO} = 194 p.p.m.,
IR: ν(CO) = 1620, 1560 cm^{-1},

(B)

δ_{CH_3} = 3.95 p.p.m.,
δ_{CO} = 152 p.p.m.,
ν(CO) = 2309 cm^{-1}.

Fig. 4 illustrates the regions corresponding to the existence of free RCOOH and the ions $RC(OH)_2^{\oplus}$ and $RCO^{\oplus}$ as a function of the acidity of the medium. As can be seen from Fig. 4, the cations $CH_3CO^{\oplus}$ are formed only for high acidities of the medium.

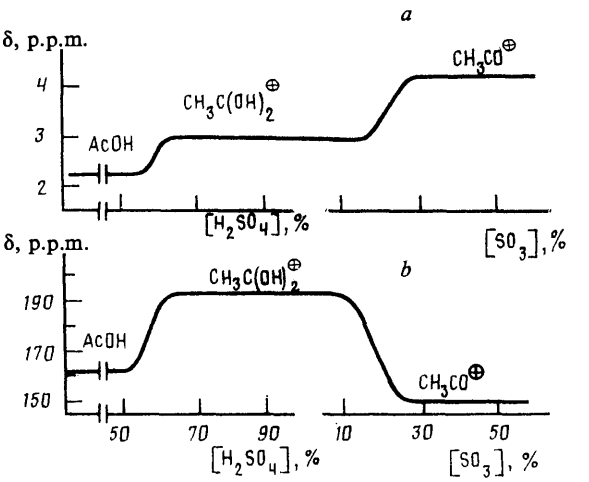


Figure 4. The region corresponding to the existence of the ions $CH_3C(OH)_2^{\oplus}$ and $CH_2CO^{\oplus}$ in the $H_2O-H_2SO_4-SO_3$ system according to ^1H NMR (*a*) [87,93] and ^{13}C NMR (*b*) [85] spectroscopic data.

The nature of the group R exerts a significant influence on the nature of the complexes formed in the RCOX.MX_n system. It follows from the analysis of spectroscopic data[5,17] that an increase in the size of the alkyl group in the sequence $CH_3 \rightarrow C_2H_5 \rightarrow CH(CH_3)_2 \rightarrow C(CH_3)_3$ leads to an increase in the content of donor–acceptor complexes (II) in the equilibrium.

Substituents R exhibiting the −*I* effect also suppress the formation of acylium salts (I). Thus a special study[94] of systems containing $AlCl_3$ and different RCOCl (R = CH_3, C_2H_5, C_3H_7, $ClCH_2$, Cl_2CH, and Cl_3C) by IR spectroscopy showed that the salts $RCO^{\oplus}AlCl_4^{\ominus}$ are not formed if pK_a < 2.9–3.2 for the corresponding RCOOH. For example, only the coordination complex $ClCH_2C(Cl)=O \rightarrow AlCl_3$ exists in the $ClCH_2COCl.AlCl_3$ system.[94]

Acylium salts with −*I* substituents can be obtained only by the reaction of RCOF with a strong Lewis acid such as SbF_5. Thus the salts $ClCH_2CO^{\oplus}SbF_6^{\ominus}$ and $BrCH_2CO^{\oplus}SbF_6^{\ominus}$ proved to be fairly stable and were isolated in a pure state.[95] The relative stability of the salts $HalCH_2CO^{\oplus}SbF_6^{\ominus}$ can be explained by the positive mesomeric effect of the halogen atoms at the α-carbon atom. According to the authors,[95] the presence of this +*M* effect stabilises to some extent the cations $HalCH_2CO^{\oplus}$ as a result of the contribution by the resonance structure in which the halogen atom acquires a partial onium character and the positive charge is delocalised:

$$Hal{-}CH_2{-}CO^{\oplus} \longleftrightarrow Hal^{\oplus}{=}CH_2{-}C{=}O .$$

Such stabilisation is insufficient for the salts $Hal_2CHCO^{\oplus}SbF_6^{\ominus}$ and they cannot be obtained. The attempts to synthesise the salt $CF_3CO^{\oplus}SbF_6^{\ominus}$ also proved unsuccessful.[28] These salts could not be detected even spectroscopically. The earlier reports by Lindner and Kranz[96] of the synthesis of $CF_3CO^{\oplus}SbF_6^{\ominus}$ at low temperatures (< −57 °C) should probably be regarded as erroneous.

The influence of the electronic effects of the substituent on the nature of the complexes formed can be traced very clearly, in our view, also in relation to the systems $SbF_5{\cdot}F(O)C-(CH_2)_n-C(O)F{\cdot}SbF_5$ (n = 2−7).[58] For $n \geqslant 3$, the formation of the salts of the dications $SbF_6^{\ominus}{}^{\oplus}CO-(CH_2)_n-CO^{\oplus}SbF_6^{\ominus}$ is observed, while for n = 2 the inductive influence of the oxocarbenium group is already so great that only the monocationic complexes $SbF_6^{\ominus}{}^{\oplus}CO-(CH_2)_2-C(F)=O \rightarrow SbF_5$ are formed.[58]

The replacement of an alkyl group by an aryl group (without substituents in the *ortho*-position) favours the formation of donor–acceptor complexes. However, one should note that the steric effects in the aryl group in ArCOX exert a decisive influence on the structure of the complexes formed. Substituents in the *ortho*-position suppress the formation of donor–acceptor complexes, promoting the formation of acyl cations, which are less sensitive to steric hindrance. Thus the interaction of $TiCl_4$ with 2,6-dimethylbenzoyl chloride or mesitoyl chloride results in the formation of mainly the salts $2,6\text{-}Me_2C_6H_3CO^{\oplus}Ti_2Cl_9^{\ominus}$ and $2,4,6\text{-}Me_3C_6H_2CO^{\oplus}.Ti_2Cl_9^{\ominus}$,[23,67] although a weak Lewis acid such as $TiCl_4$ usually forms only type (II) complexes.[7,17]

2. The nature of the solvent

Ionising solvents favour the formation of ionic complexes (I), while weakly polar solvents favour the formation of coordination complexes (II). An effective illustration of the influence of the nature of the solvent on the structure of the complexes formed in the $RCOX.MX_n$ systems may be provided by the behaviour of the $4\text{-}CH_3C_6H_4COCl.SbSl_5$ system.[17,41] Both salts (I) and complexes (II), whose structure was demonstrated by X-ray diffraction, were isolated for this system. Thus, when $4\text{-}CH_3C_6H_4COCl.SbCl_5$ was dissolved in non-polar CCl_4 (ε = 2.2),[50] orthorhombic crystals of the donor–acceptor complex (II) were isolated, while monoclinic crystals of the ionic salt (I) were isolated from the more polar $CHCl_3$ (ε = 5.05).[50] The acylium salt is converted in CCl_4 into a donor–acceptor complex, which in turn isomerises to an acylium salt on dissolution in $CHCl_3$.

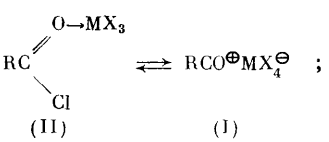
It has been established that the $RCOF.SbF_5$ systems in SO_2 consist exclusively of ionic complexes (I).[7] In liquid HF, the salts $RC(OH)_2^{\oplus}X^{\ominus}$ are also in equilibrium with the acylium salts. In polar organic solvents [nitromethane (ε = 39), nitrobenzene (ε = 35)], the $AcX.SbF_5$ (X = Cl, F) systems represent an equilibrium mixture of complexes (I) and (II). In non-polar organic solvents, the systems with SbF_5 were not investigated.

The $RCOX.AlX_3$ systems have been studied in a wide range of solvents (CH_3Cl_2, $CHCl_3$, $C_2H_4Cl_2$, CH_3NO_2). The set of the available data shows that ionic type (I) species are not formed in the solvents investigated.[9,17,63,78] Admittedly it has been reported[9] that ν(CO) = 2300 cm^{-1} vibrations with an extremely low intensity appear in the IR spectrum of a solution of the $AcCl.AlCl_3$ system in dichloroethane. However, much importance can hardly be attributed to this fact, particularly since, together with the main frequencies as regards intensity, referring to complex (II), the ν(CO) = 1800 cm^{-1} frequency of the initial acetyl chloride is present in the IR spectrum of the solution, which is usually due to secondary reactions of the $RCOX.MX_n$ systems under the influence of the salt optical components.

3. The influence of temperature

The literature data concerning the influence of temperature on the equilibria between the complexes, (I) ⇄ (II), are scanty and contradictory.

Perkampus and Weiss[97] concluded that, as the temperature is reduced, the equilibrium (II) ⇄ (I) shifts towards the formation of the type (II) complex:



(a) R = Ph, $MX_3 = AlBr_3$; (b) R = Me, $MX_3 = AlBr_3$ (−30 °C); (c) R = Et, $MX_3 = AlBr_3$ (−40 °C); (d) R = Et, $MX_3 = GaCl_3$ (−100 °C).

Thus it has been shown that the content of the salt $PhCO^{\oplus}AlBr_3Cl^{\ominus}$ is a maximum at 40–50 °C, diminishing with decrease in temperature. For other systems, such data were not quoted[97] and only the temperatures at which absorption in the region of ν(CO) for the acylium salt begins to be observed were indicated (in brackets).

On the other hand, it has been shown by ^{81}Br NQR that even at 77 K the ionic structure of the salts $CH_3CO^{\oplus}AlBr_4^{\ominus}$ is retained and that a type (II) complex is not formed.[55]

VII. The influence of the structure of acylium salts on their thermodynamic stability

The strength of the Lewis acid MX_n and the nature of the group attached to the carbonyl group exert a significant influence not only on the equilibrium between complexes (I) and (II) but also on the chemical stability of the complexes formed.

It follows from Table 1 that the maximum stability and the highest melting points are characteristic of adducts formed by the strongest Lewis acids. On the other hand, weak Lewis acids form readily fusible and relatively unstable compounds. Thus the complex $AcF.BF_3$, which has the structure of an ionic salt in the solid state, dissociates reversibly into AcF and BF_3 at 20 °C (the boiling point of AcF).

The stability of the complexes $RCOX.MX_n$ also depends on the structure of the group R. The cations $RCO^{\oplus}$, where there is no possibility of an effective stabilisation of $R^{\oplus}$, are resistant to decarbonylation. Thus thermodynamic calculation shows that the decomposition of the acyl cation is a strongly endothermic reaction and does not occur under the usual conditions:[34]

$$CH_3CO^{\oplus} \rightarrow CH_3^{\oplus} + CO,\ \Delta H = 294-340\ kJ\ mol^{-1}.$$

On the other hand, acylium salts with a group R capable of forming a relatively stable carbonium ion are extremely unstable. Thus $(CH_3)_3CCO^{\oplus}SbF_6^{\ominus}$ decomposes to a slight extent at −40 °C, while at room temperature the complex undergoes full irreversible decomposition with liberation of CO. The formation of the t-butyl cation on its decomposition has been demonstrated by NMR:[27]

$$(CH_3)_3C-CO^{\oplus}SbF_6^{\ominus} \rightarrow (CH_3)_3C^{\oplus}SbF_6^{\ominus} + CO.$$

The very high stability of the triphenylcarbenium cation is just as

responsible for the very low stability of the $Ph_3CCO^{\oplus}$ ion, which eliminates CO even at a low temperature:[98]

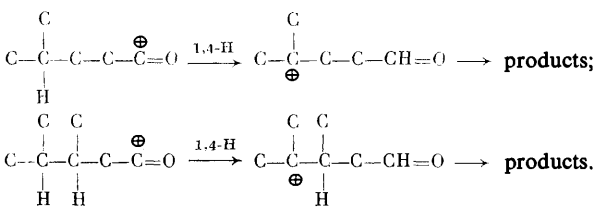
$$Ph_3C{-}CO^{\oplus} \rightarrow Ph_3C^{\oplus} + CO.$$

Similarly the complex $(CH_3)_3CCOCl.AlCl_3$ is spontaneously decarbonylated at room temperature. It is of interest that in the presence of isopentane the process is suppressed and the main pathway in the reaction of the complex becomes the formation of the ketone $(CH_3)_2CHCOCH_3$. It is believed[99,100] that the ketone detected is formed via the intramolecular 1,2-shift of the methyl group in the acyl cation, while the isoalkane is a donor of the hydride ion:

$$(CH_3)_2\overset{\oplus}{C}{-}\overset{\oplus}{C}{=}O \xrightarrow{\sim 1,2\text{-Me}} (CH_3)_2\overset{\oplus}{C}{-}C(=O){-}CH_3 \xrightarrow{+H^{\ominus}} (CH_3)_2CH{-}C(=O){-}CH_3.$$

Similar intramolecular rearrangements apparently occur in the familiar alkane carbonylation reactions catalysed by Lewis acids.[101]

Together with the intermolecular hydride transfer from RH to $RCO^{\oplus}$, an intramolecular 1,4-hydride shift from the tertiary carbon atom to the carbonyl carbon atom of the $RCO^{\oplus}$ cation can take place at temperatures in the range 60–100 °C:[102]



On the other hand, if the tertiary carbon atoms are not located in the 4-position, then an intermolecular hydride shift takes place in which another $RCO^{\oplus}$ species functions in all probability as the $H^{\ominus}$ acceptor.[102] In the case of n-alkyl groups, both intramolecular and intermolecular hydride shifts are suppressed and such cations n-$RCO^{\oplus}$ do not change under the conditions indicated.

The presence of atoms with a $+M$ effect at the α-carbon atom in the cations $RCO^{\oplus}$ destabilises the cation and, with increase in the number of such groups, the instability also increases. The salts $CF_3CO^{\oplus}SbF_6^{\ominus}$ and $F_2CHCO^{\oplus}SbF_6^{\ominus}$ cannot be detected even at −70 °C, while at −60 °C CF_4 and CF_3H—the products of the decarbonylation of these salts—were identified respectively.[28]

VIII. Conclusion

The complexes of acyl halides with Lewis acids, $RCOX.MX_n$, have a hundred year's long history. The wide scale employment of metal complexes in synthetic organic chemistry began with these particular systems.

During the 50 years which have elapsed since the synthesis of the first well characterised complex $Ac^{\oplus}BF_4^{\ominus}$, extensive factual data have accumulated in this field: a large series of ionic complexes $RCO^{\oplus}MX_{n+1}^{\ominus}$ and donor–acceptor complexes $RC(X)=O \rightarrow MX_n$ have been synthesised, the characteristic features of the structures of complexes of both types in the solid state and in solution have been investigated, spectroscopic methods for the identification of these complexes have been developed, and factors influencing the equilibrium between them have been discovered. However, many problems in this field still remain unsolved and many contradictions in the literature concerning the complexes $RCOX.MX_n$ have not been explained. The equilibria between ionic and donor–acceptor complexes have not been studied systematically, the investigations having been carried out mainly at a qualitative level. There are almost no literature data on the coordination complexes $RC(O)Cl \rightarrow MX_n$ and their role in the equilibrium

$$RCO^{\oplus}MX_{n+1}^{\ominus} \rightleftarrows RC(X)=O \rightarrow MX_n.$$

Overall, one may conclude that the $RCOX.MX_n$ systems have been studied fairly well at a qualitative level. The next stage in their investigation will probably lead to the determination of quantitative data on the equilibria existing in these systems, including equilibria with participation of relatively unstable complexes formed as intermediates.

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Translated from *Uspekhi Khimii* **60** 1077–1103 (1991) U.D.C. 621.357.12:546.62

Electrolytic deposition of metals on aluminium and its alloys

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ABSTRACT. The directions of the development of the technology of the deposition of galvanic coatings on aluminium and its alloys are examined. Attention is concentrated on the immersion method with preliminary contact segregation of metallic films, which has nowadays found the greatest practical application. Studies in the theory and practice of the electrodeposition of metals on preoxidised aluminium and also the direct deposition of galvanic coatings, whose main advantage is its universality and the simplicity of the technological process, are considered.

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I. Introduction

Among metallic constructional materials, aluminium has found extensive application. During the period 1950–1980, its world prodution increased almost by a factor of 12.[1] According to forecasts,[2] the requirement for aluminium in the year 2000 will increase by a factor of 4 compared with 1980. Thus multilayer copper–nickel–chromium and nickel–chromium (or binickel) coatings are deposited on it in the production of the protective, decorative trim. In order to protect the surfaces of articles against mechanical wear, thick layers of chromium are deposited and coatings consisting of lead–tin and copper–tin alloys are used to impart antifraction properties. In order to facilitate the welding of articles, use is made of tin–lead, tin–bismuth as well as nickel and silver coatings. The latter are employed to achieve contact and surface electrical conductivity in articles. Brass coatings are deposited on aluminium to facilitate the firm adhesion of its surface to rubber in hot pressing. Threaded aluminium articles are zinc-plated to prevent seizing. Protective cadmium and zinc coatings have been recommended for units where the aluminium components are coupled to components made of other metals in contact with which the corrosion of aluminium is intensified. Aluminium with coatings tinted to simulate "old bronze" or "old silver" are used in the making of artistic articles.[3–9]

However, aluminium has many properties which hinder the formation of high-quality metallic coatings on its surface. These include the high affinity of aluminium for oxygen, as a result of which its surface is rapidly covered by an oxide film in aqueous solutions, and the high negative potential of the activated surface which promotes the segregation of the contact metal. Furthermore, the possibility of the harmful influence of a number of physico-mechanical factors has been noted: such as the difference between the coefficients of the thermal expansion of aluminium and the metals deposited on it, the difference between their crystal lattice parameters, and the presence of hydrogen in the main metal and in the electrolytic deposits.[3,4,9,10] Different workers assess in different ways the importance of the above factors in particular situations. However, a decisive role is attributed to the first two factors: the presence on the coated surface of an oxide film, which prevents the firm adhesion of the coating to the base, and the negative potential of aluminium following its activation, as a consequence of which the corrosion of the metal constituting the base in electrolytes is accompanied by the formation of a porous, frequently powdery, contact deposit, which only weakly adheres to the aluminium surface.

As a consequence of the above difficulties, the attempts to treat aluminium using the same procedure as in the deposition of coatings on metals such as copper or iron have not led to satisfactory results. The electrolytic deposits had an unsatisfactory structure, adhered only weakly to the main metal, and did not meet other operating requirements. Special electrolytes and procedures for the treatment of the surface to be coated are therefore used to coat articles made of aluminium and its alloys. The general problems of the technology of the deposition of galvanic coatings on aluminium have been considered in a series of monographs and review articles.[3–5,8–17,etc.] In accordance with the nature of the preparatory operations and the surface obtained as a result of the preparation, the proposed methods for the deposition of coatings on aluminium are classified as follows:[4,11]

1) deposition of coatings on a rough surface;
2) deposition of coatings on a film of contact metal;
3) deposition of coatings on an oxide film;
4) direct method;
5) other methods.

However, the change in the state of the surface during the preparatory process cannot alone solve all the problems arising in the deposition of coatings on aluminium. Certain changes are in one way or another necessary also in the deposition stage. In a series of procedures, an additional heat treatment operation, usually for the coating of components, is also introduced into the technological scheme. The practical success of a particular process is determined by the extent to which account is taken in its individual stages of the

specific properties of aluminium and of the changes in these properties on passing from one alloy to another.

II. Deposition of galvanic coatings on a rough surface

The deposition of coatings on a rough aluminium surface is apparently the oldest method. The first studies date back to the beginning of this century.[3,4,9] The roughness of the coated surface is increased by mechanical, chemical, or electrochemical treatment. The adhesion increases as a result of the greater surface area of the cathode and the creation of additional bonding with the base as a result of the mechanical fixation ("anchoring") of the deposit in hollows on the surface. Solutions of hydrochloric, hydrofluoric, and chloroacetic acids or their mixtures with sulphuric, nitric, and phosphoric acids are usually employed for the chemical treatment. Electrochemical anodic etching is generally carried out in chloride solutions, sometimes with addition of other salts and acids. Sand blasting and hydroabrasive mechanical treatments are used to increase roughness.[3,4,17,18]

The systematic studies of this method[18–24] are associated with the development of electrochemical etching processes. It has been shown that electrochemical anodic dissolution ensures a greater number, compared with chemical dissolution, of etching sites on the aluminium surface and a greater uniformity of the etching.[20] Best results have been achieved using a hot (70–90 °C) solution of sodium chloride. The introduction of sulphates and tartrates into the solution leads, according to Batashov et al.,[20] to an increase in the ionic conductivity of the surface oxide and promotes the formation of a larger surface. The etching coefficient increases approximately by an order of magnitude and reaches 30–35, which makes it possible to obtain high quality, as regards adhesion, coatings of aluminium from the usual electrolytes: copper coatings from a pyrophosphate solution or nickel coatings from a sulphate solution.[18,20]

The method involving the formation of a rough surface, as an independent type of preparation of aluminium before the deposition of galvanic coatings, is nowadays finding a very limited application for the following reasons:[3,4,9,22,23]

1) insufficient reliability in ensuring a firm adhesion of the coating to the aluminium base;

2) difficulties in obtaining lustrous decorative coatings;

3) weak protective properties of rough coatings.

However, additional electrochemical or more often chemical etching in order to increase somewhat the roughness of the surface is frequently employed as an auxiliary operation in the preparation of aluminium and its alloys for coating by other methods.[5,24–26]

III. Deposition of galvanic coatings with an intervening film of contact metal

The deposition of a film of contact metal before the electrolytic deposition of coatings on aluminium is sometimes referred to as the immersion treatment or immersion preparation. The essential feature of the method is that aluminium is immersed in a corrosive solution containing the ions of a more positive metal M^{z+}. As a result of the action of the corrosive component of the solution (OH^- ions in an alkaline medium and F^-, Cl^-, and BF_4^- ions in an acid medium), the surface of aluminium is activated, the corrosion potential shifts in the negative direction, and a contact exchange reaction takes place:

$$zAl + 3M^{z+} \rightarrow zAl^{3+} + 3M.$$

One selects conditions such that the contact metal is segregated as a thin compact film and can serve as a base on which the galvanic coating is subsequently deposited.

The appearance of the immersion method is associated with the development of the chemical treatment method. In the early studies by Work, designed to achieve a rough surface by chemical methods, it was noted that certain etching solutions with a high content of a salt of a more positive metal not only make the surface of aluminium rougher but also form a contact film, which facilitates the electrodeposition process.[9] At the present time, there exist recommendations concerning the deposition of zinc, tin, nickel, copper, and other metal films. However, only some of them have found a wide-scale practical employment. The technological process involving the deposition of coatings includes the cleaning of the coated surface, the deposition of a film of contact metal, and the electrodeposition of the coatings. In some processes, provision is made for a concluding heat treatment.

The following factors which make it possible to obtain high quality galvanic coatings have been noted. When aluminium is immersed in a corrosive solution for the segregation of the contact metal, a passive film prevents the normal course of the deposition of the metal and the adhesion of the deposit to the base is removed from its surface. The contact metal protects the surface of aluminium against reoxidation. The etching of the aluminium surface in the course of the contact exchange is non-uniform, which results in an increase of its microroughness and improves the conditions for the preparation of coatings firmly adhering to the base. The principal disadvantage of the method is associated with the fact that the contact exchange process and hence the structure of the film depend on the composition of the alloy to be coated. In the deposition of films on different aluminium alloys, it is therefore necessary in many instances to alter the composition of the solutions, the conditions, and sometimes also the procedure for the preparation of the surface.

1. Alkaline solutions

OH^- ions are the strongest activators of aluminium. The activating capacity of alkaline solutions reaches maximum values at pH 15–16 (concentration of alkali 5–7 M). Under these conditions, the rate of the self-dissolution of aluminium at a corrosion potential of $-(1.4-1.8)$ V is 150–170 g $m^2 h^{-1}$.[27–29] The decrease in the rate of dissolution at higher concentrations of alkali is mainly attributed to the formation on the surface of the metal of solid aluminates or their hydrolysis products.[27] $[Al(OH)_4]^-$ is usually quoted as the final product of the overall aluminium dissolution reaction in alkalis:

$$Al + 4OH^- \rightarrow [Al(OH)_4]^- + 3\bar{e}.$$

Another formulation of this reaction, in which the final product is the anion AlO_2^-, can also be encountered. However, this form of formulating the reaction is more arbitrary, because the existence of the above species in aqueous solutions is regarded as unlikely.[30]

The study of the mechanism of the corrosion of aluminium in alkaline solutions has led most investigators to the conclusion that this process proceeds via a stage involving the formation of an

intermediate passive oxide or hydroxide film.[31–33] According to the results of Heusler and Allgaier,[33] in weakly alkaline solutions the film has the structure of bayerite while in strongly alkaline solutions it has the structure of hydrargillite, the rate of corrosion being limited by the process

$$Al(OH)_3 + OH^- \rightarrow [Al(OH)_4]^-.$$

The rate of self-dissolution remains constant within a wide range of potentials. The possibility of the dissolution of aluminium via an active mechanism even at very negative potentials is doubtful[34] and this term is frequently used merely to characterise the high rate of the process. Studies with the aid of rotating disc electrodes have demonstrated a significant influence of the diffusion factor—the supply of OH^- ions to the corroding metal—on the rate of dissolution. It has been suggested that contact films of zinc, tin, copper, and nickel be deposited on aluminium from alkaline solutions.

The commonest method of deposition of a contact metal film on aluminium is the zincate treatment. This method (it has been described in detail[3,9]) was proposed in the USA by Hewitson in 1927. In the USSR, the zincate preparation was first studied in detail by Lainer.[9] At the present time, most publications are devoted to this process. Wide-scale studies are being carried out on the mechanism of the zincate treatment process and new improved electrolytes are being proposed.[35,36]

The zincate treatment involves the immersion of the aluminium article in a solution of sodium zincate. In an alkaline solution of sodium zincate, the surface of aluminium is activated and a film of contact zinc is formed. In an alkaline solution, zinc exists in the form of complex ions and its deposition potential is very negative, which promotes the formation of a compact and thin contact film without deep etching of the main metal. Account is also taken of the favourable ratio of the crystal lattice parameters of the two metals.[3]

In the simplest case, the zincate solution consists of sodium hydroxide and zinc oxide. The thickness and compactness of the zinc film depend on the concentration of the solution, the ratio of the components, temperature, and the period during which the aluminium articles are maintained in the solution. Solutions containing from 5 to 100 g $litre^{-1}$ of ZnO are employed. In concentrated zincate solutions, it is easier to obtain high quality films. Such solutions do not require frequent changing or correction but their high viscosity hinders the washing of the surface and the treatment of articles with a complex profile. On the other hand, dilute ZnO solutions require more careful technological monitoring. The higher the concentration of OH^- ions, which form a complex with zinc, the smaller the thickness and the greater the compactness of the film. It is therefore recommended that a higher ratio of OH^- to zinc ions be maintained in dilute zincate solutions. With increase in process temperature and the exposure time, the thickness of the films increases. The process is generally carried out at room temperature. The duration of the treatment depends on the composition of the coated alloy. For an inadequate exposure, there is insufficient time for the contact coating to cover the main metal and, when the exposure is too long, a thick loose film is produced.[9]

An advantage of the zincate treatment is that it is possible with its aid to coat articles made of both pure aluminium and its alloys. The solutions employed are simple in composition and are cheap. The principal disadvantages are associated with the high percentage of rejects, because of poor adhesion of the coating in the treatment of many alloys,[5,37] and with the low corrosion stability of the zinc film.[3,38,39] In order to obtain a film firmly adhering to the base, careful maintenance of the treatment conditions is required. Best results are obtained on alloys containing copper and manganese. On high-silicon alloys (more than 12% of silicon), it is not possible to achieve a satisfactory adhesion.[9] According to the literature,[8,38] the greatest wastage is on alloys containing electronegative metals: zinc and particularly magnesium. In such cases it is recommended that the treatment be carried out in other contact zinc-plating solutions.[8] The low corrosion stability of the aluminium–zinc–galvanic coating system is associated with the fact that the zinc layer behaves in most cases as the anode both in relation to the coating and to the main metal. In the presence of perforating pores in the coating, the zinc film begins to dissolve vigorously in the first place exerting a protecting effect against the corrosion of the base and the coating. The corrosion of zinc leads to the swelling of the coating caused by the corrosion products.[38,39] Studies carried out to improve the zincate preparation are designed to eliminate the above disadvantages.

The main aspect of the improvement of the zincate treatment consists nowadays in the use of modified zincate solutions, which contain modifying additives: iron, nickel, copper, cobalt, lead, and other metal salts and nitrates, sulphides, and cyanides. The addition of metal ions improves the corrosion properties and structure of the zinc film, as a result of the latter becoming alloyed. Organic compounds are also introduced into zincate solutions: amines, acids, alcohols, and others. A correlation has been noted between the quality of the film and the corrosion potential difference between the film and the coated alloy in the zincate solution. The lower this difference, the sooner should the zinc displacement process be completed and the denser and thinner the zinc film. Although this postulate cannot be regarded as rigorous, it usually holds.[8] It has been shown[40] that, under the conditions of diffusion-dependent limitations, a loose zinc film is formed, whilst under the conditions of kinetic limitations to the rate of the process a compact film is produced. In the presence of modifying agents, the initial potential difference between the zinc film and aluminium diminishes and in the course of the contact treatment it approaches zero, which leads to the retardation of the contact exchange in the course of time. In modified zincate solutions a rigorous maintenance of the duration of the operation is therefore not required and it depends less on the type of alloy to be coated.[41] At the same time, the small potential difference between the zinc film and the aluminium base in the modified solutions, in the treatment of alloys containing magnesium and zinc, leads to the need for additional cathodic polarisation of the aluminium components in the zincate bath.[38]

One of the first most successful modified zincate solutions contains added iron(III) chloride and a tartrate salt.[9] The zinc film deposited from this solution contains a small amount of iron, which increases the corrosion resistance and compactness of the film. The tartrate salt binds the iron ions into a complex, preventing their precipitation in the alkaline solution, and also regulates the rate of formation of the deposit and its structure. The solution can be used to coat alloys which are coated unsatisfactorily in the unmodified zincate solution. Very satisfactory results have been noted for alloys containing magnesium or both magnesium and silicon.

Modified zincate solutions containing copper and nickel complexes (mainly cyanide complexes) have come to be most widely used abroad in recent years. It has been noted that these additives regulate the potential difference between the aluminium alloys and the zinc film,[41] diminish the thickness of the film,[36,42] improve the

lustre of the electrolytic metal deposits,[36,43] and appreciably increase the strength of the adhesion of the coating to aluminium.[36,42,44] Copper and nickel are also effective alloying components which increase the corrosion resistance of the films.[36] For example, in the "Bondal" process, the compact deposit consists of 86% of zinc, 8% of copper, and 6% of nickel, while in the "Bettel" process it consists of 90% of zinc, 5% of copper, and 5% of nickel.[36] It has been noted[38,42,45] that zincate solutions modified by copper and nickel cyanides can be used to coat aluminium alloys containing silicon, magnesium, and zinc.

Organic components are sometimes introduced into the zincate solutions. A wide range of organic additives, functioning as complex forming ligands and surfactants, have been investigated.[3,46] Organic additives make it possible to use more economical dilute zincate solutions and ensure the formation of a thin, compact zinc film strongly adhering to the base.

In a series of technological processes using the zincate method for the preparation of aluminium, provision is made for the treatment of the articles after the deposition of the electrolytic coatings. The influence of such treatment on the quality of the coatings has been investigated by Lainer.[8] Lainer attributes the increase in the strength of adhesion during the heat treatment to the formation of a diffusion layer at the main metal–coating interface. A temperature of 200–250 °C and a treatment time of 30 min are recommended as the optimum conditions for the heat treatment in the nickel plating of aluminium.

Coatings with a more stable quality are obtained in the double zincate treatment of aluminium. It involves the removal of the contact zinc film from the article in nitric or sulphuric acid solutions and the retreatment of the article in a zincate solution. The potential difference between the base and zinc in the case of the double zincate treatment is smaller than in the single treatment. A thinner and denser film is obtained. The process was first investigated by Edwards and Swanson.[47] At the present time, this procedure is applied widely when both the usual and modified zincate solutions are employed.[5,43,48,49] It has been noted that in a number of instances, when after the single treatment the coatings adhere inadequately to the base, the double zincate treatment yields satisfactory results. In some instances, the double zincate treatment ensured the same strength of adhesion of the coating to the base as the single treatment with subsequent heat treatment.[9,50] According to Ref. 51, the use of the double zincate treatment makes it possible to obtain a strength of adhesion which is not inferior to the strength of the main metal. The disadvantages of the double zincate treatment are the increase in the number of technological operations and the additional consumption of reagents.

Aluminium articles coated by a zinc film are frequently copper-plated and electrolytically and chemically nickel-plated; chromium, cadmium, and silver plating as well as coatings consisting of other metals are used more rarely. For the deposition of electrolytic and chemical coatings on a zinc film, both the usual universal electrolytes and special electrolytes yielding better results are employed. These electrolytes are less corrosive to the thin zinc film, which is easily damaged and decomposed in many solutions. The film is deposited immediately after the zincate treatment and careful washing of the components. It has been noted that[52,53] even a short exposure of components with a zinc film to air can reduce greatly the strength of adhesion. The characteristics of a set of special electrolytes are presented below.

Weakly alkaline cyanide electrolytes with pH < 10 having an increased content of free cyanides and added tartrates are recommended for copper plating. It is also recommended that the components be immersed in the electrolyte with current flowing as well as an initial current pulse.[4,5,36,54]

Special electrolytes have been recommended for the deposition of thin electrolytic nickel coatings ("overcoats") on articles with a zinc film. Electrolytes containing citrates, which inhibit the contact exchange between the film and the nickel-plating electrolyte, have been proposed.[8] However, citrate electrolytes are expensive and unstable. Sulphate electrolytes, whose pH is in the range from 5.3 to 5.7, are more convenient for practical use. The electrolysis is carried out at 18–25 °C and at a low cathodic current density (0.5 A dm^{-2}).[52] The chloride-free sulphate matt nickel-plating electrolyte is recommended[55] for the covering of a zinc film by a thin (approximately 1 μm thick) nickel layer. An acetate-glycolate electrolyte, in which Ni^{+} ions are bound in the complex with glycollic acid, has been proposed for the deposition of a thin (2–3 μm) layer of nickel. It differs from sulphate solutions by being less corrosive and less stringent requirements have therefore to be met by the quality of the zinc film.[22,53] The electrolyte has been used successfully for the deposition of electrolytic coatings on aluminium in automatic apparatus. The mechanism of the deposition of nickel on a zinc film from such an electrolyte has been considered.[56]

As noted by Schmeling,[57] the zincate treatment is the most reliable procedure for the preparation of aluminium before chemical nickel plating. In this case, relatively non-corrosive weakly acid and weakly alkaline solutions are used for the deposition of nickel.[55,57–60] In order to reduce the corrosiveness, nickel is introduced in the form of acetate and a large amount of ligands, for example, citrates[59] or lactates,[60] is introduced. When aluminium components with a zinc film are immersed in a chemical nickel-plating solution, the nickel deposition process does not begin immediately. The induction period, lasting usually 10–20 s, is caused by the negative potential of the surface of the component (about −0.75 V), which arises on dissolution of the zinc film. The dissolution of zinc is accompanied by the contact liberation of nickel and the gradual displacement of the potential into the positive region as far as −(0.4–0.45) V (depending on the composition of the aluminium alloy, the thickness of the zinc film, and the composition of the chemical nickel-plating solution). The potential stabilises at this value and the chemical nickel-plating process begins.[58–61]

It has been established[58–61] that the zinc film dissolves almost completely in the chemical nickel-plating solution, but most of the dissolved zinc is subsequently chemically reduced forming the so called "zinc-enriched layer". The thickness of this layer varies from 50 to 300 nm. At the same time, the correlation between the thickness of the "zinc-enriched layer", on the one hand, and its zinc content and its adhesion, on the other, has not been observed. In order to increase the reliability of the adhesion of chemical nickel coatings, it is recommended[55] that, after the zincate treatment, the components be activated for 10–15 s in very dilute sulphuric or sulphamic acid solutions.

Analysis shows that the zincate treatment is widely used both in the USSR and abroad. This procedure is proposed as the main method or one of the main methods for the preparation of aluminium and its alloys before the deposition of electrolytic coatings in modern textbooks of electroplating,[8,62,63,etc.] in monographs,[3,4] in review articles on the coating of aluminium,[48,64–66,etc] and in the Standards of the USSR,[67] the USA,[65] and other countries. The compositions of modern zincate solutions are not as

a rule fully revealed by foreign firms. The solutions are prepared from compositions made up by the producer firm in a dry form or in the form of concentrated solutions.[48] The "Bondal", "Bettel", "Persal", and other processes have found extensive applications. At the same time, the disadvantages of the zincate treatment noted above have stimulated studies designed to devise other processes. This trend is particularly characteristic of the Soviet Union, where the number of studies on the zincate treatment since the 1950's has diminished sharply and the efforts of investigators are concentrated on the development of new technological processes.

In the 1960's, treatment in another type of alkaline solutions (stannate solutions) began to be applied—here aluminium components are coated by a film of contact tin. These films have been mainly used as independent coatings for the improvement of the antifriction properties of the aluminium surface.[3,9,68] The first communications[69,70] concerning the successful use of the stannate treatment before the deposition of electrolytic coatings on aluminium date back to 1964–1965.

The technological process for the coating of aluminium using the stannate treatment includes the cleaning of the aluminium surface by traditional methods, contact treatment in the stannate solution, coating with bronze in a cyanide electrolyte, and copper plating in a cyanide bath.[41,48] In order to avoid the hydrolysis of stannate in the film of solution on the surface of articles, it is recommended that they be transferred to the bronze-coating bath without preliminary washing.[41,48,71] Stannate treatment processes ("Alstan 80" and "Alstan 80A"), in which the thin film is deposited electrochemically in a stannate solution, have appeared in recent years.[48]

Studies[72,73] have demonstrated an appreciable influence of the kinetics of the tin liberation process on the adhesion of the coatings. It has been noted[73] that, in the stannate treatment, there is an initial rapid dissolution of aluminium induced by the high content of free alkali and the elevated temperature of the solution. During the first 10–20 s of the process, about 2000 aluminium atoms are dissolved per deposited tin atom. Subsequently this ratio is altered rapidly, reaching 1:6. At the same time the rates of dissolution of aluminium and of the evolution of hydrogen are reduced, which can be explained by the coverage of the main metal by the contact deposit of tin. The tin deposition process begins on the electropositive components of the alloy. The marked influence of impurities and alloy components on the stannate treatment process is responsible for the dependence of the conditions in the stannate treatment on the type of coated alloys.

Compared with the deposition of zinc from zincate solution, the contact deposition of tin from stannate solution is much slower and less uniform, while the films formed are thinner and more porous. In order to accelerate the deposition of tin and to increase the number of crystallisation centres, the aluminium particles in stannate solutions are sometimes subjected to additional cathodic polarisation. After coating with bronze and subsequent copper plating, the intervening layer between aluminium and copper consists of a tin-enriched bronze.[39]

Modern solutions for stannate treatment contain, together with the main components (sodium stannate and the free alkali), mixtures of additives, usually organic ligands and surfactants, which regulate the structure of the deposit.[74] The solutions used in the technological process are prepared as a rule from compositions supplied by the manufacturers. The commonest compositions are Alstan and Alstan 20 and 30 for the cleaning of the surface, Alstan 70, 75, 80, and 80A for the deposition of tin, and Alstan 71 for the electrolytic coating of tin by a layer of bronze.[39,42,75,76]

The main advantage of the stannate treatment over the zincate treatment is that it can be used to deposit coatings on articles employed under more severe climatic conditions. The tin film is more resistant to corrosion than the zinc film. However, more expensive and scarce reagents are used for the preparation of stannate solutions and the latter are relatively unstable, being hydrolysed, and therefore have to be changed frequently. The conditions in the stannate treatment also depend on the type of alloy coated. Thus, in the coating of aluminium–silicon and aluminium–magnesium alloys, such treatment yields unsatisfactory results. Although the stannate process produces contact films of higher quality, it is therefore recommended only in special applications where a high cost is justified.[39,41,77]

The stannate treatment has not found extensive applications in the USSR. Studies on the stannate treatment process have been carried out at the Academy of Sciences of the Lithuanian SSR and at the Leningrad Polytechnic Institute. The possibility of using pyrophosphate electrolytes in the stannate method for the electrolytic deposition of bronze and copper coatings has been demonstrated.[71,78]

Alkaline solutions are also recommended for contact deposition of copper and nickel films on aluminium, but their use is more limited compared with zincate and stannate solutions. In order to ensure the solubility of Ni^{2+} and Cu^{2+} compounds in an alkaline medium, an excess of ligands is introduced into the solution. It has been suggested in studies carried out in recent years that amines be employed as such ligands. An ammine electrolyte for the contact copper plating of aluminium and its alloys has been developed at the Kharkov Polytechnic Institute.[79,80] In this solution the OH^- ions have a decisive influence on the morphology of the deposit: at pH < 11.9, copper is hardly deposited, while at pH > 13.5 a dark, loose coating is produced. Thus the working pH range is 11.9–13.5. The optimum thickness of the copper deposit is 1.3–1.5 μm. The sublayer of copper ensures the firm adhesion of the subsequent electrolytic deposit to aluminium, although it can be used also as an independent coating. A similar electrolyte for the contact nickel plating of aluminium and its alloys has been proposed in the USA.[81] Ammonia and organic amines are used as ligands in this instance. The treatment is carried out at a pH of about 12 and at room temperature. According to the authors data, the contact nickel film ensures the effective adhesion of the subsequent electrolytic nickel coating to the base.

2. Acid fluoride and fluoroborate solutions

Aluminium dissolves in acid media also with formation of an intervening oxide film.[31] The activating capacity of H^+ ions is much lower than that of OH^-. According to the studies of Thomas and co-workers,[82,83] this factor can be explained by the fact that in the presence of H^+ only the hydroxo-groups forming part of the compositon of the surface oxide are highly reactive, the $Al-\underset{\displaystyle H}{\underset{|}{O}}-Al$ groups are stable, while the $Al-\underset{\displaystyle Al}{\underset{|}{O}}-Al$ oxo-groups are very stable.

Anions may catalyse the aluminium dissolution process. Among them, fluorides are the most effective. In the presence of fluoride, the rate of dissolution of aluminium increases greatly, while the corrosion potential shifts to the negative region as far as −(1.2–1.35) V. The activating capacity of fluorides increases with increase in concentration but in highly concentrated solutions it falls again owing to the formation of a film of fluoroaluminates.[84] The intervening oxide film on aluminium also contains fluorides, whose

concentration diminishes from the outer surface to its barrier component.[85] According to Wiedmer and Grauer,[86] the rate of the dissolution is limited by the supply of the fluoride to the surface of aluminium and by the heterogeneous-phase interaction of the fluoride with the oxide.

Heiman[87] demonstrated the possibility of the contact deposition on aluminium of zinc, cadmium, tin, and copper films from fluoride-containing solutions and their use for the subsequent electrolytic deposition of other metals.

A new technology for the tinning of aluminium wire has been introduced. It involves the contact deposition on a pre-cleaned surface of the metal of a sub-layer of tin from a highly acid fluoride solution. The tin sublayer is coated with copper in a cyanide bath and the wire is then tinned in a fluoroborate electrolyte.[88] A technology for the tinning of aluminium wire has been developed and tested under semi-industrial conditions. Its main operations are the deposition of a film of zinc–nickel alloy from a weakly acid fluoride-containing solution, electrolytic copper plating in a pyrophosphate electrolyte, and tinning.[89] It was noted that both technologies ensure the formation of high quality coatings which withstand welding.

A series of fluorobroate solutions have been proposed for the contact deposition of zinc and its alloys with nickel. Fluoroborates are also effective activators of aluminium, being somewhat inferior in this respect to fluorides.[87] High quality deposits of contact zinc can be obtained from a solution of zinc fluorobrate at pH 3.0.[8] In order to improve the quality of the film, nickel and ammonium fluoroborates are added to the solution.[3,90,91] A solution proposed in a patent[91] is used in the Limeda Al biological process for the deposition of a zinc–nickel alloy film (30–40% of nickel) on aluminium. The articles are immersed in the solution initially without a current and then a brief electrodeposition of the alloy is carried out. In order to increase the strength of adhesion of the film to aluminium, it has been suggested that triethanolamine[92] or Sintanol DS-10[10] be introduced into the solution. It is recommended that, before the contact treatment, etching be carried out in a solution containing fluoroboric acid.[25] Electrolytic coatings can be deposited on the contact film of the zinc–nickel alloy from relatively non-corrosive electrolytes whose pH is in the range 4–10. Best results are obtained for copper plating in a pyrophosphate electrolyte and for nickel plating in a sulphate electrolyte.

By virtue of certain advantages over the zincate treatment, the Limeda Al technology has found applications in a number of undertakings in the USSR. The lower porosity of the film and the improved corrosion reistance of the coatings should be included among the advantages of this technology,[93–95] while its disadvantages comprise the more complex preparation and use of the solutions and also the need to maintain different treatment conditions for different aluminium alloys.[41]

The influence of various factors on the adhesion of electrolytic coatings to aluminium, treated in fluoroborate solutions for contact deposition, has been investigated in recent years.[95–101] According to the authors of these studies, the adhesion of coatings to the main metal is determined by the compactness of the structure of the contact film and is independent of its thickness. If the contact film is not continuous, then on the sections where it is absent the adhesion is unsatisfactory. On the other hand, on the sections where the zinc–nickel alloy film is in contact with the base, the strength of adhesion exceeds the intrinsic strength of aluminium. The adhesion can be impaired by partial etching of aluminium under the contact deposit caused by over-exposure to the fluoroborate solution or by the treatment with a corrosive electrolyte in the deposition of the coating.

3. Acid chloride solutions

Chlorides are effective activators of aluminium in an acid medium. According to the classification proposed by Davydov and Kamkin,[102] chlorides are anodic-anionic activators. In this case activation takes place as a result of the electrical breakdown of the passive film, which can occur even at stationary potentials of $-(0.4-0.65)$ V. It has been noted[103] that, for the activation mechanism indicated, there is a possibility not of a decrease of the thickness of the passive film but merely of an increase in its defectiveness. The latter factor leads to the local character of the dissolution of aluminium accompanied by an increase in the roughness of its surface. Chloride solutions have been proposed for the contact deposition of nickel, iron, manganese, copper, and a number of other metals.[3,9] The contact deposition of nickel on aluminium from a solution of nickel chloride in phosphoric acid has found the greatest practical application in the USSR.[104,105] The nickel film serves as a base for the subsequent chemical or electrochemical nickel plating. The corrosion resistance of the coatings deposited on contact nickel is much higher than that of the analogous coatings deposited on a zincate film.[106,107] However, the employment of the method on a wider scale is prevented by the inadequate reliability of the adhesion of the coatings to the base comprising certain alloys.[108] In a number of instances, it is altogether impossible to obtain high quality contact films. It has been shown that heat treatment improves the strength of adhesion of the coatings to the base.

Solutions for the contact copper plating of aluminium, containing chlorides as activators, have been investigated.[79,109–111] Thus an oxalate electrolyte, incorporating a small amount of chlorides, has been recommended for this purpose.[111] Copper deposits up to 5μm thick adhere satisfactorily to the base and can be used both as a sublayer for the subsequent deposition of electrolytic coatings and as an independent coating, for example, for welding.

IV. Deposition of galvanic coatings on oxidised aluminium

The method consists in the anodisation (sometimes chemical oxidation), after preliminary cleaning, of the surface to be coated followed by the deposition of the electrolytic coating. The process was developed in the 1930's mainly as a result of the studies of Fischer (quoted after Ref. 17), Travers,[112] and Kudryavtsev.[113] Phosphoric acid (more rarely oxalic, sulphuric, chromic, and other acids) is usually employed nowadays to obtain the anodic oxide, but mixtures of acids are also used.[3,17,24,60] Nickel, copper, cadmium, silver, iron, zinc, and chromium are deposited on the anodised aluminium.[11,17,114] Copper plating in a pyrophosphate electrolyte and nickel plating in a sulphate or sulphamate electrolyte are commonest. Apart from the operations indicated, the technological process sometimes involves additional etching before oxidation or after it[9,113,115–118] and a concluding heat treatment of the coatings.[119,120]

An advantage of the method is the improved protecting capacity of the coatings associated with the presence of an oxide film on the surface to be coated. A disadvantage is its high sensitivity to the smallest changes in the composition of the treated alloys. The purer the aluminium, the greater the difficulties arise in its coating. For pure aluminium, anodic treatment altogether fails to yield positive

results. Certain copper-containing and cast alloys are not always coated satisfactorily. The disadvantages of the process are its relatively high cost and the need to have for anodisation special power supply sources with an increased voltage.[3,9,10] For these reasons, the method is nowadays finding only a limited application compared with the immersion method.[48] Modern studies of the deposition of metals on oxidised aluminium are directed towards the investigation of the process mechanism and the improvement of the technology in order to eliminate the above disadvantages.

1. Mechanical theory of the adhesion of electrolytic metal deposits to oxidised aluminium

The commonest is the mechanical theory of the adhesion of an electrolytic deposit to the anodic oxide film. The foundations of the theory were laid by Keller et al.,[121] who noted the dependence of the structure of the anodic oxide on the composition of the anodisation electrolyte and a number of other factors and put forward the hypothesis that the structure of the anodic oxide is the determining factor in the deposition of metallic coatings on it. It was suggested that, since the films obtained in phosphoric acid are distinguished by the presence of numerous large-diameter pores, they should yield best results also on anodisation of aluminium before the deposition of electrolytic coatings on the latter.

The theory treats the anodic oxide as a dielectric having a discrete structure. During the deposition of coatings, the electric current passes mainly through "weak sites" in the oxide layer, which consists of pores, micro-cracks, and sometimes the inclusions of more noble metals. The electrolytic deposit begins to be formed initially within the pores as finely dispersed fibres, which then grow together, forming bridges across the film. Adhesion is achieved as a result of the mechanical fixation of the coating within the pores of the oxide film, which in turn adheres firmly to the main metal.[5,9,122] These postulates have been confirmed by a number of experimental data. At the beginning of the electrolysis, the formation of an electrolytic deposit is observed only at individual points on the cathode. Owing to the high true current density, the first layers of the metal in deposition on an oxide layer have a dark and even black colour regardless of whether copper, nickel, or silver is deposited and acquire the normal form only as the coating grows. According to data of Schardein[122] and Lashmore,[123] firm adhesion is achieved when the pores of the anodic film have been completely filled with the electrolytic deposit. The electrolytic deposits obtained in the pores under these conditions have the form of intertwined tree roots.[124,125] It has been established that the complete filling of the pores of the anodic oxide by the electrolytic deposit takes place in the deposition of coatings at low current densities, apparently owing to the elimination of diffusional limitations. It has been recommended in a number of publications[123,126,127] that, in the deposition of coatings on an anodic oxide, the cathodic current density be gradually and slowly increased (in the first minutes of the electrolysis) from zero to a stationary value. A correlation has been noted between the geometrical size of the pores and the quality of the coatings. It has been confirmed that the largest and most uniformly distributed pores are present in films obtained in phosphoric acid and this explains the finding that, when the latter is used, high quality coatings are obtained.[17,24,121]

It has been established[122] that the pore diameter increases with increase in the anodisation potential. At the same time an improvement in the adhesion of the coatings to aluminium has been noted.[122,123] However, the cathodic electrocrystallisation of metals on films obtained at very high potentials (60–80 V and above) is difficult apparently due to the appreciable thickness of the barrier layer. This feature together with the decrease in the total number of pores leads to a diminution of the number of centres for the electrocrystallisation of the electrolytic deposit and to a decrease in the strength of adhesion.[24,122]

High quality coatings can be obtained starting from a specific thickness of the anodic film.[24,123] For a small thickness (i.e. for a short anodisation time), the adhesion is unsatisfactory. Kishi[24] compares this kind of coating with a tree having weak, shallow roots. Lashmore[123] suggests that the side walls of the pores make the main contribution to adhesion. With increase in the thickness of the anodic film, the lateral surface of the pores increases and thus ensures the necessary strength of adhesion. For a greater thickness of the oxide film, the electrodeposited coatings become non-continuous as a result of the decrease in the number of crystallisation centres.[24,128,129] This phenomenon is usually observed for anodic films obtained in sulphuric acid.

However, certain experimental results cannot be explained satisfactorily on the basis of the mechanical theory of adhesion. According to a number of workers,[24,123,128,129] the difference between the structures and pore sizes of the films obtained in phosphoric acid and other acids (sulphuric, oxalic, and chromic) is small. The pores in the films obtained in these acids can also be completely filled with the electrolytic deposit.[17,124,125] Nevertheless the anodic films formed in phosphoric acid ensure a much greater strength of adhesion of the coatings to aluminium. The structures of sufficiently thick anodic films on different aluminium alloys also differ little,[122] while the strength of the adhesion depends greatly on the type of alloys coated.[9,126]

It has been noted that the electrodeposition of a metal can occur not only in the pores but also on the outer surface of the film[123] as well as on the sharp edges between the hollows in the oxide.[24] These observations led to the creation of the chemical theory of the adhesion of electrochemical metal deposits to anodised aluminium.

2. Chemical theory of the adhesion of electrolytic deposits of metals to anodised aluminium

Aleksandrov, Bogoyavlenskii, and Khudyakov and co-workers[130–137] have developed a chemical theory of the adhesion of coatings to the anodic oxide film. The principal postulates of this theory have been described also in studies by foreign authors.[24,128,129,138] The theory treats the anodic oxide as a colloidal-polymeric formation with semiconducting properties, containing inclusions of anions from the anodisation electrolyte and the components of the aluminium alloys.

According to this theory, the formation of the electrolytic deposit begins simultaneously both in the pores of the oxide and on its surface. The strength of adhesion of the electrolytic deposit to the base is determined not by the mechanical fixation of the deposit within the pores of the oxide layer but by the presence of chemical bonds between the deposited metal and the components of the anodic oxide, mainly the inclusions of anions from the oxidation electrolyte.

The greatest strength of adhesion of the coatings observed when the oxide is formed in phosphoric acid is attributed to the fact that phosphate ions readily penetrate into the anodic oxide during anodisation and create active centres for the electrocrystallisation of metals. The number of crystallisation centres on such oxides is much greater than on oxides obtained in solutions in other acids. It has been observed by the tracer atom method that the number of phosphate ions incorporated in the anodic oxide can be increased by introducing a series of additives (zinc sulphate, polyethyleneimine) or

diminished (sulphuric acid) and hence the strength of adhesion of the coatings to the anodised aluminium can be correspondingly altered.[130,139–141]

The inclusion of the components of the aluminium alloys and their oxidation products in the anodic oxide creates additional crystallisation centres for the deposited metal and hence promotes an increase in the strength of adhesion of the coating to the base. It has been established that the content of the phosphate ions in the oxide increases somewhat with increase in the concentration of the alloy components, which is also accompanied by an increase in the strength of adhesion. Various alloy components promote to different extents the increase in the concentration of phosphate ions in the anodic oxide. These data make it possible to explain, from the standpoint of the chemical theory, also familiar facts such as the difficulties arising in the coating of anodised high-purity aluminium and the dependence of the strength of adhesion on the type of alloy coated.

According to the chemical theory, although the pores in the oxide film do participate in the electrodeposition process they do not play a decisive role. It has been established by X-ray diffraction and electronic spectroscopy[131] that a satisfactory adhesion of the coatings to anodised aluminium can be achieved even when the pores are only slightly filled by the electrolytic deposit. However, the details of the chemical theory have so far been insufficiently worked out to be able to reject the role of pores in the electrocrystallisation processes and in the adhesion of coatings to aluminium oxide.

A positive aspect of the chemical theory is the fact that it creates a basis for the development of a general approach to the analysis of the electrodeposition of metals on oxidised aluminium. The literature of recent years contains data confirming the postulates of both the chemical and the mechanical theory of the adhesion of galvanic coatings to anodised aluminium. It is noteworthy that fundamentally the two theories do not conflict with one another.

3. The development of technological processes for the electrodeposition of metals on oxidised aluminium

Although for reasons indicated, the method involving the deposition of metals on preoxidised aluminium is so far finding limited applications, nevertheless during the last 10–15 years the number of studies devoted to its investigation and improvement has greatly increased. The main bulk of publications were in the USSR, the USA, and Japan. Thus the American Electroplating Society included the study of the electrodeposition of metals on anodised aluminium in its main research projects: Project 41 and Project 61. The results of studies in the USA have been examined by Lashmore,[123,142] Schardein,[122] and Thomas.[143]

Analysis shows that the improvement of the processes for the deposition of coatings on aluminium with preliminary anodisation has the following main aspects: 1) the development of new electrolytes for the deposition of coatings on anodic aluminium oxide and of anodisation procedures; 2) improvement of additional operations for the modification of the anodic oxide and the preliminary preparation of the surface; 3) oxidation and deposition of electrolytic coatings in one bath; 4) combination of the anodisation process with the preliminary liberation of the metal.

Among the current studies devoted to the first aspect, mention should be made of a new technology for the silver plating of anodised aluminium in a highly productive sulphate-ammonia electrolyte,[144] a technology for the nickel plating of anodised aluminium alloys in a sulphate-tartrate electrolyte,[145] a technology for the stepwise anodisation of aluminium articles (reflectors) in a phosphate bath and for the subsequent nickel plating in a citrate electrolyte,[146] and a technology for the copper plating of anodised aluminium alloys.[147] Technological processes for anodisation and subsequent deposition of a series of electrolytic coatings (copper–nickel–chromium, copper–silver, copper–cadmium) on various aluminium alloys have been studied in detail at the Kazan Institute of Aviation and are being introduced into industry.[148–150]

Studies on the partial or complete replacement of phosphoric acid in the anodisation of aluminium by cheaper, mainly sulphuric acid, solutions are being continued. Lukashchuk and Marchenko[151,152] developed a technology for the anodisation of aluminium alloys in a sulphuric acid electrolyte with subsequent electrochemical copper plating. In order to improve the properties of the oxide films, it was suggested that activators—fluorides and fluorosilicates—be introduced into the anodisation solution. These additives increase severalfold the active surface area of the oxide and improve the strength of adhesion to aluminium and its alloys.

The technology for the coating of motor car bumpers made of high-strength aluminium–copper–magnesium alloys with nickel and chromium, developed by Wittrock,[153] has found practical applications in the USA. The first nickel layer is deposited from a sulphamic acid electrolyte on a base anodised in a mixture of phosphoric and sulphuric acids. It was noted that the use of a copper sublayer is undesirable owing to the decrease in the protecting capacity of the coating as a consequence of the enhancement of the contact corrosion in its pores. In one of the latest studies,[126] Wittrock recommends that the anodisation be carried out in a very dilute (3%) solution of phosphoric acid at a high temperature (about 60 °C) with activation of the resulting oxide in sulphamic acid. It is suggested that a sulphamate electrolyte be used for the subsequent nickel plating. The high strength of adhesion of the nickel deposits to the aluminium–zinc–magnesium alloys was noted.

The studies on the second aspect of the modification of the oxide film before the deposition of electrolytic coatings are not fundamentally new. The films are modified in the course of the activation of anodised aluminium—by treatment in dilute acid solutions. The operation became a component of the first technological processes proposed in the 1930's.[3,17] It was established[130] that, after activation, there is an increase in the number of crystallisation centres for the subsequent electrodeposition of the metal, which has a favourable effect on the strength of adhesion of the coating to the base. Best results were noted on treatment of the oxide film in fluoride solutions.

Sulphamic or sulphuric acid solutions have been proposed for the activation of the oxide films.[142,144] It has been noted[154] that the activation of the oxide in sulphamic acid makes it possible to carry out the anodisation process in sulphuric acid and to deposit the electrolytic coatings from electrolytes with the usual composition.

The oxide films can also be activated in the electrolytes for the deposition of electrolytic coatings via a.c. polarisation or by brief electrochemical treatment in solutions for chemical nickel plating.[155,156] In the new technology for the deposition of an iron–nickel alloy on aluminium anodised in phosphoric acid, the activation is carried out in the acid sulphate electrolyte for the deposition of electrolytic coatings.[157] The anodic activation in a dilute solution of hydrofluoric or sulphamic acid after anodisation in a phosphoric acid bath greatly increases the strength of adhesion to aluminium of the nickel coatings obtained in the sulphamate electrolyte.[123]

There have been studies designed to improve the preparatory operations before the deposition of the oxide film. According to Aleksandrov and co-workers,[26,158] etching in 15% hydrochloric acid before anodisation makes it possible to expand the range of permissible phosphoric acid concentrations, the current density, and the process time and also makes it possible to obtain high quality coatings, as regards adhesion, on articles anodised in other acids: sulphuric, chromic, and oxalic. The positive effect of the preliminary etching has been attributed to the increase in the porosity of the oxide films by 5–7%. There is a simultaneous increase in the roughness of the surface, which increases the area of the actual contact between the anodic oxide and the galvanic coating.[141]

The third aspect—anodisation and deposition of galvanic coatings in a single bath—is a comparatively new technological procedure proposed by Mondolfo,[159,160] Bogoyavlenskii and Khudyakov,[161–163] and others. The combination of these two operations is achieved by switching the polarity of the power source. A technology has been developed for the anodisation and deposition of a galvanic coating in a single bath in the preparation of zinc,[164] copper,[160,165–167] cadmium,[165,166] iron,[168] and chromium[169,170] coatings. It was established[164,171] that the nature of the metal cation in the oxidising bath has different effects on the properties of the anodic oxide and the adhesion of the electrolytic deposits obtained from the same electrolyte. The favourable effect of cations is attributed to their incorporation in the oxide film. On deposition of the metal, these cations are reduced, generating additional crystallisation centres and promoting the improvement of the adhesion of the coating to the base.

The advantages of the method involving oxidation and electrodeposition in a single bath consist in the absence of intermediate operations, in which the oxide can undergo undesirable changes, and in a decrease in the total number of operations.[165] However, the operation of a bath in which both oxidation and deposition of the metallic coating take place is fairly complex.

A fundamentally new aspect of the development of the method for the electrodeposition of a metal on oxidised aluminium constitutes the combination of the process involving the preliminary deposition of metals on aluminium films and subsequent anodisation. This aspect is associated with the work of the Japanese investigators Akijama, Yasuchara, and others.[138] It has been established by electron microscopy, X-ray diffraction, and spectroscopic studies that thin films of metals as well as alloy components can be incorporated on anodisation in the oxide film formed in phosphoric acid and can subsequently serve as additional crystallisation centres in the deposition of metals. Japanese workers[138] and subsequently Meckelburg[128] proposed a technology for the copper plating of anodised aluminium involving the preliminary deposition (by a contact or electrolytic process) of iron. On anodisation, the main bulk of the iron coating dissolves but a proportion of it remains as an admixture in the oxide. The preliminary iron plating increases the strength of adhesion of the electrolytic deposits to aluminium and its alloys.

In order to improve the adhesion of the coating the following treatment has been recommended: chemical zinc plating, the removal of the zinc film and anodisation in phosphoric acid, and electrolytic nickel plating.[172] It has been suggested[119] that aluminium can be subjected to an a.c. treatment in a nickel plating electrolyte. A layer of aluminium and nickel oxides is then formed on the surface of aluminium. The current is then changed from a.c. to d.c. and nickel is deposited. It was noted that the metal electrodeposition process can also be carried out in a special bath. In order to improve the adhesion between nickel and aluminium, a final heat treatment of the articles at 100–300 °C is recommended.

An advantage of the above procedure is that it makes it possible to solve the problem of the deposition of galvanic coatings with an oxide sublayer on pure non-alloyed aluminium, while a disadvantage is the increase in the complexity of the technological process.

It is noteworthy that all the proposed improvements have not so far permitted the complete elimination of the main disadvantage of the method—the dependence of the quality of the deposit on the composition of the alloy to be coated.

V. Direct method for the deposition of galvanic coatings

The direct method for the deposition of galvanic coatings on aluminium and its alloys is characterised by the absence of preliminary operations involving the modification of the surface of the base (immersion treatment, anodisation, etc.). The conditions needed to obtain firmly adhering coatings are created directly in the deposition electrolyte by selecting its composition and the electrolysis conditions, while the preliminary preparation of the articles reduces to the cleaning of the surface.

The first attempts at the deposition of electrolytic coatings on aluminium by the direct method refer to the beginning of our century. However, according to Heiman,[87] tests of old patents show that the adhesion of the coatings obtained to the aluminium base does not meet the necessary requirements. Only the direct zinc plating of aluminium in a cyanide electrolyte, proposed by Work,[173] and the Vogt process, quoted after Wernik and Pinner,[3] have found practical applications. Work[173] discovered that, when a cyanide electrolyte is used, it is possible to obtain a satisfactory deposit of zinc on a smooth aluminium surface. In order to improve the quality of the coating, he proposed the replacement of sodium hydroxide in the electrolyte by ammonium hydroxide and the introduction of gelatine as an additive. The subsequent heat treatment of the articles improved the quality of the coating.

The direct zinc plating process in a cyanide electrolyte had been used previously for practical purposes involving the preparation of multilayer coatings.[174] However, the low thermal stability of the resulting coatings and the impossibility of depositing coatings with a thickness greater than 20–30 μm was noted. According to Gruev,[175] heating of the articles above 160–170 °C leads to blistering of the electrolytic deposits.

The Vogt process, developed in 1929 (quoted after Wernik and Pinner[3]), consists of the following main operations: direct electrolytic deposition of a thin layer of zinc from a cyanide electrolyte, brief brass plating in a cyanide bath, and nickel plating in a sulphate electrolyte. In order to strengthen the adhesion of the coating to the base, the articles are subjected to a heat treatment at 230 °C. When necessary, the articles can be additionally chromium-plated. Certain improvements to the Vogt process, concerning the composition of the electrolytes and the electrolysis conditions, were subsequently introduced by Ore[176] and also Edwards and Swanson.[47] Ore[176] recommended that the articles be washed between zinc plating and brass plating and a second heat treatment after chromium plating. The principal change proposed by Edwards and Swanson[47] consists in the additional zincate treatment of aluminium and the removal of contact zinc before the direct electrolytic zinc plating. However, these improvements did not eliminate disadvantages of the Vogt process such as the impossibility of coating alloys with a high

magnesium content (in excess of 3%) and the necessity for the careful maintenance of the recommended treatment conditions.

Among the latest studies on the direct depositions of metals on aluminium, mention should be made of those of Atkinson,[177–179] which provide a preliminary basis for the selection of conditions in the electrodeposition of metals. Atkinson proposed a sulphate nickel plating electrolyte containing fluoroborate ions as the activator and polyligand pyrophosphate–oxalate–amine copper plating electrolytes. However, there is no information about the practical use of these electrolytes.

The principal disadvantage of the methods for the direct electrolytic deposition of metals on aluminium proposed previously, namely the inadequate stability of adhesion of the coatings to the main metal, can apparently be accounted for by the empirical nature and the limiting extent of the studies made.

Since the 1950's, systematic research has been prosecuted at the Ivanovo Institute of Chemical Engineering into the theory and practical application of the direct method for the electrolytic deposition of metals on aluminium.[4] The required electrochemical activity of the surface to be coated was achieved in two ways: by the corrosive interaction of the surface with the electrolyte and by the cathodic activation after switching on the current. Cathodic activation makes it possible to use less corrosive electrolytes and thus reduce the rate of the contact exchange between aluminium and the ions of the metal being deposited. A combination of the two factors indicated above yields stable results as regards the adhesion of galvanic coatings to the base, which are independent of the composition of the aluminium alloy. Under optimum conditions, the strength of adhesion is not inferior to the strength of the main metal.

The present authors' own studies demonstrated the influence of the anionic and cationic compositions of the solutions on the corrosion and cathodic activation of aluminium.[4,180–191] Fluorides are effective activators of aluminium for the deposition on the latter of galvanic coatings. It was recommended that they be introduced into the composition of the electrolytes for this purpose. The characteristics of the influence of these activators on the electrodeposition of metals and the adhesion of coatings as well as the mechanism of their action were investigated over a wide concentration and pH range. The characteristics of the contact exchange between aluminium and the ions of more positive metals present in the electrolyte were studied.

The possibility of the cathodic activation of aluminium in the direct deposition of galvanic coatings had not been established before our investigations, but in a number of instances an increase in the rate of corrosion on cathodic polarisation of the metal was noted. This effect was attributed to a change in the pH of the layer near the cathode as a result of the incorporation of protons in the passive film and its decomposition by hydrogen and also the incorporation of alkali metals into the surface of the aluminium.[192–197]

Our investigations of the cathodic activation of aluminium in the electrocrystallisation of metals[198–201] showed that, in conformity with the ideas of Kabanov and co-workers,[197] Li^+ ions exhibit the most effective catalytic activity.

On the basis of experimental studies on the adhesion of coatings, it was established that it is influenced by electrolytic saturation with hydrogen, as suggested previously. The accumulation of hydrogen at the main metal–coating interface leads to the partial pealing of the coatings in the form of hydrogen blisters. The probability of the formation of blisters increases with increase in current density and depends on the composition of the electrolyte, especially on the presence of hydrogen saturation catalysts or inhibitors. The positive influence of low concentrations of oxidants such as $K_2S_2O_8$ (in the nickel plating electrolyte) and KNO_2 (in the pyrophosphate copper plating electrolyte) has been established.[4,185,202,203] It was also shown for the first time that the introduction into the solutions for the deposition of coatings of small amounts of oxidants can reduce the rate of the contact exchange reaction as a result of the depolarisation of the cathodic corrosion process without appreciable passivation of the main metal.[4,204]

An increase in the adhesion of coatings as a function of time, associated with the escape of adsorbed hydrogen from the main metal–coating interface into the surrounding medium (ageing), has been observed.[205] This process intensifies significantly in the heat treatment of the coated articles, which is frequently used as the final operation in various procedures for the deposition of galvanic coatings on aluminium.

The specific features of the deposition of multilayer coatings on aluminium have been studied. It has been shown that the deposition of upper layers of the coating can lead to a decrease in adhesion and to the formation of blisters as a result of saturation with hydrogen and the corrosion interaction between aluminium and the electrolyte in the pores of the first layer of the coating.[4] The deposition of the upper layer of the coating, for example, cadmium, which can retain hydrogen in the system, can fully suppress the positive influence of the concluding heat treatment on the adhesion of coatings. The conditions and the sequence of the technological operations, which rule out the negative influence of the factors indicated, have been determined on the basis of the studies made.[4,206,207]

Electrolytes for the direct nickel plating, copper plating, and zinc plating have been developed at the Ivanovo Institute of Chemical Engineering and on their basis technological processes for the deposition of single layer and multilayer coatings on various aluminium alloys both in a suspended form and in a loose form in drums have been devised. The technologies thus developed have been included in the USSR Government Standards GOST 9.047-75 and GOST 9.035-84 as well as branch standards and have been applied in industrial undertakings concerned with machine construction, instrument making, and other industries.[4]

In recent years, studies in the field of the direct electrolytic deposition of metals on aluminium have expanded and a considerable proportion of new research has been carried out in the USSR. Attention has been concentrated on the technology of the copper plating and nickel plating of aluminium.

A number of investigations[208–215] were directed towards the further improvement of electrolytes for the coating of aluminium and its alloys, developed at the Ivanovo Institute of Chemical Engineering and also towards their practical application under specific industrial conditions. Thus it has been recommended that sodium sulphate be introduced as a further additive to nickel plating electrolytes;[208] the possibility of replacing sodium chloride by nickel chloride,[209] of sodium persulphate by ammonium persulphate, and of boric acid by sodium acetate[210] has been reported. Data have been published[211–213] concerning the practical use of the electrolyte for the direct nickel plating of articles in a suspended form and in a loose form in drums. It has been suggested that chlorides be used instead of zinc and ammonium sulphates in weakly acid fluoride-containing zinc plating electrolytes.[214,215]

As a result of the study of the properties of polyligand solutions, electrolytes have been developed at the Kharkov Polytechnic Institute for the direct copper plating, bright nickel plating, and

brass plating of cast aluminium alloys.[216–218] A highly productive acid electrolyte based on copper nitrate has been proposed for the direct copper plating of silumin (with subsequent nickel plating and chromium plating).[219]

A patent[220] recommends the use of a pyrophosphate electrolyte for the high speed copper plating of aluminium alloys. The strength of adhesion of the coating to the base is ensured, according to the authors, by the use of a high current density (5–10 A cm^{-2}) in the initial stage of the electrolysis, which leads to the decomposition of the oxide film on aluminium. In a series of reports,[221–224] weakly alkaline electrolytes, containing mixed copper ammine and amine complexes, have been proposed for the copper plating of aluminium articles (especially aluminium sheets). Monoethanolamine, ethylenediamine, pyridine, etc. can be used to prepare the electrolytes. The necessity for the introduction of fluorides into electrolytes in order to improve the adhesion of copper to the base has been pointed out.[223]

Riger[225] suggested a sulphate electrolyte for the direct nickel plating of aluminium and its non-highy alloyed compositions which, together with the traditional chloride and fluoride additives, contains sodium hypophosphite. When this electrolyte is used, high quality coatings up to 40 μm thick, firmly adhering to the base, are obtained. The electrolyte can also be used to deposit wear-resistant composite nickel coatings containing silicon or boron carbide particles. It has been reported[226] that a nickel coating firmly adhering to aluminium is obtained in any electrolyte of the Watts type at a temperature in excess of 150 °C. Kochman et al.[227] recommended a sulphuric acid electrolyte for the direct zinc plating of aluminium, which makes it possible to deposit both bright and black zinc deposits. This electrolyte has found practical use. A complex Niostin electrolyte, based on divalent lead salts and incorporating a reductant and surfactants, has been developed at the Institute of Inorganic Chemistry of the Academy of the Latvian SSR. The application of Niostin ensures the formation of bright coatings on a series of metals, including aluminium alloys.[228]

Technologies have been proposed in which the surface of aluminium is coated by one or two thin layers of metals deposited electrolytically directly on a cleaned surface of the base, after which other coatings are deposited on the surface treated in this way. A technology for the copper plating of aluminium wire, according to which a thin layer (up to 0.1 μm) of tin is deposited electrolytically, before applying the copper coating, from a fluoride electrolyte prepared in a mixed solvent containing ethylene glycol and water has been developed at the Cable Industry Research Institute.[229] It has been recommended[230] that a thin layer of tin be deposited on aluminium articles from an acid fluoroborate electrolyte with subsequent deposition of a bronze (from a pyrophosphate electrolyte) and other coatings from the electrolytes usually employed. In order to increase the strength of adhesion of the coatings to the base, the articles are heat-treated in the concluding stage at 275 °C for 30 min.

A method for the copper plating of aluminium involving the coating of the latter in two stages has been developed in the German Democratic Republic: aluminium is initially coated with a zinc–tin alloy (0.1–0.2 μm) from a fluoroborate electrolyte and then with copper (0.3–0.6 μm) from a pyrophosphate electrolyte at pH 8–8.5. The main copper plating is carried out in a sulphate electrolyte. This procedure is recommended for the copper plating of wire and for the deposition of multilayer protective-decorative coatings.[90] According to the data in Ref. 231, before depositing galvanic coatings the aluminium surface is covered by a layer of iron (up to 1 μm) from a sulphate electrolyte containing fluoroborates or fluorosilicates. After the deposition of the required coatings from the electrolytes usually employed, the articles are heat treated at 150–500 °C. The possibility of using the iron plating electrolytes for the deposition of independent very thick coatings has been noted. Gaynes[232] describes a technology for the iron plating of aluminium alloy with silicon in order to increase their hardness and wear-resistance. This procedure involves the initial electrolytic covering of the base with zinc and then with copper from cyanide electrolytes. Iron plating is carried out in a hot chloride electrolyte. A Hungarian patent recommends that, before depositing a thin layer of nickel from an electrolyte containing fluoroborates, the surface of aluminium should be subjected to additional electrochemical activation in an alkaline solution using non-stationary forms of current.[233]

The development of the direct method for the deposition of electrolytic coatings on aluminium has been stimulated by its simplicity, universality, and the low cost of the technology. At the same time, a considerable proportion of the processes described have been a result of empirical studies. For the development of new highly effective processes, it is desirable to investigate in greatest detail the scientific foundations of the method. There is a prospect of the development of universal electrolytes for the deposition of electrolytic coatings on steel, copper, and aluminium. The use of such electrolytes would make it possible to treat articles made of different materials on a single electroplating line and would ensure greater efficiency of the process.

VI. Other methods

In conclusion we shall consider studies unrelated to the methods listed above. For example, the electrolysis of melts[234] and preliminary deposition of a metal sublayer *in vacuo*[235] or a sublayer of chemical nickel[236] have been proposed for the deposition of coatings on aluminium. It has been recommended[237] that the surface of aluminium be subjected to cathodic activation in hydrochloric acid before depositing a nickel coating. It is suggested that in this case a metastable layer of aluminium hydride is formed on the surface of the specimen. It decomposes during the deposition of nickel, which results in the formation of a strong metal–metal bond. In connection with expansion of the employment of non-aqueous solutions, the corresponding studies devoted to the deposition of galvanic coatings on aluminium have been published.[109,238,239]

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Translated from *Uspekhi Khimii* **60** 1105–1127 (1991) U.D.C. 541.1

The photochemistry of uranyl: spin selectivity and magnetic effects

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ABSTRACT. The very large range of photochemical reactions of uranyl conforms to certain general principles; and these are summarised, correlated, and from them the main types of photochemical reactions are classified. It is shown that the primary fundamental photoreactions of uranyl are selective with respect to electron spin and are therefore magnetosensitive. In these reactions there are found to be magnetic effects, including the most important—a magnetic isotope effect which is accompanied by the separation of uranium isotopes (magnetic ^{235}U and nonmagnetic ^{238}U).

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I. Introduction

Uranium is famous for its ^{235}U isotope, whose natural content is about 0.72%; and on increasing its content by a factor of only 2–3, nuclear fuel is obtained.[1] Salts of the uranyl ion UO_2^{2+}, in which uranium is in a hexavalent state, are common compounds of uranium. The main "non-nuclear" application of uranium compounds is related to the utilisation of the photochemical properties of these salts, which absorb ultraviolet and visible light and have a green luminescence.

Both the luminescence of uranium and its photochemistry have been studied for over fifty years[2] and a large amount of information has been obtained (see a monograph[3] and four reviews[2,4–6]). However a number of questions that are fundamental to the photochemistry and photophysics of uranyl remain:

—whether the large range of photochemical reactions of uranyl conforms to certain general principles, what are these principles (if, of course, they exist); is it possible to predict the photochemical behaviour of uranyl;

—which photochemical reactions of uranyl are primary and which are secondary, which of the photoreduction reactions of uranyl—through electron transfer or through hydrogen atom transfer—predominates; in which reactions is the UO_2 atomic shell of uranyl preserved and in which is it destroyed;

—what is the nature of the spin of the excited state of the uranyl ion UO_2^{2+}; is it singlet or triplet or is it altogether impossible to assign a definite spin multiplicity to this state (such a view has in all seriousness been expressed);

—what are the magnetic properties of the uranoyl ion UO_2^+, formed in the fundamental reaction of excited uranyl; what are the geminate reactions of this ion; are they magnetosensitive, and does the magnetic moment of the uranium nucleus have an effect on the spin behaviour of radical pairs involving the paramagnetic uranoyl ion UO_2^+?

The present article discusses the answers to these questions. The answers to some of them are clearer, while to others they are less certain.

II. Photochemistry of uranyl salts

1. Photoreduction of uranyl salts

The photoexcited uranyl ion participates in processes that are typical for many electronically excited molecules, namely, luminescence and radiationless deactivation. The decrease in intensity of luminescence and the reduction in lifetime of the excited state in the presence of many chemical reagents is regarded as an indication of "chemical" or "physical" quenching of excited uranyl. In its ground state uranyl is a weak electron acceptor (E^0 = 0.06 V relative to a standard hydrogen electrode); on excitation of the uranyl ion its electron affinity increases substantially (E^0 = 2.6–2.7 V).[4–6] In terms of its oxidising properties photoexcited uranyl is similar to molecular fluorine.[7] Therefore the main photochemical reaction of the uranyl ion is removal of a hydrogen atom (or electron) from the donor SH_2:

$$(UO_2^{2+})^* + SH_2 \rightarrow UO_2^+ + SH^\cdot + H^+. \quad (1)$$

This reaction is similar to the reaction of aromatic ketones or quinones excited to the n,π^* state.[4] For them the following general rule is typical: there is an increase in the rate constant with an increase in donor properties and a decrease in ionisation potential (or redox potential) of the donor and a decrease in energy of dissociation of the bond undergoing attack.[2,8–14]

Molecules of solvent (including water) can, in particular, act as a hydrogen donor.[9,15] The reaction of $(UO_2^{2+})^*$ with water

$$(UO_2^{2+})^* + H_2O \rightarrow UO_2^+ + OH^\cdot + H^+ \quad (1a)$$

occurs with a rate constant of $k \cong 10^2$ litre mol^{-1} s^{-1}.[9] Recently it was possible to record the spin adducts of the hydroxyl radical on photoexcitation of uranyl nitrate in water in the presence of a spin trap, providing additional evidence for reaction (1*a*).[15] The lifetime

of luminescence of uranyl in aqueous solution is of the order of several microseconds, so that the quantum yield of reaction (1*a*) is of the order of several percent.[16]

Added quantities of chemical compounds to solutions of uranyl salts also quench $(UO_2^{2+})^*$ in a "physical" manner—without the formation of chemical products:

$$(UO_2^{2+})^* + SH_2 \rightarrow UO_2^{2+} + SH_2. \qquad (2)$$

In the discussion of "reaction" (2) arguments have been more or less developed concerning the formation of exciplexes $[(UO_2^{2+})^*...SH_2]$ [5,10,13,18–20] and complexes in the ground state $UO_2^{2+}...SH_2$.[21] In particular, in the presence of aromatic compounds the formation of π-complexes has been postulated.[10,13,19]

The quantum yields of the reaction products of (1) vary over a wide range—from zero to unity—depending on the nature of SH_2, the solvent, and other conditions.[16–18,22,23]

Uranyl has luminescence in the region 490–650 nm; the absorption spectrum of $(UO_2^{2+})^*$, which was first recorded by Allen et al.,[24] has an absorption maximum at λ = 580 nm.[2,25,26] The kinetics of reactions (1) and (2) can be studied from luminescence quenching (during steady-state or pulsed excitation) or from the kinetics of luminescence decay of $(UO_2^{2+})^*$. A large number of studies have been devoted to the luminescence quenching of uranyl by different organic compounds, metal ions, halide ions, etc. In these experiments either the rate constants of quenching $k_q = k_1$ and k_2 or the Stern–Volmer constants K_{SV} have been determined. In the luminescence quenching the general principle noted above was found: k_q and k_{SV} are higher, the greater the electron-donating properties of the quencher (see, for example the studies of Sandhu et al;[8,10] a summary of k_q values is given by Hoffman et al.[27]).

2. Dualism in the reactivity of photoexcited uranyl

A very large number of organic and inorganic compounds,[2–6,28–33] alcohols,[13,20,33,34–40] organic acids,[24,36,38,41–48] amines,[25] amides,[28] cellulose,[28] phenols,[25,49] benzhydrol,[48] hydroquinone,[50] and others[8,10,14,36,51–58] participate in photooxidation with uranyl salts. The results of detailed EPR studies of the reaction products of (1) involving a very wide range of chemical compounds in the solid state and at low temperatures have been reported by Kemp et al.[28,29] We will not present the results of these detailed studies but will merely discuss the general properties of the reactions of excited uranyl.

Two principal mechanisms of the reactions of the electronically excited uranyl ion can be stated. On the uranium atom in the uranyl ion there are five coordination sites[59] to which ligands add (five water molecules in the complex $[UO_2(H_2O)_5]^{2+}$, two carboxyl anions and one water molecule in the complex $[UO_2(RCOO)_2.H_2O]$, two acetylacetone anions and one tetrahydrofuran molecule in $[UO_2(acac)_2.THF]$, etc.). All of the ligands lie in a single equatorial plane; the O–U–O axis is perpendicular to this plane and the "yl" oxygen atoms are situated at the poles. Hence a dualism is possible in the reactivity of the ion; electronically excited uranyl reacts either on the "equator", involving the uranium atom and the ligands, or on the "pole", involving the oxygen atoms. The first reactions occur intramolecularly, as a rule, and the second reactions are intermolecular. Furthermore, electron transfer from a ligand to the central atom is characteristic of the first reactions (U^{6+} is converted to U^{5+} as a result of this intramolecular transfer), while for the second reactions, hydrogen atom transfer to an "yl" oxygen is a typical feature. A typical example of the first reaction is the photodecarboxylation of salts of carboxylic acids, an example of the second is the photoreduction of uranyl in alcohols. In far from every case has it been possible to distinguish these two routes. Thus, generation of the ·OH radical on photolysis of uranyl salts in water [reaction (1*a*)] can occur by both routes—either by electron transfer from an equatorial ligand and the subsequent deprotonation of H_2O^+ or by an intermolecular reaction involving hydrogen atom transfer from a water molecule to an "yl" oxygen of uranyl. The dualism in the reactivity of excited uranyl is particularly clear when it is possible to establish competition between the two reaction routes. For example, in pure methanol the photolysis of UO_2^{2+} generates $CH_3O^{\cdot}$, while during photolysis in water–methanol mixtures (2:1 by volume) when the equatorial plane of UO_2^{2+} is occupied by water molecules, photoreduction occurs on the "polar" oxygen of uranyl to form the radical $\dot{C}H_2OH$.[34] It is clear that in the first case reaction mainly occurs on the "equator" through electron transfer and subsequent deprotonation while in the second case intermolecular photoreduction of uranyl on the "pole" occurs preferentially.

The photooxidation of lactic acid occurs by different mechanisms at different pH values: at pH > 3.5 it is accompanied by decarboxylation and the formation of acetaldehyde:[41]

$$UO_2^{2+} + CH_3CH(OH)COOH \xrightarrow{h\nu} U^{4+} + CH_3CHO. \qquad (1)$$

at pH 0 dehydrogenation occurs without decarboxylation and a keto acid (pyruvic acid) is formed:

$$UO_2^{2+} + CH_3CH(OH)COOH \xrightarrow{h\nu} U^{4+} + CH_3C(O)COOH. \qquad (2)$$

In the first case lactic acid is present in the form of lactate anion $CH_3CH(OH)COO^-$ and reacts in the coordination sphere (on the "equator") by electron transfer and decarboxylation followed by conversion of $CH_3\dot{C}HOH$ to acetaldehyde.

At low pH values in aqueous solution lactic acid is predominantly in the molecular form and photoreduction occurs on the pole to form the radical $CH_3\dot{C}(OH)COOH$, which is then converted to the keto acid.

On photoreduction of alcohols an isotope effect occurs. In the pairs of systems CH_3OH-CD_3OH and CH_3OD-CD_3OD the isotope effect has a normal sign of $k_1(CH)/k_1(CD) = 2.4–2.9$.[41] In the pairs CH_3OH-CH_3OD and CD_3OH-CD_3OD the isotope effect is very small (0.98 and 0.85) and has the reverse sign.[41] It is clear that the reaction of excited uranyl on the C–H bonds occurs on the "pole" as an intermolecular hydrogen atom transfer while the reaction on the O–H bonds occurs as an intramolecular electron transfer ("equatorial" reaction).

Thus, the dualism in the reactivity of photoexcited uranyl is determined by the competition of reactions along two pathways—on the equatorial plane of the ion and on a "polar" oxygen atom. These routes have a different sensitivity to the reaction conditions and this phenomenon is the reason for the very considerable variability in the chemical behaviour of uranyl.

In certain cases when the formation of U(IV) and new chemical products is recorded using conventional steady-state methods but the formation of primary products of one-electron oxidation or removal of a hydrogen atom is not detected, two-electron oxidation or oxygen atom transfer processes are postulated.[8,10,51,52,60] For

example, according to Sandhu et al.,[60] the oxidation of dialkyl sulphides occurs according to the following reaction:

$$(UO_2^{2+})^* + R_2S \rightarrow U^{4+} + R_2SO. \quad (3)$$

It has been proposed that the same reaction involving oxygen atom transfer [reaction (3)] occurs by reaction of $(UO_2^{2+})^*$ with triphenylphosphine, triphenylarsine, triphenylbismuth, and certain other compounds. However, in the oxidation of dicyclohexyl sulphide in dry acetone the cationic species UO_2^+ are formed,[17] while in the oxidation of a number of other disulphides, radical cations are formed.[18] Addition of dilute hydrochloric acid to a solution of dicyclohexyl sulphide in acetone is accompanied by the formation of U(IV), but only in secondary reactions:

$$UO_2^{2+} + R_2S \overset{h\nu}{\rightleftharpoons} [UO_2^{2+} \ldots R_2S]^* \quad (3a)$$

$$[UO_2^+ \ldots R_2S^+] \xrightarrow{H_2O,\ H^+} UO^{2+} + R_2SO\,. \quad (3b)$$

There is a high probability that all of the remaining reactions of type (3) occur via a one-electron transfer to form UO_2^+ [reaction (1)].

The photoreduction of uranyl nitrate with tri-n-butyl phosphate is accompanied by the formation of nitrite and nitrous acid, which oxidise U(IV). The combination of primary and secondary reactions leads to the results having poor reproducibility and a strong dependence of the yield of U(IV) on temperature, wavelength of exciting light, etc.[23] Moreover, the photolysis of uranyl nitrate can lead to formation of the pair $[UO_2^+, NO_3]$ and nitrite can be formed directly by photoexcitation of nitrate.[23,61]

Uranoyl is an intermediate in the photolysis of a number of uranyl compounds in the solid state.[62,63]

Above, there has mainly been a discussion of the photoexcitation of uranyl in water or other homogeneous solvents. The luminescence of uranyl and its photochemical reactions in heterogeneous and microheterogeneous solutions have also been investigated.[25,64–67] The photochemistry of uranyl adsorbed on colloidal silicon, zeolites, and alumina has been studied in relation to the possible photocatalytic effect of such systems.[65,66] Moreover, it is well known that in heterogeneous media (including micelles) conditions are favourable for the display of different magnetic effects in spin-selective reactions,[68–71] and this circumstance has stimulated additional interest in such studies. However, in principle, the photochemistry of uranyl in heterogeneous systems repeats the normal "homogeneous" chemistry.

3. The radical pair uranoyl–free radical

The primary product of excited uranyl with a donor is the radical pair (RP) $[UO_2^+, \dot{S}H]$, which either dissociates or its partners react together (forward or reverse electron transfer or disproportionation):

$$[UO_2^+, \dot{S}H] \begin{cases} \xrightarrow{k_4} UO_2^+ + \dot{S}H, & (4) \\ \xrightarrow{k_5} UO_2^{2+} + SH_2, & (5) \\ \xrightarrow{k_6} U^{4+} + S. & (6) \end{cases}$$

From a knowledge of the redox potentials of the pairs $E^0(UO_2^{2+}/UO_2^+) = 0.06$ V and $E^0(UO_2^+/U^{4+}) = 0.55$ V relative to a standard hydrogen electrode,[2–6] it can be predicted that oxidising radicals (with a potential $E^0 > 0.06$ V) will regenerate the initial reagents, while the strong oxidising agent—uranoyl—will oxidise many radicals to tetravalent uranium compounds. It is necessary to bear in mind that the values of the redox potentials are significantly dependent on the pH of the solution and the reagents.

Little is known about the cage reactions of the uranoyl ion and therefore different ideas have been put forward. There is definite interest in recording them directly. The cage reactions (4)–(6) are exhibited during laser photolysis, in particular in the photooxidation of the leuco base of a thionine dye (SH_2) sensitised with uranyl nitrate. The conversion of SH_2 to $\dot{S}H$ and S is accompanied by marked spectroscopic changes.[26] In the first instant after a flash the excited state $(UO_2^{2+})^*$ is formed, the "physical" (2) and "chemical" (1) destruction of which lasts 800 ns (Fig. 1). By this time $\dot{S}H$ has accumulated and, what is significant, S is formed in appreciable concentration (Fig. 1). Thus, these direct results demonstrate the occurrence of a successive two-stage oxidation of SH_2 by photoexcited uranyl with primary formation of the uranoyl ion. The quantity of $\dot{S}H$ oxidised in the cage comprises about 5% of the quantity of $\dot{S}H$ formed in bulk [reaction (4)].[26]

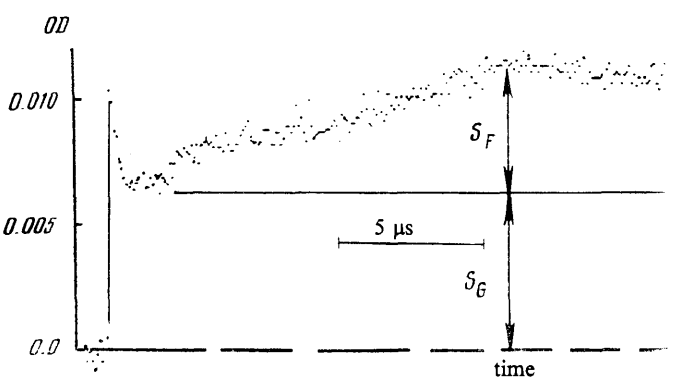


Figure 1. Changes in the optical density *OD* of aqueous solutions of uranyl nitrate in the presence of leucothionine which occur during laser photolysis with $\lambda = 600$ nm.[26] Here S_G is the optical density due to S formed in the cage; S_F is the optical density of S formed in extracage reactions.

The kinetics of the geminate recombination (5) of the pair $[UO_2^+ . .(C_6H_5)_2NH^{+\cdot}]$ obtained by pulsed laser photoexcitation of uranyl nitrate in the presence of diphenylamine in reverse micelles of sodium di(2-ethylhexyl)sulphosuccinate (Aerosol OT) (AOT) have been recorded.[25] In this case uranyl nitrate occurs in aqueous solution inside the micelles. The destruction of the RP is given by a first-order kinetic equation with a constant $k_q = k_4 + k_5$ and depends on the ratio $[H_2O]/[AOT]$, namely, on the size of the micelles. The cage effect in all of the experiments was approximately 0.9.[25] Such experiments are for the time being scarce in number, but they make it possible to record directly both the kinetics of geminate recombination and the magnitude of the cage effects.

There are many indications that excited uranyl has a triplet state, and when it undergoes photoreduction in a triplet RP is formed (see later).

III. Reactivity of the uranoyl ion

There is no doubt that the primary photoprocess—transfer of a hydrogen atom or electron to the uranyl ion [reaction (1)]—occurs with retention of the monolithic shell of UO_2 (see Section II.2). Destruction of this shell occurs in secondary, mainly dark, reactions, about whose mechanism little is known for certain. Amongst these is disproportionation of uranoyl ions

$$UO_2^+ + UO_2^+ + 4H^+ \rightarrow UO_2^{2+} + U^{4+} + 2H_2O, \qquad (7)$$

with regeneration of uranyl and the readily hydrolysed ion of oxygen-free tetravalent uranium. Despite its outward simplicity, the mechanism of reaction (7) is quite complex and has not been completely elucidated.[72] The reaction is significantly accelerated with a decrease in pH, occurs more rapidly in heavy water than in normal water, and is accelerated in the presence of fluoride ions.[72,73] Kinetic schemes that involve the formation of the dimer of UO_2^+ in protonated form UO_2H^{2+} represent the experimental data to the most adequate degree. In the region of pH 2–3 the UO_2^+ cation is relatively stable; in more acidic media the approximate relationship $k_7[H^+]^{-1} \cong 5.0 \times 10^2$ litre^{-2}mol^{-2}s^{-1} (water, 293 K, ionic strength 2.5) is valid.[72]

Another reaction involving destruction of the shell is the exchange of oxygen atoms between uranyl and water molecules. It was known some time ago (see for example, Okuyama et al.[74]) that the dark exchange which is extremely slow ($\sim 10^4$ h) in acid solution is markedly accelerated (by many orders) on irradiation with light in the absorption band of uranyl. It was proposed that exchange occurs in the electronically excited state of the uranyl ion,[74] but doubts about this mechanism arose straight away since no correlation was found between the rate of exchange and the lifetime of the excited (luminescent) state. In strongly acid solutions the rate of exchange decreased substantially, although the lifetime of the excited state increased.[75]

This phenomenon was noted in a series of outstanding studies by Suglobov et al.[16,22,55,58,76,77] on the kinetics and mechanism of photostimulated oxygen exchange between uranyl and water. The kinetic features of the exchange reaction were reliably established: 1) isotopic exchange ($^{16}O-{}^{18}O$) between uranyl oxygen and water is only induced by light that is photochemically active towards UO_2^{2+}; 2) the quantum yield of exchange (the number of fundamental exchange reactions per photochemically active quantum) is considerably greater than unity and amounts to tens or even hundreds in water (depending on the pH), and in the presence of ethanol reaches 3500; this indicates that the exchange reaction is a chain process; 3) the quantum yield has a linear dependence on the concentration of the initial uranyl; 4) it is inversely proportional to the square root of the light intensity; 5) the quantum yield decreases sharply in the presence of small quantities of added persulphate, whose ions do not quench the luminescence of UO_2^{2+} but oxidise uranoyl ions:

$$UO_2^+ + S_2O_8^{2-} \rightarrow UO_2^{2+} + SO_4^{\cdot} + SO_4^{2-}. \qquad (8)$$

All these features clearly demonstrate that the uranoyl ion UO_2^+ (or its protonated form), in which the triatomic shell becomes unstable, is responsible for oxygen exchange:

$$U^{18}O_2^+ + H_3^{16}O^+ \rightleftarrows U^{18}O_2H^{2+} + H_2^{16}O, \qquad (9)$$

$$U^{18}O_2H^{2+} + H_3^{16}O^+ \rightleftarrows U^{16}O_2H^{2+} + H_3^{18}O^+. \qquad (10)$$

Let us adopt the following kinetic scheme of exchange

$$[UO_2^{2+}]^* + H_2O \xrightarrow{W_i} UO_2^+ + OH^{\cdot} \qquad (1a)$$

(The photochemical generation of the uranoyl ion occurs with rate W_i);

$$UO_2^+ + UO_2^{2+} \rightleftarrows UO_2^{2+} + UO_2^+ \qquad (11)$$

the reaction of electron recharging (electron exchange) ensures the propagation of the kinetic chain of oxygen exchange:

$$UO_2^+ + UO_2^+ + 4H^+ \rightarrow UO_2^{2+} + U^{4+} + 2H_2O \qquad (7)$$

(disproportionation, destruction of the uranoyl ion, termination of the kinetic chain).

The scheme assumes a rapid oxygen-isotope exchange of each UO_2^+ ion with water (its mechanism has so far not been discussed), propagation of the chain through electron recharging between the isotopically exchanged UO_2^+ and "native" $UO_2^{2+}$and termination of the kinetic chain through disproportionation of uranoyl ions.

The rate W_i of generating UO_2^+ is equal to φI, where φ is the quantum yield of generation of UO_2^+, I is the intensity (number) of quanta absorbed. The quantum yield of oxygen exchange can be given in the form

$$\Phi = W_i\nu/I = \varphi\nu, \qquad (12)$$

where ν is the length of the kinetic chain. The lifetime of an individual uranoyl ion $\tau^* = \{k_{11}[UO_2^+]\}^{-1}$, while the lifetime of the kinetic chain $\tau = \{k_7[UO_2^+]\}^{-1}$, where the steady-state concentration of $[UO_2^+] = (W_i/k_7)^{1/2}$. Hence we can readily obtain the length of the kinetic chain

$$\nu = \tau/\tau^* = \frac{k_{11}[UO_2^+]}{(k_7W_i)^{1/2}} = \frac{k_{11}[UO_2^+]}{(k_7\varphi I)^{1/2}} \qquad (13)$$

and the quantum yield

$$\Phi = \frac{W_i}{I} = \frac{\varphi^{1/2}k_{11}[UO_2^+]}{k_7^{1/2}I^{1/2}} \qquad (14)$$

The dependences of Φ on $[UO_2^+]$ and I as predicted by Eqn. (14) are consistent with experiment and quantitative determinations of Φ (with the current uncertainty in the constant k_{11}) are in reasonable agreement with the experimental values of Φ.[16]

In solutions of uranyl in perchloric acid ([$HClO_4$] = 0.1 M), Φ = 43, while under the same conditions but in the presence of ammonium persulphate, which suppresses the chain process through reaction (8), Φ^* = 0.08.[16] Since in this case ν = 1, it is easy to determine that the length of the kinetic chain of oxygen exchange of uranoyl in water is equal to $\nu = \Phi/\Phi^* = 540$.

The physical meaning of the dependence of Φ on I is also clear. The greater the intensity of light, the higher the steady-state concentration of UO_2^+ ions, and hence, the rate of quadratic chain termination, and the lower the yield of oxygen exchange.

It is clear that the limiting quantum yield ($\Phi = \varphi\nu$) when φ = 1 is equal to the length of the kinetic chain of oxygen exchange Φ = 540. However, in aqueous ethanol solutions Φ increases with an increase in concentration of ethanol and reaches a maximum value of Φ = 3500.[16] This considerably exceeds the expected value of 540 and would appear to indicate that in aqueous ethanol solutions an increase in φ to unity is insufficient and that it is necessary also to

assume that the rate constants k_7 and k_{11} vary (relative to purely aqueous solutions of uranyl) in Eqns. (13) and (14).

On addition of metal salts to the solutions being studied in perchloric acid there is a change in Φ.[58] The introduction of ions that reduce $(UO_2^{2+})^*$ (Fe^{2+}, Ce^{3+}, Mn^{2+}) leads to an increase in Φ, whereas the introduction of ions that oxidise UO_2^+ (Fe^{3+}, Ag^+) leads to a decrease in Φ.[58]

The most unclear stage in this mechanism is the actual reaction of oxygen exchange in the UO_2^+ ion, namely, destruction of the UO_2 shell. The rate of exchange is strongly dependent on the pH of solution. For example, when $[UO_2^{2+}] = 0.1$ M, with an increase in acidity from 0.01 to 0.4 $HClO_4$ the quantum yield increases from 10 to a maximum value of 80, and then with a further increase in $HClO_4$ concentration it decreases to $\Phi = 1$ at 12 M $HClO_4$. In solutions with pH $\leqslant$ 0.4 both of the oxygen atoms of uranoyl are exchanged (two-oxygen exchange) and the quantum yield of this exchange $\Phi_2 \approx [H^+]^2$.[16] When pH > 1.5 the exchange involves one oxygen, i.e. each oxygen atom is exchanged independently and the quantum yield of exchange $\Phi_1 \approx [H^+]$.[16] It is clear that singly or doubly protonated forms of the uranoyl ion participate in exchange (the reaction occurs on a single oxygen atom [Eqn. (10)] or on both simultaneously) and that exchange is catalysed by hydroxonium ions. Reasonable and plausible chemical schemes of catalytic exchange can be put forward,[77] but they should be treated with caution. Direct methods are needed (with a time resolution of the order of picoseconds) for detecting the intermediate species and their dynamics.

As was mentioned above, in the photoreactions of uranyl with Ph_3P, Ph_3As, R_2S, and R_2SO, transfer of an oxygen atom occurs.[8,10,51,52,60] In this case phosphite is converted to phosphate, sulphide to sulphoxide, sulphoxide to sulphone, and the Ph_3As group to Ph_3AsO. The quantum yield of these reactions is low and equals 0.01–0.05. Photooxidation of sulphoxide to sulphone with uranyl is a thermally activated reaction and required an energy of activation of about 25 kJ mol^{-1},[52] which is unusual for photoreactions. It must be assumed from these characteristics that transfer of oxygen in these reactions is a secondary reaction that occurs with the involvement of the resulting uranoyl ion UO_2^+. In certain cases there is direct evidence for this mechanism (see above).

There is no doubt that destruction of the shell also occurs in $^{235}U-^{238}U$ isotope exchange[54]

$$^{235}UO_2^{2+} + {}^{238}U^{4+} \rightleftarrows {}^{238}UO_2^{2+} + {}^{235}U^{4+} . \qquad (15)$$

For a solution of uranyl in hydrochloric acid (8.0 M), $k_{15} = 7.17 \times 10^{-4}$ litre mol^{-1} min^{-1}.[54] Reaction occurs via the formation of uranoyl and is markedly accelerated by visible and UV light.[54] In the absence of other donors uranyl is photoreduced by U(IV) to form a superequilibrium concentration of UO_2^+.[50,54]

The mechanism of reaction (11), in which electron exchange and hence isotope exchange occur is debatable. The reaction occurs either by one-electron transfer, as according to Eqn. (11),[78] or via a stage involving the formation of a complex[16]

$$UO_2^+ + UO_2^{2+} \rightleftarrows UO_2^+ \ldots UO_2^{2+}, \qquad (16)$$

$$UO_2^+ \ldots UO_2^{2+} \rightarrow UO_2^{2+} + UO_2^+. \qquad (17)$$

The values of the rate constants have been determined: k_{11} = 1–10 litre mol^{-1} s^{-1};[78] k_{16} = 16–30 litre mol^{-1} s^{-1},[16,72] $k_{17} = (1.0 \pm 0.1) \times 10^3$ s^{-1}.[16]

Of the other reactions of uranoyl we should mention the formation of a binuclear complex [reaction (16)] which stabilises uranoyl.[72,79] It is assumed that formation of the complex between uranoyl and the radical resulting from photooxidation of a donor also stabilises UO_2^+.[17,80]

In the photoreduction of (8-crown-6)uranyl perchlorate in acetonitrile, a U(V) compound is obtained which has the formula $UO(18\text{-crown-6})(ClO_4)_3$.[81] It is relatively stable and does not disproportionate, being shielded by the macrocyclic ligand.[81]

The UO_2^+ formed in the primary photochemical reaction, in addition to disproportionation and isotope exchange, participates in reactions with the initial SH_2

$$UO_2^+ + SH_2 \rightarrow U^{4+} + SH_2^{\cdot} \qquad (18)$$

and with the corresponding radical $SH^{\cdot}$ ($SH^{\cdot}$)

$$UO_2^+ + SH^{\cdot} \rightarrow \text{products}. \qquad (19)$$

The latter reaction is rapid,[82–84] and it is frequently geminate. The routes of reactions of the type (18) and (19) can be predicted from the one-electron redox potentials of the reactants.[26,57,58,84]

It was shown by Sergeeva et al.[50] that UO_2^+ oxidises ethanol, ascorbic acid, and hydroquinone. It is very probable that it is reaction (18) involving ethanol that is responsible for the excess value of the quantum yield of U(IV) of 0.5 in the photoreduction of uranyl in aqueous solution containing a high concentration of ethanol rather than the transfer of two electrons as was proposed by Suglobov et al.[22]

Values of k_{19} ranging from 10^4 to 10^9 litre mol^{-1} s^{-1} have been obtained for a number of organic and inorganic radicals acting as partners of uranoyl.[50,82,84]

We should note in conclusion that the whole range of photochemical reactions for the reduction of uranyl is reduced to two key processes—oxidation of the substrate in the inner sphere by one-electron transfer (reaction on the "equator", reaction of the U atom) and removal of a hydrogen atom on the "pole" (reaction of an O atom). These reactions of photoexcited uranyl are primary and are accompanied by retention of the triatomic shell of UO_2. Break-up of this shell occurs in secondary reactions of the further reduction of U(V) to U(IV), occurring both inside the cage and in extracage reactions. Of the latter the most characteristic is disproportionation of U(V) [reaction (7)], which results in the formation of the final photoreduction product of uranyl—uranium(IV).

IV. Spin and magnetic properties of excited uranyl and the uranoyl ion

1. The lowest excited state of uranyl

The question of the spin state of the reacting excited ion of uranyl is of fundamental significance—it determines the spin selectivity of the reactions and the scale of the magnetic effects. A solution to the problem of the nature of the spin state of $(UO_2^{2+})^*$ can be provided by quantum-chemical calculations, an analysis of the lifetimes of luminescence, experiments on energy transfer, and research into magnetic and spin effects in the photochemical reactions of uranyl.

The absorption of uranyl in the visible region is mainly due to transitions from the highest occupied molecular orbital located primarily on the oxygen atoms to the 5*f* orbitals of uranium.[85–92]

These transitions are symmetry-forbidden and have low intensity (extinction coefficient $\varepsilon \cong 10-50$ litre mol^{-1} cm^{-1}). The substantial spin-orbit coupling (SOC) in the uranium atom (it is thought that in the uranium atom the SOC constant is in the region of $\zeta = 1740-2000$ cm^{-1})[87] places in doubt the possibility of assigning a definite spin state to $(UO_2^{2+})^*$. The authors of two studies[93,94] believe that singlet and triplet are so highly mixed and indistinguishable that there is no point in raising the question of the spin state of excited uranyl. However, such a conclusion is scarcely constructive. Thus, detailed calculations[85] indicate that both schemes (interelectron repulsion of the terms greater than the spin-orbit coupling between the terms and *vice versa*) represent the excited states of the uranyl ion, with the first scheme representing them even better. Attempts to determine experimentally the nature of the excited states of the uranyl ion in liquid solution during energy transfer experiments involving organic molecules and molecular oxygen proved unsuccessful.[95,96] The luminescence of uranyl is hardly excited at all by other donors, and there is hardly any evidence of energy transfer from photoexcited uranyl salts (energy of the lowest level $E = 20500$ cm^{-1})[4,96,97] to typical acceptors of triplet energy. In particular, molecular oxygen even at a pressure of 2×10^6 Pa does not quence the luminescence of uranyl.[96] Similar results led Sergeeva et al.[95] to assume that the excited state of the uranyl ion is singlet. However, the low efficiency of energy transfer from $(UO_2^{2+})^*$ to acceptors is a weak argument for such a conclusion, since it may be related to shielding of excitation to the 5*f* orbitals by the outer filled orbitals and the orbitals of the oxygen atoms.[96] Such a cause of inertness in energy transfer is not new, it is known for complex compounds with localised excited states.[2] Claudel et al.[63] have also proposed (without careful reasoning) that the reactive state of $(UO_2^{2+})^*$ in the solid state is singlet.

However, the idea of the triplet nature of $(UO_2^{2+})^*$, first put forward by McGlynn and Smith,[104] has been accepted by the majority of research workers (see, for example, several studies).[48,54,61,76,98–103] Moreover, there is experimental evidence for it, obtained in magnetic circular dichroism at low temperature for uranyl compounds.[98] A number of indications suggest a triplet as the excited reacting state of uranyl. First of all the lifetime of the excited state (2–10 μs in water[2] and 440 μs (!) for a colloidal solution of uranyl bonded to silicon[65]) is too great to belong to a singlet—especially when the presence of the uranium atom with strong spin-orbit interaction (~2000 cm^{-1}) is taken into account. It is true that it still does not follow from this fact directly that this luminescent state is reactive or responsible for the reaction of excited uranyl.

There is other also indirect evidence resulting from the reaction characteristics of excited uranyl. This relates in particular to photoreduction reactions on the "pole", namely, reactions on "yl" oxygen (see Section II.2). As was mentioned above, these are almost identical to reactions of triplet benzophenone: the same H/D isotope effects and reactions on the C–H bonds of alcohols, the same order of increase in quantum yields of photoreduction in the series methanol < ethanol < isopropanol (0.15, 0.31, and 0.34 respectively)[4] and the same absolute values of the rate constants k_1 of photoreduction (about 10^6 litre mol^{-1} s^{-1}). Even in its ground state UO_2^{2+} is similar to benzophenone. For example, it is an acceptor of a hydroxy hydrogen atom (see below), removing it from the radicals $(C_6H_5)_2COH$, CH_3COH, and $CH_3C(OH)COOH$. None of this evidence can be regarded as reliable confirmation; the latter only developed out of magnetic spin effects in reactions of uranyl (see Section V).

2. Magnetic and other physical properties of the uranoyl ion

The uranoyl ion is a primary product of the photoreduction of uranyl salts; it is also obtained by electrochemical or chemical reduction of uranyl.[105] the reducing agents can be free radicals such as $(CH_3)_2COH$, $CO_2^{\cdot-}$, etc.[44,47,106] Uranoyl is a labile species whose lifetime is mainly dictated by the disproportionation reaction

$$UO_2^+ + UO_2^+ + 4H^+ \rightarrow UO_2^{2+} + U^{4+} + 2H_2O. \qquad (7)$$

Its rate constant depends on the pH of the aqueous solution, the solvent, and the composition of the solution, so it is possible to find the conditions under which it achieves a high (up to 10^{-2} M) steady-state concentration of uranoyl[17,51,53,78–81,105,107] (for more detail, see Section III).

The absorption spectrum of uranoyl extends into the visible and infrared regions. The positions of the absorption maxima and values of the extinction coefficients of uranyl are given in several studies.[17,51,53,78,80,103,107–113]

The absorption spectra of UO_2^+ are sensitive to the solvent and depend on the nature and concentration of SH_2 and the concentration of UO_2^{2+}, and these dependences result from the complexation of UO_2^+. The absorption spectra of UO_2^+ are mainly used for identification of this intermediate compound. From the existing data it is possible to distinguish U(V) from U(IV) and U(VI) in the absorption spectra with complete confidence.[17,51,53]

The uranoyl ion has the electron shell [Rn]$5f^1$ and is a free radical. Its EPR spectrum has been recorded at low temperature (77 and 153 K) during electrochemical and photochemical reduction of $UO_2(dmf)_5(ClO_4)_2$ in *N*,*N*-dimethylformamide (dmf) and also $UO_2(dmso)_5(NO_3)_2$ and $UO_2(tep)_2(NO_3)_2$ in dimethyl sulphoxide (dmso) and triethyl phosphate (tep) respectively, which enter into the coordination sphere of uranyl.[110,114] Miyake et al.[110,114] consider that there are two types of spectra comprising isolated lines with the parameters $g_\perp = 2.5$, $g_\parallel \approx 0$, line width 150 mT, symmetrical line (spectrum of the first type) and $g_\perp = 1.97$, $g_\parallel \approx 1.3$, line width 10 mT, asymmetric line (spectrum of the second type). An average value of the *g* factor of $\bar{g} = 1.7$ corresponds to both type of spectrum. Spectra of the first type are obtained by photo- or electro-chemical reduction of perchlorates, and in these the perchlorate anion always remains outside the first coordination sphere and the equatorial plane is occupied by molecules of the organic solvent,[114] while spectra of the second type are obtained by photoreduction of nitrates. In this case the nitrate anion is situated in the equatorial plane of the complexes and remains in it during photoreduction, giving rise to the asymmetry of the EPR spectrum. This interpretation of the spectra is very much in doubt. Firstly, the EPR line ascribed to UO_2^+ is always asymmetric (even in the case of uranyl perchlorate); secondly, the theoretical interpretation of the spectrum is complex and ambiguous and requires a number of doubtful assumptions and approximations concerning the strength and symmetry of the crystal field and the spin-orbit coupling in the UO_2^+ ion. It is all the more difficult to correlate the theoretical and experimental EPR spectra.

It may also be doubtful that the isotropic *g* factor of UO_2^+ has a value close to 1.7, although the fact that it is less than the *g* factor of a free electron (2.0023) has been confirmed with complete reliability.[115–117] It was shown in these three studies[115–117] that the uranoyl ion has a considerable effect on the magnetic resonance parameters of organic radicals that are complexed with it.[28,115–117] Thus, in complexes of UO_2^{2+} with a phenanthrenequinone radical anion PQ^- and neutral radical

$HPQ^{\cdot}$, the g factors and electron relaxation times T_1 differ considerably from the g-factor and T_1 of free $PQ^{\cdot-}$ and $HPQ^{\cdot}$: $T_1(PQ^{\cdot-}) = 4-10$ μs, $T_1([UO_2PQ]^{+}) = 0.8$ μs, the g factors for $PQ^{\cdot-}$, $[UO_2PQ]^{+}$ and UO_2HPQ^{2+} are 2.0045, 1.9940, and 1.9945 respectively.[116] The presence of the uranium atom with its spin-orbit interaction opens up an additional route for paramagnetic relaxation and reduces the electron relaxation times of the complexes. In complexes of substituted *o*-benzo-semiquinones with uranoyl T_1 is even less (<0.2 μs).[117] The decrease in the g factor of the complexes results from the delocalisation of the spin from the organic anion to uranoyl. This means that the g factor of uranoyl is less than the g factor of a free electron.

Evidence for this assertion is provided by the EPR spectrum of the radical pair $^3[UO_2^+, NO_3]$ which is formed by photolysis of a monocrystal of the triethyl phosphate complex of uranyl nitrate $UO_2(NO_3)_2.2OP(OC_2H_5)_3$.[61] The angular dependence of the spectrum is dictated by the anisotropy of the g factor (its primary values lie within the region of 1.996 to 1.871). Even the largest of the components of the g factor is less than 2.0023. The additional interaction between the electrons in the pair has an angular dependence, with its maximum value amounting to 87 mT. This corresponds to a distance of 2.8 Å between the electrons, and it is approximately equal to the distance between the partners in the pair. In itself the observation of the EPR spectrum of a radical pair at the low temperatures used (less than 10 K) is an indication of a triplet precursor of the excited ion $(UO_2^{2+})^*$. However, strictly speaking the sign of the exchange interaction J and hence the spin state of the pair cannot be deduced from the EPR spectrum. Moreover, Giacometti et al.[61] did not estimate the value of J either, although this is possible by comparing the value of a_N—the ^{14}N hyperfine interaction in NO_3. If $J \gg a_N$, the ^{14}N hyperfine splitting in the pair must be $\frac{1}{2}a_N$ in the individual NO_3 radical; if $J \ll a_N$, a_N in the pair must coincide with a_N for the free NO_3 radical.

It is of course necessary to have reliable information about the g factor and hyperfine electron-nuclear interactions on the ^{235}U nucleus in the uranoyl ion. Further efforts are needed to obtain the EPR spectra of this ion in an oriented state—in monocrystals, in liquid crystal systems or by photolysis with polarised light, i.e. under conditions of photoselection with respect to orientation.

The question of the hyperfine coupling (HFC) on the magnetic nucleus of ^{235}U is very important. It is known that in UF_5 radical located in crystal lattices of halides of alkali or alkaline earth metals, the isotropic HFC is 5 mT on average. For UO_2^+ the hyperfine coupling is quite unknown and new measurements of EPR spectra of this ion with an enriched content of magnetic isotope are needed.

The paramagnetism of UO_2^+ is also detected in NMR spectra. This was first demonstrated by Pershin et al.[39] On irradiation of uranyl nitrate in ethanol, paramagnetic shifts and broadening of the NMR lines of ethanol appeared on the recording unit of the NMR spectrometer. The kinetics of the shifts and broadening on turning the light on and off clearly corresponded to the kinetics of the photochemical formation and dark destruction of the paramagnetic UO_2^+ ion. This indicates that the shifts and broadening of the NMR lines of the solvent occur when these molecules enter into the coordination sphere of the UO_2^+ ion and by a rapid exchange of the coordinated molecules with free ones.

The patterns of shifts and broadening are distinctive. The NMR line of the protons of the CH_3 group is hardly shifted and is not broadened, the line due to CH_2 is broadened and shifted downfield, but the hydroxyl protons of ethanol undergo the most broadening and a shift upfield. These are all indications that the paramagnetic shifts are due to contact hyperfine coupling of the unpaired electron with the nuclei of the ligand and that the ligand adds to the UO_2^+ ion via its hydroxyl group and through it spin density from the UO_2^+ ion is partially transferred to the ligand.[39]

Paramagnetic shifts and broadening of the NMR lines of the solvent were also observed in the photolysis of UO_2^{2+} in dimethyl sulphoxide.[80] The resonance lines due to the methyl groups in the ^1H and ^{13}C NMR spectra were shifted upfield (the magnitude of the shift was proportional to the concentration of paramagnetic UO_2^+ ions). In this case also the shifts and broadening occur on introduction of a solvent molecule into the coordination sphere of the UO_2^+ ion, but they are induced by a pseudocontact interaction (the same sign of the ^1H and ^{13}C shifts indicates this). In other words, in complexes of UO_2^+ with DMSO spin density is not transferred to the ligand (in contrast to complexes of UO_2^+ with ethanol). It is difficult to identify clearly the reason for these differences, but it is most likely that ethanol adds as a ligand to an oxygen atom of UO_2^+ on the pole while DMSO enters the plane of the coordination sphere on the equator.

V. Spin-selective reactions of uranoyl and magnetic effects

Let us return again to the question of the spin state of the excited uranyl ion. It was previously argued that this state has a given multiplicity, namely, a triplet. Since the spin is retained in fundamental reactions, the spin state of the excited ion is converted unchanged into the primary photoreduction product of uranyl—a radical pair—and therefore manifests itself in the spin selectivity of the photochemical reactions of uranyl.

A feature of spin-selective chemical reactions is their magneto-sensitivity, i.e. the sensitivity to the magnetic interactions of electrons and nuclei with an external magnetic field and to electron-nuclear hyperfine coupling. Energetically the magnetic interactions are small, but they are unique in the sense that it is only they that can change electron spins and remove the spin restriction in the spin-selective reaction. The spin restriction means that not all spin states can react, i.e. there are states that are reaction-forbidden.

The notable phenomena related to spin restriction are chemical polarisation of nuclei and electrons (CPN and CPE), the magnetic field effect (MFE), and magnetic isotope effect (MIE).[68–71] The most interesting of these is the MIE, namely, the dependence of the rate of reaction of paramagnetic species on the spin and magnetic moment of their nuclei.[70] It leads to a separation of magnetic and nonmagnetic isotopes in chemical reactions. A magnetic isotope effect has been detected for carbon, oxygen, silicon, and sulphur.[70,119,120] It would be tempting to find this effect also for reactions involving uranium compounds, in which one of the isotopes—^{238}U—is nonmagnetic, while the other—^{235}U—is magnetic (nuclear spin $I = {}^7/_2$, magnetic moment $\mu_I = -0.36\ \mu_N$).[121]

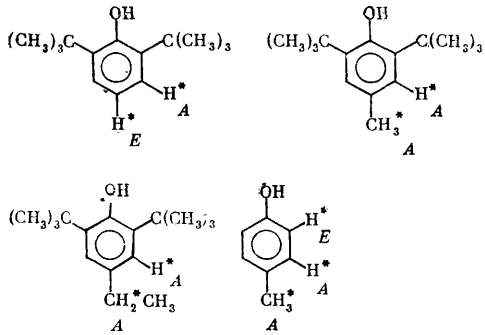
Research into the MIE in uranium aims to reach the solution to three problems: 1) to find reactions of uranium compounds involving paramagnetic intermediates; 2) to find the spin-selective stages in the reactions of these species and to establish the initial spin multiplicity in these stages; 3) to study the distribution of isotopes in the products of these reactions.

A solution to the first problem is evident. It is clear that photoreduction reactions of uranyl give radical pairs with the paramagnetic UO_2^+ ion and that these reactions are most suitable for

solving the subsequent two problems. We shall discuss below the methods for solving them through magneto-spin effects.

1. Chemical polarisation of nuclei in photoreduction reactions of uranyl salts

Chemical polarisation of ^1H nuclei has been observed in the photoreduction of uranyl nitrate with a number of alkyl-substituted phenols, benzilic acid, and benzhydrol (Figs. 2 and 3).[48,102] The polarisation indicators are shown below on the diagram (A = enhanced absorption E = emission):[102]



Polarisation of the extracage products of the recombination of the resulting phenoxyl radicals has also been detected. The reaction involves the fundamental stages (22), (23), and (24) (see section V.3). Phenoxyl radicals are poor electron donors and good acceptors, so the spin-selective reaction (24), resulting in the formation of a phenol with polarised nuclei takes place in the cage.

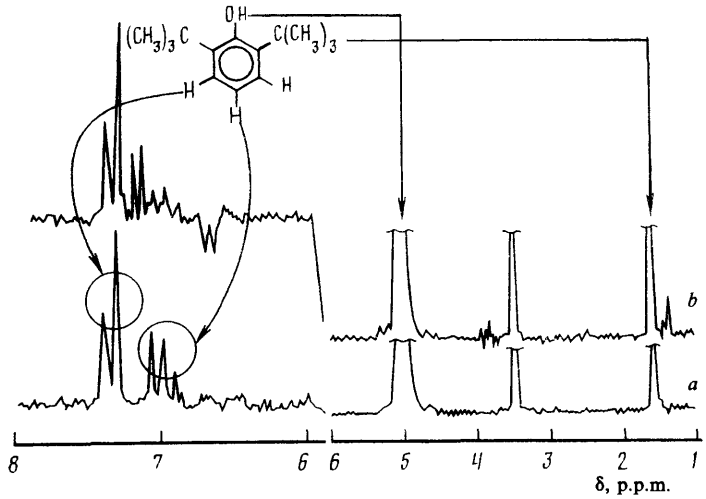


Figure 2. PMR spectrum of a solution of 2,6-di-t-butylphenol and uranyl nitrate in methanol-d_4 before (a) and during (b) irradiation of solution.

The fact that CPN occurs is not insignificant. It demonstrates the spin selectivity of the reaction and determines the spin multiplicity of the RP, from which the magnetosensitivity of the reactions and magnetoselectivity of the radicals is to be expected.

Chemical polarisation of the protons of the phenols accurately reproduces the polarisation in reactions of the same phenols with triplet benzophenone,[102] and this provides a firm (but not conclusive) basis for the assertion that uranyl reacts in a triplet state and generates a triplet RP.

The ketyl radical of benzophenone is formed as an intermediate on oxidation of benzhydrol and benzilic acid.[48] This radical, on the other hand, is a good donor[44,47] and oxidation of ketyl to ketone occurs in the cage (see scheme below).

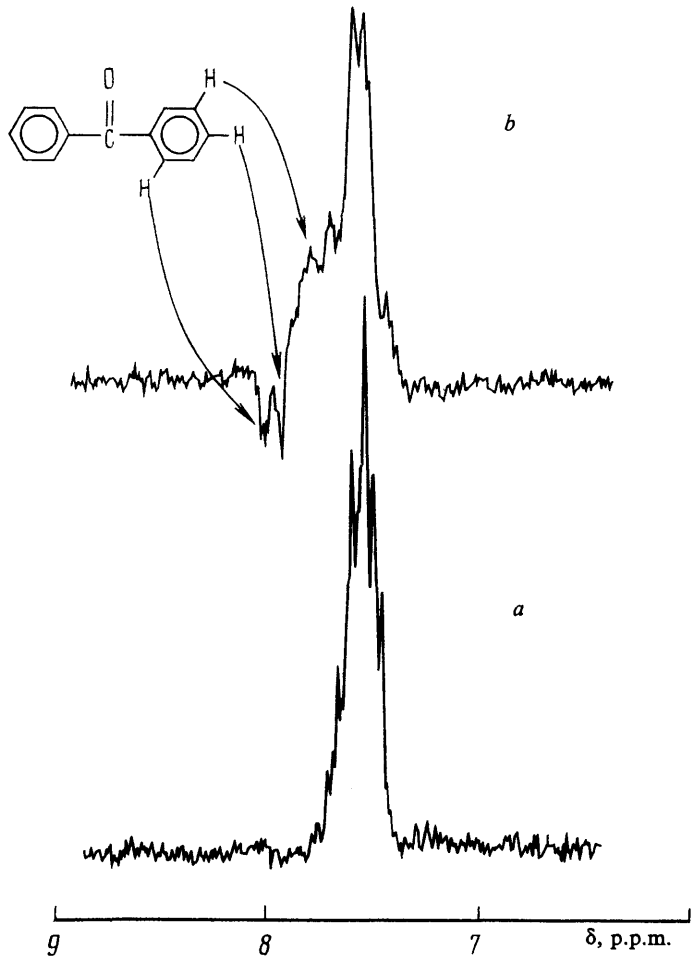
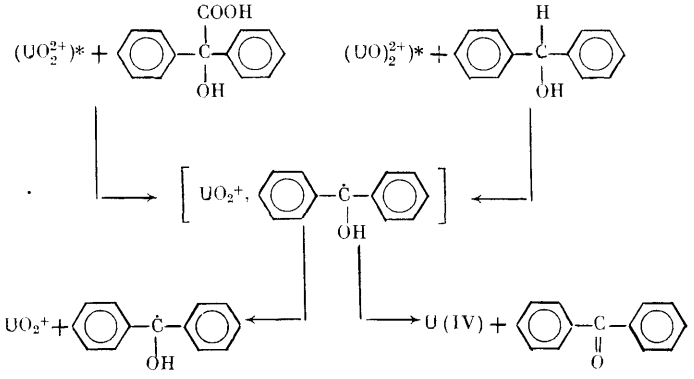


Figure 3. PMR spectrum of a solution of benzilic acid and uranyl nitrate in methanol-d_4 before (a) and during (b) irradiation of solution.[48]

The resulting benzophenone proves to be polarised (Fig. 3). The polarisation signs of the phenols and benzophenone are in agreement with the theoretical values on the basis of the following assumptions:

1) the RP is triplet; 2) the cage product is polarised; and 3) the g factor of uranoyl UO_2^+ is less than the g factor of phenoxyl (ketyl). The latter assumption was substantiated to a sufficient degree of reliability in section IV.1. Thus, the CPN data indicate that the predominant contribution to the reactive form of uranyl is provided by its triplet state, which is preserved during its chemical conversion to an RP.



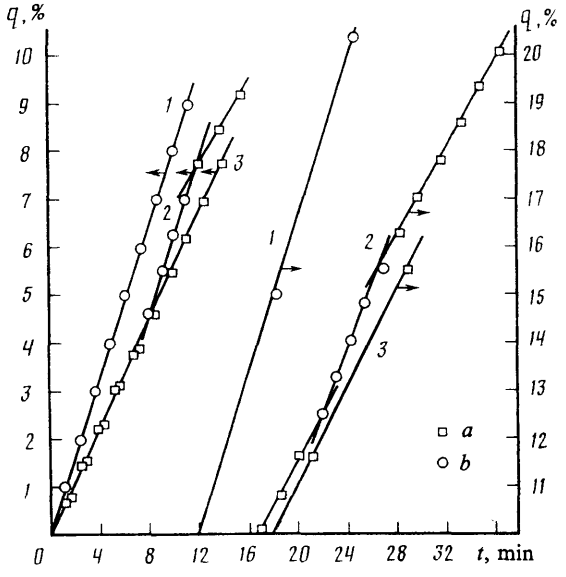


Figure 4. Dependence of conversion (q) on time in the polymerisation of *N,N,N,N*-dimethyldiallylammonium chloride in the earth's field (a) and in an external magnetic field (b):[101] *1*, polymerisation in the magnetic field; *2*, polymerisation with alternate installation and removal of the magnet; *3*, polymerisation in the earth's field.

2. Effect of an external magnetic field

Photochemical reactions that occur via the formation of triplet radical pairs are known to demonstrate significant magnetic field effects (MFE).[1,68–71] It may be expected that the spin-selective photochemical reactions of uranoyl will also be sensitive to an external magnetic field. A clear indication of the triplet multiplicity of the reacting photoexcited uranyl and the subsequent RP is the MFE in the photopolymerisation of *N,N,N,N*-dimethyldiallylammonium chloride photoinitiated with uranyl acetate.[101] The effect is clearly visible in Fig. 4. An external magnetic field (B = 0.17 T) causes a 10–40% acceleration of polymerisation. This result is reproducible regardless of when the field is applied or disconnected. At the same time as an increase in the rate of polymerisation, the molecular weight of the resulting polymer decreases in the field. Both of these results clearly suggest that: 1) initiation is the spin-selective stage, i.e. the UO_2^+ ion and the monomer molecule radical are partners of the primary RP; 2) this primary pair is a triplet, since only under this condition does the magnetic field suppress its conversion to a singlet, which increases the yield of radicals and the efficiency of initiation resulting in an acceleration of polymerisation and a decrease in the kinetic length of the polymerisation chain (or the molecular weight of the polymer). During the reaction there is an accumulation of U(IV) formed in both cage and extracage reactions: the yield of U(IV) decreases in the field.[101] The photodecomposition of uranyl oxalate (or oxalic acid in the presence of uranyl nitrate and a mineral acid) is of considerable interest. This reaction forms the basis of the uranyl oxalate actinometer. By titrating oxalic acid it is possible to determine its decomposition on photolysis with great accuracy. The reaction mainly involves the uranyl-sensitised oxidation of oxalic acid:[3,28,38,45]

$$H_2C_2O_4 \longrightarrow \begin{cases} \longrightarrow CO_2 + CO + H_2O\,, \\ \longrightarrow CO_2 + HCO_2H\,. \end{cases} \qquad (20)$$

Moreover, there is no doubt that an RP involving $CO_2^{\cdot-}$ and UO_2^+ is formed in this reaction. The EPR spectrum of the $CO_2^{\cdot-}$ radical anion in this system was recorded at low temperature.[28] A radical anion released from the cage recombines and oxalic acid (after protonation) is regenerated. An external magnetic field could affect the outflow of radicals from the cage and the rate of consumption of oxalate ions on photolysis, but no effect from a magnetic field on the rate of this reaction involving uranyl containing 10% ^{235}U was found (within the limits of an experimental error of ~2%).[15] A previously unexplained phenomenon was also reported: the strong oxidising agent uranoyl oxidises the strong reducing agent $CO_2^{\cdot-}$ in the cage with low efficiency:[28]

$$^3[UO_2^+,\ CO_2^{\cdot-}] \rightarrow U^{4+} + CO_2. \qquad (21)$$

The reason for this phenomenon and the absence of an MFE in uranyl oxalate reactions would appear to have a common origin. For reaction (21) to occur it is necessary for the triplet pair to evolve into a singlet, which is made difficult because of the lack of hyperfine coupling between the two radical partners, and therefore the RP $[UO_2^+,\ CO_2^{\cdot-}]$ mainly participates in other reactions.[28]

Within the limits of experimental error (2–5%) no MFE was detected by Khudyakov et al.[25,26] in the outflow of free radicals from the solvent cage during pulsed photooxidation of a number of donors in homogeneous and micellar solutions of uranyl salts containing a natural percentage of magnetic isotope.

Triplet–singlet transitions in the pair $[UO_2^+,\ SH^{\cdot}]$ can be induced not only by hyperfine electron-nuclear coupling. Thus, in the photoreduction of uranyl nitrate with hydroquinone and *p*-methoxyphenol at 285–293 K in a viscous solvent, a negative MFE for the outflow of aromatic radicals into the bulk of the solvent was

found.[122] The reason for the negative MFE may be either a triplet mechanism (if the magnetosensitive stage is the action of the magnetic field on mixing of the triplet levels of the exciplex) or a Δg mechanism in the RP.[68] The large difference between the g factors of an organic radical and uranoyl may lead to measurable MFE effects through a Δg mechanism even in a moderate field.[122]

An increase in the content of ^{235}U isotope in the salt from 0.7 to $\approx$10% leads to a build-up of a positive MFE.[122] In fact, increasing the content of magnetic isotope leads to an increase in the content of $[^{235}UO_2^+, SH^{\cdot}]$ pairs, which have more effective HFC constants in both partners than $[^{238}UO_2^+, SH^{\cdot}]$ pairs. With a 10% content of ^{235}U isotope, the effect of the opposite sign is approximately balanced and the magnitude of the MFE is within the limits of experimental error.[122]

Strictly speaking, from the results discussed it is not possible to make any definite quantitative conclusions about the magnetic interactions in an RP involving uranoyl, but the characteristics of the dependence of the MFE on the isotopic composition of uranyl provides a basis for the expectation that HFC with the ^{235}U nucleus contributes to the spin dynamics of the pair, and hence a magnetic isotope effect can be anticipated.

3. Magnetic isotope effect

The photoreduction of uranyl with phenols, as demonstrated above, is a spin-selective reaction; and therefore, in addition to an MFE, an effect from the internal magnetic field of the ^{235}U nucleus, namely, an MIE, can be expected in these reactions. A magnetic isotope effect was detected in the photoreduction of uranyl nitrate with *p*-methoxyphenol (PhOH) in heavy water in the presence of ammonium fluoride.[49] In this system the following fundamental stages occur:

$$(UO_2^{2+})^* + PhOH \rightarrow {}^3[UO_2^+, PhO^{\cdot}] + H^+, \quad (22)$$

$$^3[UO_2^+, PhO^{\cdot}] \longrightarrow UO_2^+ + PhO^{\cdot}, \quad (23)$$

$$^3[UO_2^+, PhO^{\cdot}] \longrightarrow UO_2^{2+} + PhOH, \quad (24)$$

$$UO_2^+ + UO_2^+ + 4HF \rightarrow UO_2^{2+} + UF_4 + 2H_2O. \quad (25)$$

The *p*-methoxyphenoxyl radical formed in the reaction has relatively small HFC constants from the *ortho*-protons and it may be assumed that the a_U constant in $^{235}UO_2^+$, even if it is not that large, will contribute to the effective HFC constant of the radical pair. With conversions of uranyl of less than 20%, Khudyakov et al.[49] detected the depletion of ^{235}U isotope in the precipitate of UF_4. In the initial uranyl nitrate the ratio of $^{238}U:^{235}U$ was 8.93 $\pm$ 0.01, while in the UF_4 reaction product this ratio occurred within the limits 8.970 $\pm$ 0.005 to 8.945 $\pm$ 0.008.[49] This corresponds to an enrichment of the initial unreacted uranyl with ^{235}U isotope and agrees in sign with that expected theoretically: a triplet pair with "magnetic" ^{235}U nuclei should undergo reductive reaction (24) more rapidly, and then the ^{235}U nuclei will separate into regenerated uranyl. The magnitude of the effect is small (apparently, the electron-nuclear interaction in the ^{235}U ion is small in reality), but it exceeds the experimental error of isotopic analysis.

The coefficient of isotope separation determined by us was α = 1.02. This value is small, but significantly exceeds the value of the classical isotope effect, determined, for example, as $(238/235)^{1/4}$ = 1.006. The reaction was conducted in pulsed mode so as to increase the contribution of disproportionation of uranyl [reaction (25)] and to decrease the contribution of the exchange reaction between uranyl and uranoyl [reaction (11)], which is accompanied by a loss of the effect (see Section III).

In the patent literature there are two reports on the separation of uranium isotopes based on the MIE. In one patent[123] the separation of isotopes by photoreduction of uranyl acetate in water or water containing "complexing" components (fluoride, carbonate, oxalate, etc.) is reported. Judging from the description, it appears that the authors[123] started from general conclusions rather than the experimental data.

According to another patent,[124] separation of the isotopes occurs by photopolymerisation of uranyl acrylate in a strong magnetic field in a solution of ethanol. The precipitate is enriched with ^{235}U isotope up to a 50% level. The content of this isotope in the initial nitrate is not reported. It was not possible[15] to reproduce the results of this patent.

Independently and at the same time as the study of Khudyakov et al.[49] a reliable MIE in uranium was detected in the decomposition of uranyl oxalate.[125] On photolysis of acid solutions containing 10% ^{235}U, enrichment of the precipitate—uranium(IV) oxalate—and depletion of the initial uranium(VI) occur.[125] For example, with 18% conversion of uranyl having a ratio of $^{238}U:^{235}U$ = 10:1, it becomes depleted in magnetic isotope (this ratio becomes equal to 10.2:1). For U(IV) this ratio is 9.4:1, the fundamental coefficient of isotope separation being α = 1.08.[125] It is logical that the product of the cage reaction—uranium(IV)—should be enriched. Cage reaction (21) occurs more rapidly for uranoyl containing magnetic isotope (see above).[125] The "destructive" isotopic exchange (11) in extracage reactions is apparently inhibited because uranyl is present as a complex with oxalate. The degree of enrichment decreases with an increase in conversion.[125] The results of this study were subsequently reproduced by Klimchuk.[15]

VI. Conclusion

Certain general principles are in evidence amongst the very large range of photochemical reactions of uranyl.

Firstly, the primary reactions almost always occur with transfer of an electron or hydrogen atom from the partner to uranyl to form the UO_2^+ radical ion.

Secondly, in these reactions the UO_2 shell is preserved, destruction of which occurs in secondary reactions (disproportionation of uranoyl ions, exchange of oxygen atoms, etc.).

Thirdly, the majority of the reactions can be differentiated according to a single important criterion—whether the reaction occurs in the equatorial plane of the uranyl ion (i.e. involving equatorial ligands) or whether it takes place on the "pole" (i.e. involving the oxygen atoms of uranyl). The first reactions take place preferentially as electron transfer, the second occur as a hydrogen atom transfer from the reagent to an "yl" oxygen atom (these latter are almost identical in many respects to the reactions of triplet benzophenone). It is true that the question of transfer of an electron or hydrogen atom, as always, is unclear and the preference for a given route remains uncertain in many cases.

Fourthly, the excited reacting uranyl ion can be confidently assigned a given spin state, namely—triplet. A number of indirect findings (the lifetimes, radiospectroscopy of radical pairs, chemical properties) as well as direct evidence [magneto-spin (CPN) and magneto-field effects] attest in favour of this assertion. Thus,

reactions of excited uranyl are spin-selective and hence magnetosensitive.

In this respect the magnetic properties of the uranoyl ion UO_2^+ become important, and in this case there is considerable uncertainty and much needs to be done to measure the *g* factor and hyperfine coupling in this ion in molecularly oriented systems.

The contribution of the magnetic moment of the ^{235}U nucleus and hyperfine coupling to the spin dynamics of pairs involving a uranoyl radical is of particular interest. The separation of uranium isotopes in spin-selective reactions of uranium compounds based on an MIE over a period of fifteen years has proved to be a vital problem.[71,126] It must be assumed that the presence of a heavy uranium atom and the danger of spin-orbit coupling has deterred researchers of the MIE. However, the scale of the MIE does not vary very much throughout the series of elements for which it was detected (^{13}C, ^{17}O, ^{29}Si, ^{33}S), although the spin-orbit coupling constant in this series increases by a factor of more than ten—from $\zeta = 28$ cm^{-1} (for carbon) to $\zeta = 382$ cm^{-1} (for sulphur).[119,120] This means that the role of spin-orbit coupling in spin dynamics has been exaggerated. At the present time the MIE and separation of uranium isotopes based on it have been detected in two reactions—the photoreduction of uranyl with a substituted phenol and the uranyl-sensitised photodecomposition of oxalic acid. This is, of course, an outstanding result, and it will stimulate interest in heavy multielectron atoms and a measurement of the magnetic resonance parameters of the $^{235}UO_2^+$ ion involving its hyperfine coupling with the ^{235}U nucleus.

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Translated from *Uspekhi Khimii* 60 1128–1154 (1991) U.D.C. 541.11–541.49

The formation of weak complexes by metal ions in aqueous solutions

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ABSTRACT. The modern approaches to the determination of the composition and the stepwise stability constants of weak metal complexes (K_n = 0.1–5.0) with ionic and molecular ligands in aqueous solutions are discussed. The difficulties in the unambiguous separation of the effects of the medium from those of the short-range specific interaction, described by equilibrium constants, and the consequent unreliability of the lower values of the formation constants, even when the latter are selected on the basis of a critical assessment, are examined. It is recommended that the linear relations between the algebraic sums of the logarithms of the activity coefficients of the components of the equilibria investigated and the ligand concentrations, the standard isotherms, or the measurement of the properties of all the components of the complex formation equilibria be employed for the separation of the long-range and weak short-range interactions.

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I. Introduction

The majority of processes in nature, analytical chemistry, and chemical engineering take place in aqueous solutions. Many characteristic features of such processes are determined by weak ion–ion and ion–molecule interactions leading to the formation of relatively unstable complexes. These complexes are formed and decompose via rapid reactions so that many of their properties are determined by thermodynamic functions. The most important thermodynamic parameters of the complexes in solutions are the equilibrium constants of their formation processes.

The determination of the composition and stability constants of complexes in solutions is one of the problems in physicochemical analysis[1] and constitutes the basis of the chemical theory of solutions,[2] which relates the properties of the solution to its composition. In this theory, the solution is regarded as a system where there are equilibria, obeying the Law of Mass Action, between the initial components and the products of their chemical interaction. However, when weak complexes are formed in aqueous solutions, the effect of the specific interaction is difficult to separate from the influence of the aqueous salt medium whose composition varies.

The thermodynamic functions for the formation reactions of a large number of weak complexes have been compiled in modern handbooks.[3–6] Metal cations M^{z+} with z = 1–4 usually play the role of coordination centres in the compounds considered, while polar molecules A or anions A^{z-} with z = 1–3 serve as the ligands. Analysis of data in handbooks[6] and in original studies (quoted below) shows that the current information about the thermodynamics of weak complex formation and even about the composition of weak complexes in aqueous solutions is extremely contradictory. Even many of the critically selected[5] values of the stepwise stability constants of weak complexes, for example $TlNH_3^+$, are doubtful. This is considered in Section IV of the present review.

During the last 20 years, there has been a renewed growth of interest in the thermodynamics of weak complex formation by metals. Numerous studies of outersphere association,[7–11] detailed investigation of non-aqueous solutions,[12,13] and the development of the theory of homogeneous catalysis[9] played a major role in this connection. The improvement of the level of studies on weak complex formation has been promoted by the application of microwave spectroscopy and computer techniques[14,15] and also by the use of the method involving the measurement of the activities of individual ions.[16]

Numerous new investigations[17–26] have been carried out to revise the information on the thermodynamics of repeatedly investigated complexes with low stabilities. Bjerrum discussed[27,28] the limits of the possibilities for the estimation of low stability constants of associated species in aqueous solutions. A controversy has recently arisen[26,29,30] concerning the reliability and accuracy of the determination of the stepwise formation constants of the weak complexes $CuCl_n^{2-n}$ with n = 1–4. Studies have been published[31–40] in which it is recommended that the compositions of weak associated species be determined taking into account the non-ideality of aqueous solutions with high constant ionic strengths (0.5–4.0). A new standard state has been proposed[41–43] (isopiestic solutions) for the investigation of weak complex formation. The possibilities for the quantitative investigation of weak metal ammines have been expanded.[25,44–47] A similar approach has been extended[48–50] to other ion–molecule complexes with low stabilities. Numerous free energies of transfer of ions from water to non-aqueous and mixed solvents have been surveyed and analysed.[51–53] The practical role of the thermodynamic functions of individual ions has been demonstrated.[54–56]

The most common one-centre complex formation reactions of metal (M) ions with ligands (A) in aqueous solutions are represented by the following reaction equations at the present level of development of chemistry:

$$M(H_2O)_{N,\,solv} + nA_{solv} \rightleftarrows MA_n(H_2O)_{N-nd,\,solv} + ndH_2O_{solv}, \quad (1)$$

where N is the limiting coordination number according to Werner's theory and d is the number of water molecules displaced by one

ligand A from the hydration shell of the central cation M. The ionic charges in Eqn. (1) and whenever possible in the text below are omitted to simplify formulation. The subscripts *solv* in the reactants involved in equilibrium (1) show that the latter interact in a definite sequence with all the remaining components of the solution and in the first place with solvent (water) molecules and with the ions of the supporting electrolyte and the excess ligands. However, these interactions are not included in Eqn. (1) in order to simplify the treatment of the properties of the system. They are frequently referred to as non-specific and are assigned to the effect of the medium or to changes in the activity coefficients.[57]

The constants β_n^0 of type (1) equilibria are expressed by the following relation for any standard state (designated by the superscript 0):

$$\beta_n^0 = \frac{[MA_n(H_2O)_{N-nd}][H_2O]^{nd}}{[M(H_2O)_N][A]^n} \cdot \frac{y_{MA_n(H_2O)_{N-nd}} y_{H_2O}^{nd}}{y_{M(H_2O)_N} y_A^n} = \beta_n \left(\prod_i y_i^{\nu_i}\right)_n, \quad (2)$$

where the square brackets and y_i denote the equilibrium concentrations and the activity coefficients of reactants i, β_n is the product of the concentrations or equilibrium function (but is not a constant! [1]), and ν_i are stoichiometric coefficients. The values of β_n in type (2) equations remain constant only when the concepts of the reactants and the effect of the medium, included in the symbol *solv* or in the values of y_i, are assumed to be fixed. The quantities β_n^0 are standardised in terms of temperature, pressure, and the medium selected as the standard with $I = 0$, I = const., etc. (I = ionic strength).

Whatever the standard state chosen for the study of weak complexes in aqueous solutions, the constancy of the activity coefficients in Eqn. (2) cannot be maintained. Their variation must be taken into account in the determination of n and β_n^0 for type (1) equilibria from "property–composition" diagrams because β_n and $\left(\prod_i y_i^{\nu_i}\right)_n$ are frequently comparable when the stability of the associated species is low.

There is a limitation as regards energy[7] (p. 196) in the determination of the composition and formation constants of weak complexes in solutions using the thermodynamics of reversible processes. To a first approximation, the energy of the thermal motion of the solvent, i.e. water, molecules may be adopted as a measure of this limitation, because complex formation via reaction (1) is studied in an aqueous medium. The energy of the thermal motion of solvent molecules is minimal in the ideal gas model. Such energy is defined as $1.5RT$ and at 298 K it amounts to 3.7 kJ mol^{-1}. The energy of the thermal motion of water molecules in water is comparable to the strength of the hydrogen bond and is approximately equal to 20 kJ mol^{-1}. Assuming that the energies indicated (3.7 and 20 kJ mol^{-1}) are equal to the changes in the Gibbs free energy (ΔG_n°) (it is more correct to compare them with enthalpy changes) during the stepwise occurrence of reaction (1), we obtained from the relation

$$\Delta G_n^0 = -RT \ln {}^{y}K_n^0 \quad (3)$$

where ${}^{y}K_n^0$ are unitary stepwise constants of equilibrium (1), the values of $\lg {}^{y}K_n^0$ at $T = 298$ K, which lie in the range 0.7–3.5 if d in Eqn. (2) is unity and $[H_2O] = 55.5$ M. Hence it follows that cratic stepwise stability constants, varying approximately from 0.1 to 50, correspond to the energy level of the thermal motion of solvent molecules in the ideal gas model and of water molecules under the conditions indicated. The tabulated stepwise stability constants of weak complexes[3–6] lie within these limits. The stepwise stability constants below 0.1, which are frequently quoted in handbooks,[3–6] cannot be regarded as an adequate demonstration of the formation of complexes, which has been emphasised by Krestov[58] and other investigators. Spectral additional justification of the occurrence of specific interactions is needed in systems with $K_n \leqslant 0.1$. In the absence of such justification, there is apparently no point in separating the measured effects from the changes in the activity coefficients.

The introduction of the concept of the formation constant of a complex always presupposes the presence in the solution of the initial reactants and of the molecules of the complex located at some statistical mean distance from one another. This situation is possible when there are delta-type relations between the potential energies of the associated species and the distance between M and A in reaction (1) and the separate existence of the reactants in the associated and dissociated states is likely only when the probability of the intermediate variants is zero. However, over a wide range of concentrations of electrolytes, such a situation does not arise—for example, when the ions have the electronic structure of noble gases. For systems of this kind, one should not determine the low formation cosntants of the complexes because such constants have no definite physical significance according to Kessler [see, for example, Valyashko and Kravchuk[59] (p. 7)].

This review was written with the aim of a critical consideration of the modern approaches to the determination of the composition and stability constants of weak metal complexes with ionic and molecular ligands in aqueous solutions, the analysis of a series of reliable data on the thermodynamics of weak complex formation reactions, and also the formulation of certain recommendations for new research into weak interactions in aqueous solutions.

II. Standardisation of conditions in the study of weak complex formation in aqueous solutions

The relation between the chemical potential of the component (μ_i) and its overall (c_i) and equilibrium ($\{[i]\}$) concentrations in a real solution at a constant temperature and pressure can be expressed by the equations

$$\mu_i = \mu_i^0 + RT \ln c_i y_i^* = \mu_i^0 + RT \ln [i]\, y_i, \quad (4)$$

$$\mu_i = \mu_i^0 + RT\left(\ln c_i + \sum_x b_{i,x}^* c_i^x\right) = \mu_i^0 + RT\left(\ln [i] + \sum_x b_{i,x} [i]^x\right) \quad (5)$$

where μ_i^0 are the standard chemical potentials, while $b_{i,x}^*$ or $b_{i,x}$ are virial coefficients whose values are independent of c_i or $[i]$. The differences between y_i^* and y_i and also between $b_{i,x}^*$ and $b_{i,x}$ consist in the fact that the coefficients marked with an asterisk represent the deviations in the behaviour of the reactants containing component i from ideality, while the coefficients without an asterisk in the superscript position express the analogous properties of only the conventionally free species i_{solv} constituting the system (1). If there is no chemical interaction, for example, no reaction (1), in the system considered, then $c_i = [i]$, $y_i^* = y_i$, and $b_{i,x}^* = b_{i,x}$. In any arbitrarily selected standard state for component i, we have $c_i = [i] = 1$ and $y_i^* = y_i = 1$, although it is frequently assumed that $y_i^* = y_i \to 1$ when $c_i \to 0$.

Logarithmic concentration functions enter into Eqns. (4) and (5); for this reason, real solutions with $c_i \to 0$ cannot be chosen as the standard state because $\mu_i \to -\infty$ when $c_i \to 0$. The hypothetical 1.0 M or 1.0 m (M and m represent the molarity and molality respectively) solutions, having the properties of infinitely dilute solutions, usually serve as the standard state for the determination of thermodynamic functions for the complex formation reactions. The choice of water, an aqueous salt solution at a constant of ionic strength or at a constant molarity, and also of any mixed solvent as the solvent for the system alters only the point from which the excess thermodynamic functions are reckoned or the factors designated by the subscript *solv* in Eqn. (1). A necessary requirement which must be met by the standard state is the constancy of these factors, i.e. the constancy of the concept of "*solv*" and of the quantity y_i. It must be emphasised that water is a fully legitimate reactant involved in equilibrium (1) and its concentration, which varies markedly in the study of weak complexes can be usefully expressed on the same concentration scale as that employed for the other reactants (in the study of complexes in solution, the molarity scale is usually employed) and not the mole fraction scale normally used. When the latter is used, it is incorrect to calculate ΔG_n° by Eqn. (3).[60]

It follows from Eqns. (4) and (5) that the relation between these two ways of taking into account the non-ideality of the behaviour of reactant i is defined by the relations

$$\ln y_i^* = \sum_x b_{i,x}^* c_i^x, \tag{6}$$

$$\ln y_i = \sum_x b_{i,x} [i]^x, \tag{7}$$

the first of which refers to a system with complex formation, whose parameters are included in the quantity $\ln y_i^*$ or in $\sum_x b_{i,x}^* c_i^*$.

Measurable amounts of weak complexes are formed only at high concentrations ($>0.1-0.5$ M) of M and A or of one of these substances. The majority of studies on weak interactions have been carried out hitherto[3-6] at microconcentrations of M (at $c_M \leqslant 1 \times 10^{-2}$ M) and with wide variation of c_A. Complex formation was usually studied in aqueous solutions with variable (from 1×10^{-2} to 15 M) or constant (0.5, 1.0, 3.0, 4.0, and 6.0) ionic strength maintained by inert electrolytes. Sodium perchlorate and ammonium nitrate were usually employed as the latter.

The wide variations of the concentration c_A or c_M, required to investigate weak complexes whatever the choice of the standard state, alter the factors designated by the subscript *solv* in type (1) equilibria or contributing to the activity coefficients in Eqn. (2). Such changes must be taken into account in calculations of n and β_n^0.

After taking logarithms in Eqn. (2), we obtain

$$\lg \beta_n{}^0 = \lg \beta_n + \lg y_{MA_n} + nd \lg y_{H_2O} - \lg y_M - n \lg y_A =$$

$$= \lg \beta_n + \Delta (\nu_i \lg y_i)_n, \tag{8}$$

where the symbol Δ denotes the algebraic sum. Substitution of the general Eqn. (7) in Eqn. (8) affords

$$\lg \beta_n{}^0 = \lg \beta_n + \Delta \left(2.303 \nu_i \sum_x b_{i,x} [i]^x\right)_n . \tag{9}$$

Application of Eqn. (9) to semi-ideal solutions,[61-63] i.e. the restriction of the sum in Eqn. (7) to the quantities $b_{i,1}$, leads to the equation

$$\lg \beta_n{}^0 = \lg \beta_n + \Delta (2.303 \nu_i b_{i,1})_n [i]. \tag{10}$$

If the composition of the test solution changes only as regards the ligand A concentration, then Eqn. (10) simplifies and assumes the following form:

$$\lg \beta_n{}^0 = \lg \beta_n + \lambda_n [A], \tag{11}$$

where λ_n is the algebraic sum of $b_{i,1}$ with allowance for the stoichiometric coefficients ν_i.

Potentiometric study of the equilibrium

$$Ac^-_{solv} + H_2O_{solv} \rightleftarrows HAc_{solv} + OH^-_{solv}, \tag{12}$$

where HAc is acetic acid, in 3.0 M aqueous Na(Cl→Ac) solutions with chromatographic determination of the activity coefficients of acetic acid molecules made it possible to estimate[32] the contributions of the non-ideality of the behaviour of all the reactants as the salt composition of the medium is varied. It is seen from the data in Table 1 that the replacement of chloride ions by acetate ions increases to the maximum extent (compared with other reactants) the activity coefficients of hydroxide ions, but there is at the same time an appreciable increase in the activity coefficients of acetate ions and a significant fall of y_{HAc}. On the other hand, the algebraic sum of the logarithms of the activity coefficients of the reactants ($\Delta \lg y_i$) involved in equilibrium (12), i.e.

$$\Delta \lg y_i = \lg y_{OH^-} + \lg y_{HAc} - \lg y_{Ac^-} \tag{13}$$

varies appreciably less than the activity coefficients of any individual reactant. The ratio $\Delta \lg y_i / c_{Ac^-}$ then remains almost constant and amounts to 0.07 ± 0.01 at all the concentrations of chloride and acetate ions.

Table 1. The logarithms of the activity coefficients of the reactants involved in equilibrium (12) in 3.0 M Na(Cl→Ac) solutions at 298 K.

c_{Ac^-}, M	$\lg y_{OH^-}$	$\lg y_{Ac^-}$	$-\lg y_{HAc}$	$-\lg y_i$ from Eqn. (13)	$-\lambda_i = \Delta \lg y_i / c_{Ac^-}$
0.5	0.07	0.04	0.07	0.04	0.08
1.0	0.14	0.08	0.13	0.07	0.07
2.0	0.30	0.20	0.24	0.14	0.07
3.0	0.45	0.30	0.33	0.18	0.06

Calculations have shown[31] that β_1, approximately equal to unity, changes by almost 100% if λ_1 in Eqn. (11) amounts to only ~0.2, as happens in many mixtures of uni-univalent electrolytes with I = const. Hence it is clear that, in the study of weak acido-complexes in aqueous solutions with I = const., it is essential to determine both β_n and λ_n in Eqn. (11).

The study of the behaviour of non-electrolytes in aqueous solutions of the majority of inorganic salts with variable and constant ionic strengths has recently[61] led to the equation

$$\lg y_i = \sum_j b_{i,j}^* c_j, \tag{14}$$

where the Sechenov's constants $b_{i,j}^*$ depend only on the nature of the non-electrolyte i and the ions j. Eqn. (14) is valid for all systems without strong interactions between the molecule i and the ions j.

The activity coefficients of the ion i are expressed by the following equation over a wide range of ionic strengths:

$$\lg y_i = -Az_i^2\sqrt{I}/(1 + B\mathring{a}\sqrt{I}) + b_i^*I, \quad (15)$$

where A and B are the Debye–Hückel constants calculated theoretically, $\mathring{a}$ is the conventional ionic radius, and b_i^* is the second virial coefficient. The first term on the right-hand side of Eqn. (15) is constant at I = const. if it is assumed that $\mathring{a}$ is invariant. By analogy with Eqn.(14), it is suggested that one assumes[33] that the activity coefficients of the ions and ionic strengths, which are constant in magnitude but variable as regards composition, are described by the equation

$$\lg y_i = F_i(I) + \sum_j b_{i,j}^* c_j, \quad (16)$$

in which $F_i(I)$ are characteristic constant functions of the ion i independent of the nature of the ion j.

The applicability of Eqn. (16) to mixtures of uni-univalent electrolytes with a constant molarity or molality has been repeatedly confirmed.[18,19,31] Eqn. (16) is frequently valid for mixtures of uni-bivalent and bi-univalent electrolytes of the type of sodium sulphate or barium chloride for constant overall molar concentrations[33] but not constant ionic strengths I.

Throughout many years, the model of semi-ideal solutions was used successfully[23,64] in the study of copper(II), cobalt(II), and iron(III) chloride complexes as well as other weak associated acido-species formed by reaction with the cations M in 3–12 M solutions of hydrochloric acid and lithium, magnesium and calcium chlorides as well as similar solutions[26] with variable ionic strengths. The corrections for the variation of the activity coefficients in such solutions were introduced in terms of averaged system parameters (y_{av}) expressed by the relation

$$\lg y_{av} = a + bc_{Cl^-}, \quad (17)$$

where a and b are constants for a specific salt medium with a variable ionic strength. The similarity of the methods used to take into account the non-ideality of the solutions with constant ionic strengths I = 0.5–6.0 and for variable ionic strengths $I \geqslant 3$ is clearly seen from the comparison of Eqns. (16) and (17).

The need to take into account the changes in the activity coefficients of the Cd^{2+} ions in 3.0 N aqueous solutions of sodium sulphate and perchlorate arose already in the old investigations of cadmium sulphate complexes.[65] It was established that the measured activities of sulphate ions can be accounted for by the hypothesis of the formation of only the $CdSO_4$ complexes with a stability constant of 7 ± 2, while the activities of the cadmium cations in the same solutions are reproduced by the hypothesis that the complexes $Cd(SO_4)_n^{2-n}$ [sic] are formed with ν_n = 8 ± 1, 10, and 110 for n = 1, 2, and 3 respectively.

McKay[66] cast doubt on the low thermodynamic functions for complexes standardised using solutions with high and constant ionic strengths immediately after the publication of the first edition of the Handbook of Stability Constants.[3] Pitzer and Brewer[67] pointed out as early as 1961 that there is no point in using solutions with high and constant values of I for the study of weak acido-complexes, since the Harned coefficients for I = const. = 0.1–3.0 are approximately constant.

Kul'ba and Mironov[68] noted in 1963 that the values of n and β_n for the weak acido-complexes TlA_n^{1-n} with $n > 1$, where A^- = Cl^-, Br^-, I^- or SCN^- are conventional thermodynamic parameters which include both the short-range specific interaction of Tl^+ with A^- and the changes in the activity coefficients of ions reacting in 3.0 or 4.0 M aqueous solutions of Na(ClO_4→A). It has been shown[31] that the changes in the composition of the majority of uni-univalent electrolyte solutions with I = const. make it possible to determine the stepwise stability constants of acido-complexes of ~10 with an error not less than 10% without taking into account the variability of the activity coefficients, the error increasing with decrease in K_n.

Eqn. (11) was first used for a detailed study of weak multistep acido-complex formation by Vierling,[34,69] who investigated lead(II) chloride and bromide complexes in 4.0 M aqueous Na(ClO_4→A) solutions, where A^- = Cl^- or Br^-, with complete replacement of perchlorate ions by halide ions. Potentiometric, solubility, and spectrophotometric methods were used as the basis for these investigations. Unfortunately, the relevant communications do not give a mathematical analysis of the reliability of the simultaneous calculation of β_n^0 and λ_n on the basis of Eqn. (11). The necessity to analyse the different hypotheses concerning the formation of weak acido-complexes in connection with the determination of β_n and λ_n in aqueous solutions with high ionic strengths was first confirmed by Belevantsev et al.[40] This conclusion was reached from the applicability tosolutions with constant molarities and molalities of the Harned rule with a single virial coefficient α' in the general equation

$$\lg y_{\pm}^{(I+II)} = \lg y_{\pm}^{(I)} - \alpha' c_{II} - \alpha'' c_{II}^2 \quad (18)$$

where $y_{\pm}^{I+II)}$ and $y_{\pm}^{(I)}$ are the mean ionic activity coefficients in mixtures of electrolytes (I) and (II) with I = const. and in the pure electrolyte (I) with the same ionic strength, c_{II} is the concentration of electrolyte (II) in the mixture, and α' and α'' are Harned coefficients, usually with $\alpha' \gg \alpha''$. However, the limited applicability of the Harned rule is generally known.[70,71] At the same time, Eqn. (11) is valid for many aqueous salt systems. This contradiction can be accounted for by the fact that λ_n is the algebraic sum of the Harned coefficients. The high values of the latter, as well as the terms quadratic in c_{II}, cancel out in this sum judging from the data in Table 1. It is important that Eqn. (11) is frequently applicable to solutions with variable ionic strength as a result of the applicability of the Storonkin–Lagunov rule[72] to these systems. It has been noted[40] that the values of λ_n in Eqn. (11) as well as those of $\lg y_{\pm}$ can be divided into components corresponding to individual ions. At the same time, accurate calculations of the λ_n from the mean ionic activity coefficients are by no means always possible, while the Harned coefficients for individual ions are extremely useful for the estimation of the effects of non-ideality.

The values of λ_1 for equations of type (11) have been determined[36,73] in the study of solutions with microconcentrations of outer-sphere tris(phenanthroline)iron(II) monoperchlorate complexes, keeping the ionic strength I, the normality N, and the molarity M constant using mixtures of two salts and also at a constant activity of water a_{H_2O}. It was found (Table 2) that the replacement of the constant parameters in the sequence I, N, $M \simeq a_{H_2O}$ reduces significantly the value of λ_1, i.e. diminishes the effect of non-ideality. The changes in I or N in the range 0.25–0.75 have little influence on λ_1, but none of the methods of standardising the conditions in the study of weak perchlorate complexes indicated ensures the constancy of the activity coefficients. The replacements Na(F→Cl), Na(F→Ac), and (Na_2→Li_2)SO_4, i.e. of one singly-charged ion by another singly-charged ion, had little influence on λ_1, while the replacement of fluoride or chloride ions by divalent sulphate ions did exert a significant influence.

It has been established[74–79] that the coefficients λ_1 are almost constant for the equilibria in the formation of microamounts of

$H^+ - A^{z-}$ associated species and certain metal acido-complexes in mixtures of $NaClO_4$ with NaCl, NaBr, NaI, $NaNO_3$, and $LiClO_4$ at constant ionic strengths I = 0.5, 1.0, 2.0, 3.0, 4.0, and even 6.0 (Table 3). The constancy of λ_1 is maintained also for 3.0 M Na(Cl→Ac) solutions[32] in which 0.1–3.0 M acetate ions (Ac^-) are protonated, i.e. the process takes place under the conditions of an ionic automedium (Table 1).

Table 2. The coefficient λ_1 (accuracy to within ±20%) in Eqn. (11) [36,39,73] for tris(phenanthroline)iron(II) monoperchlorate complexes.

Supporting salt	λ_1 at				
	I=0.25	I=0.75	N=0.25	M=0.25	a_{H_2O}=0.99
Na(F→0.5SO_4)	3.9	2.7*	2.6	1.5	1.8
Na(Cl→0.5SO_4)	3.6	–	2.7	1.5	1.6
Na(F→Cl)	–	0.1	–	–	–
Na(F→CH_3COO)	–	0.9	–	–	–
(Na_2→Li_2)SO_4	–	0.35	–	–	–

*At N = 0.75.

Table 3. The values of λ_n in Eqn. (11) for I = const. and T = 298 K.[78,79]

Reaction	I	Salt in the medium	$\lambda_n \pm \sigma$
$H^+ + Ac^- \rightarrow HAc$	1.0	Na(ClO_4→Cl)	0.081±0.005
	2.0	Na(ClO_4→Cl)	0.082±0.002
	4.0	Na(ClO_4→Cl)	0.069±0.004
	1.0	Na(ClO_4→Br)	0.027±0.007
	3.0	Na(ClO_4→Br)	0.036±0.005
	1.0	Na(ClO_4→I)	−0.022±0.009
	3.0	Na(ClO_4→I)	−0.021±0.003
	6.0	Na(ClO_4→I)	−0.015±0.03
	1.0	Na(ClO_4→NO_3)	0.072±0.007
	3.0	Na(ClO_4→NO_3)	0.087±0.004
	3.0	(Na→Li)ClO_4	0.068±0.003
$H^+ + HCOO^- \rightarrow HCOOH$	3.0	Na(ClO_4→Cl)	0.070±0.003
	3.0	Na(ClO_4→Br)	0.023±0.003
	3.0	Na(ClO_4→NO_3)	0.076±0.003
$H^+ + Cit^{3-} \rightleftarrows HCit^{2-}$ *	2.0	Na(ClO_4→NO_3)	0.073±0.03
$H^+ + Cit^{3-} \rightleftarrows HCit^{2-}$	3.0	Na(ClO_4→NO_3)	0.06±0.01
$2H^+ + HCit^{2-} \rightleftarrows H_3Cit$	3.0	Na(ClO_4→NO_3)	0.10±0.01
$H^+ + OH^- \rightleftarrows H_2O$	2.0	Na(ClO_4→NO_3)	0.075±0.005
$H^+ + C_2O_4^{2-} \rightleftarrows HC_2O_4^-$	3.0	Na(ClO_4→Cl)	0.075±0.003
$2H^+ + C_2O_4^{2-} \rightleftarrows H_2C_2O_4$	3.0	Na(Cl_4→Cl)	0.14±0.02
$H^+ + NH_3 \rightleftarrows NH_4^+$	0.5	Na(ClO_4→NO_3)	0.016
	1.0	Na(ClO_4→NO_3)	−0.013
	2.0	Na(ClO_4→NO_3)	0.017

*Cit^{3-} = citrate ion.

In order to reduce the activity coefficients λ_1 in Eqn. (11), recommendations have been formulated[80] concerning the rational selection of electrolytes for the study of weak acido-complexes. According to these recommendations, the difference between the logarithms of the mean ionic activity coefficients ($\Delta \lg y_\pm$) and the activities of water (or osmotic coefficients) in solutions of an inert electrolyte BX and the ligand-supplying salt BA should be minimal. Analysis of the parameters

$$\Delta \lg y_\pm = (\lg y_{\pm BX} - \lg y_{\pm BA})\, m^{-1}, \quad (19)$$

$$\Delta\varphi = (\varphi_{BX} - \varphi_{BA})\, m^{-1}, \quad (20)$$

where m is the molality and φ are osmotic coefficients, showed[63,70,71] that, for $\Delta \lg y_\pm$ and $\Delta\varphi$ tending to zero, the microcomponents of the type (1) equilibria in BX + BA mixtures induce a minimal change in the activity coefficients. For example, such changes have been observed for acetic acid (Table 3) and also for thallium(I) [24] and lead(II) [81] chloride complexes in isopiestic $NaClO_4$ + NaCl solutions which are nearly isomolar.

Krigintsev[82] and Ryazanov suggested[41–43] isopiestic solutions of mixtures of BX with BA as a new standard state. It is recommended that, when the latter is used, the entire experimental effect be included in the thermodynamic functions for equilibrium (1). On this assumption, no account is taken of the differences between the following parameters:

$$\Delta \lg y_\pm = (\lg y_{\pm MX_z} - \lg_{\pm BX})\, m^{-1}, \quad (21)$$

$$\Delta \lg y_\pm'' = (\lg y_{\pm MX_z} - \lg y_{\pm BA})\, m^{-1}\ . \quad (22)$$

The main feature is that one neglects the difference between the degrees of associaiton of ions in mixtures of the BX and BA salts, which makes an appreciable contribution even to the properties of 1.0 M Na(Cl→F) solutions[83] owing to the different strengths of the $Na^+(H_2O)_xCl^-$ and $Na^+(H_2O)_xF^-$ ion pairs.

A novel, purely chemical approach to complex non-ideal solutions put forward by Poppi[84,85] is noteworthy. It is based on allowance for the formation of solvates and transformation distributions. The non-ideality of such solutions is taken into account in terms of the hypothesis of an ideal solution of a continuous set of solvates. However, this procedure for taking into account non-ideality has not so far undergone the necessary tests on a sufficient number of specific examples. This also applies to a promising unified concept within the framework of which reduced ionic activity coefficients are used as characteristics of the non-ideality of the solutions.[86]

In many systems, the quantities λ_n in Eqn. (11) remain virtually constant when constant ionic strengths are varied in the range 0.5–4.0 (Table 3). The constancy of λ_n has been frequently demonstrated in relation to the behaviour of weak acids in mixtures of two electrolytes. The values of λ_n for the stepwise protonation of anions, i.e.

$$nH^+ + A^{z-} \rightleftarrows H_nA^{n-z} \quad (23)$$

were determined for systems with z = −1, −2, and −3. On the basis of the constancy of λ_n at constant ionic strengths I in the range 0.5–4.0, a method was developed for the separation of the medium effect from the effect of weak complex formation.

It is important to stress that the coefficients λ_n are constants even in those systems where the values of $\lg y_i$ in Eqn. (8) depend significantly on the constant ionic forces in mixtures of two electrolytes. The abolition of the differences between the values of $\lg y_i$ as a result of the cancellation of the third virial coefficients in equations of type (5) explains this finding. According to data in handbooks,[87] the quantities $b_{i,1}$ are almost constant for 0.1–0.6 m aqueous Na(ClO_4→A) solutions with A^- = Cl^-, Br^-, or I^-, but

decrease appreciably with increase in the molality of mixtures of $Li(ClO_4 \rightarrow A)$ and $K(F \rightarrow A)$. Mixtures of MSO_4 (M = Zn, Cu) with sodium, potassium, magnesium, and bismuth(II) sulphates as well as sulphuric acid can be divided into three groups as regards the nature of the dependences of $\Delta \lg y_{\pm}$ on I:[88] for the first group, the dependence has a maximum, for the second it has a minimum, and for the third the values of $\Delta \lg y_{\pm}$ remain almost constant over the entire range of ionic strengths I.

Potentiometric determinations of the activity coefficients of microamounts of tris(ethylene diamine)cadmium(II) [89] from the e.m.f.'s of cells with transport in 1 M aqueous $Li(ClO_4 \rightarrow A)$ solutions showed that b_i [Eqn.(16)] varies with increase in I in the same way as $y_{\pm}$ for $LiClO_4$ + LiA mixtures.

The influence of the charge of the ion A^{z-} in equilibrium (23) on λ_n in Eqn.(11) is of interest. There exists the view that the relation[79,90]

$$\lambda_n \simeq n\lambda_1 \qquad (24)$$

is valid, as can be seen from the data for oxalic acid, or that $\lambda_1 \simeq \lambda_2 \simeq \lambda_3$, as can be seen from the values of λ_n for citric acid (Table 3). Preference is usually given to Eqn.(24), but, unfortunately, the experimental data concerning the influence of ionic charges in equilibrium (1) on the λ_n are not unambiguous[90] and have been obtained only in isolated studies. In a new investigation,[26] Bjerrum notes that the following relation is valid for weak acido-complexes in solutions with high variable ionic strengths:

$$(y_{M^{z+}}y_{A^-})/y_{MA^{z-}} \approx (y_{MA^{z-1}}y_{A^-})/y_{MA_2^{z-2}} \approx \ldots \approx y_{MA_n^{z-n}}y_A/y_{MA_{n-1}^{z-n+1}}.$$

Allowance for the non-ideality of solutions with the aid of Eqns.(4), (5), or (11) does not meet the entire set of Guggenheim's requirements[61] (p. 5) for semi-ideal mixtures. This set includes the requirement that the solutions, for example, of BX and BA, at constant temperatures and pressures be mixed without a heat or volume change. Comparison of the data in Tables 3 and 4 shows that the substitution $Na(ClO \rightarrow A)$ at constant values of I in the range 1.0 – 6.0 hardly affects the values of λ_1 in Eqn.(11) but does alter appreciably $\lambda_{1(H)}$ in the equation

$$\Delta H_1^{\upsilon} = \Delta H_1 + \lambda_{1(H)}c_{Ac^-} \qquad (25)$$

where ΔH_1 and ΔH_1° are the enthalpy changes standardised by I M $NaClO_4$ and $Na(ClO_4 \rightarrow A)$ solutions, while $\lambda_{1(H)}$ are coefficients taking into account the influence of the non-ideality of the behaviour of H^+ and Ac^- in $Na(ClO_4 \rightarrow Ac)$ solutions on the coefficient λ_1. It is important to note that the values of $\lambda_{1(H)}$ are much higher than those of λ_1 (see the data in Tables 3 and 4).

Analysis of the heats of protonation of NH_3 and OH^- shows[91] that $\lambda_{1(H)}$ for ammonia is appreciably lower than for the OH^- ion, while the influence of the ionic strength I on these coefficients $\lambda_{1(H)}$ is consistent with the equation of Pitzer's theory (with the exclusion of concentrated nitrate solutions).

The absence of an appreciable influence of constant ionic strength on λ_1 at I = 0.5 – 6.0 (Table 3) led to the conclusion[40,79] that it is desirable to investigate weak acido-complexes at high ionic strengths of solutions with the replacement of a small proportion (< 10 – 20%) of the inert anions by the ligand ions. This conclusion is valid because the ions of any inert salts are little inferior to reactants forming weak complexes as regards their capacity for complex formation. In the light of the Storonkin – Lagunov rule[72] and Bjerrum's studies,[18,29,64] solutions with a variable ionic strength are more suitable as the standard state for the study of weak acido-complexes in aqueous solutions than a medium with a constant ionic strength. A correction for the non-ideality of the behaviour of the reactants involved in the type (1) equilibrium on formation of weak acido-complexes can be introduced, to a first approximation, on the basis of Eqn.(11) even at $I \neq$ const.

Table 4. The value of ΔH_1^0 for the reaction $H^+ + Ac^- \rightleftharpoons HAc$ and $\lambda_1(\Delta H)$ for I M aqueous solutions of NaA and $Na(ClO_4 \rightarrow A)$ at 298 K.[78]

I	A	ΔH_1^0, kJ mol^{-1}	$-\lambda_1(\Delta H)$
1.0	Cl^-	0.83	0.16±0.02
3.0	Cl^-	3.31	0.42±0.04
1.0	Br^-	0.72	0.07±0.03
3.0	Br^-	3.20	0.35±0.02
1.0	I^-	0.69	0.04±0.03
3.0	I^-	2.83	0.26±0.02
6.0	I^-	5.17	0.52±0.05
1.0	ClO_4^-	0.65	0
3.0	ClO_4^-	2.05	0

III. Classification of experimental methods

Various classifications of experimental methods for the study of complex formation in solution have been proposed in the literature,[3,92–94] but they do not take into account the specific features of the weak interaction in terms of type (1) reaction equations. The latter include four types of substances: (1) a simple or complex coordination centre M; (2) a ligand A; (3) the complex MA_n or the complexes $\sum_n MA_n$ formed; (4) the solvent H_2O. Measurement of the equilibrium concentrations [M], [A], $[MA_n]$ or $\sum_n [MA_n]$, and $[H_2O]$, i.e. of any of the reactants, and also of the functions $F\{[M]\}, F\{[A]\}, F\{[MA_n]\}$ or $F(\sum_n [MA_n])$, and $F\{[H_2O]\}$ sets limits, in our view, to the first group of methods for the study of weak complex formation in aqueous solutions. The second group comprises methods in which measurements are made of the acitivities (designated by braces) of the reactants or the functions of their activities, i.e. $F(\{M\})$, $F(\{A\})$, $F(\{MA_n\})$ or $F(\sum_n \{MA_n\})$, , and $F(\{H_2O\})$. This is the group of methods involving the measurement of activity.

The approaches to the mathematical analysis of experimental data for weak complex formation, for example, the determination of n and β_n^0, change on passing from concentration methods to activity measurement methods. The separation of experimental methods into the group of concentration methods and the group of activity measurement methods is associated with the need to take into

account the changes in the activity coefficients of the reactants in Eqn. (2) for any choice of standard state.

In a number of studies[7,37,95–98] on weak acido-complexes, fundamentally different information has been obtained about the values of n and β_n^0 for type (1) equilibria, which can be explained by failure to take into account the specific features of the experimental methods, noted above, in the mathematical treatment of the results. The differences are observed most often[95–98] when data obtained by the $F(\{M\})$ methods, for example the potentiometric method using an electrode reversible with respect to M, are compared with data obtained by the $F(\{A\})$ or $F\{[A]\}$ methods, for example the potentiometric method using an electrode reversible with respect to A or the method involving the measurement of solubility. The contribution of the disregarded changes in the activity coefficients of the ions M in the $F(\{M\})$ methods has frequently led to higher values of n and β_n^0 for halide, thiocyanate, and sulphate complexes than those obtained by treating the data in terms of the $F(\{A\})$ methods. A similar difference has been observed in the analysis of the results obtained by the $F\{[M]\}$ and $F(\{M\})$ methods or the $F\left(\sum_n [MA_n]\right)$ and $F(\{M\})$ methods.[7,97] The conventional parameters of the complex formation equilibria, involving both chemical interaction and the effect of the medium, have been determined in numerous investigations,[7] although their conventional nature has been rarely mentioned. The differences between the values of n and β_n^0 considered usually disappeared in the mathematical analysis of the experimental data using Eqns. (11) or (17). However, additional parameters then appeared in the form of the quantities λ_n or "b", whose values depended on the type of experimental method.[96]

An unusual case of the scatter of the values of n and β_n^0 for weak complexes has been observed[99–101] when the extraction method was used. The replacement of one extractant by another frequently alters the thermodynamic parameters of the equilibria investigated in the aqueous phase. For example, the extraction of traces of tris(phenanthroline)ruthenium(II) perchlorate from 0.75 M aqueous solutions of sodium sulphate with chloroform or acetophenone led[101] to significantly different values of the logarithms of the stepwise formation constants of the outer-sphere complexes $[RuPhen_3](ClO_4)_n^{3-n}$ (Phen = phenanthroline) for $n = 1$ and 2; these values proved to be 2.38 and 1.73 or 5.43 and 2.49 for extraction with chloroform and acetophenone respectively. Such differences are caused by the change in the standard conditions on replacement of the type of extractant. Aqueous solutions saturated by the extracting solvent constitute the standard state when extraction methods are used to investigate complex formation in aqueous solutions.

In an attempt to obtain more objective information about weak complexes in aqueous solutions, investigators have sometimes used[81] in Eqn. (2) the concentrations of some of the reactants involved in equilibrium (1) and the activities of others. Such calculations yielded estimated thermodynamic parameters of the type (1) equilibrium, the extent to which they are conventional being difficult to estimate.

For the experimental study of weak complex formation by concentration methods, it is useful to employ in the mathematical treatment of the experimental data the activity coefficients of one or several (but not all) components of the equilibria. In particular, one should avoid using the mean ionic activity coefficients in the study of weak stepwise complex formation, although some investigators[102] do not agree with this claim. From our point of view, their information about the stability constants of weak complexes can be regarded as merely qualitative but not quantitative.

The application of experimental activity methods is complicated by the need to carry out all the calculations in terms of activities or to obtain additional information about the activity coefficients of the reactants whose activities have been measured experimentally. The determination of reliable values of n and β_n^0 for weak complexes by the activity methods involves direct or indirect determination of the activity coefficients of both molecules and individual ions.[25]

The $F\left(\sum_n [MA_n]\right)$, methods, in which measurements are made for example, of the optical densities of solutions, chemical shifts, heats of reaction, etc., are sometimes (especially for $n = N = 1$) most useful for the experimental study of weak complex formation. However, these methods, which yield the dependence of the given parameter $\bar{P}$ on c_A, entail the necessity to solve equations of the type

$$\bar{P} = \sum_{n=0}^{N} (P_n [MA_n])/c_M, \qquad (26)$$

where P_n are the molar coefficients of the parameter $\bar{P}$ of the complexes MA_n. The solution of type (26) equations for weak complexes is associated with the need to find simultaneously n, β_n^0, and λ_n, as well as P_n and $\lambda_{n(P)}$, where the coefficients $\lambda_{n(P)}$ reflect the influence of the medium on the values of P_n. Judging from data (Table 4) for the influence of the medium on the enthalpy of protonation of acetate ions, the values of $\lambda_{1(\Delta H)}$ in this system are several times higher than the values of λ_1. Hitherto, in studies on weak complexes by the $F\left(\sum_n [MA_n]\right)$ methods, the influence of the medium on $\lambda_{n(P)}$ was usually disregarded. Such neglect of the values of $\lambda_{n(P)}$ has frequently led to significant differences between the constants for the protonation of strong acid anions in aqueous solutions[103] (p. 40) in calculations based on values of $\bar{P}$ obtained by different methods. The simultaneous determination of n, β_n^0, P_n, λ_n, and $\lambda_{n(P)}$ from a single smooth curve relating P to [A] for $n > 1$ has not been carried out and, judging from the first attempts,[90] is scarcely possible. The use of the $F\left(\sum_n [MA_n]\right)$ methods for the study of type (1) equilibria can be specially recommended in combination with the measurements of λ_n, P_n, and $\lambda_{n(P)}$ independent of the parameter $\bar{P}$. Such experimental methods must be sought. Electrodes reversible with respect to weak complexes MA_n may be useful, in addition to different types of molecular, microwave, and ultrasonic spectroscopy, but in such experiments it is essential to take into account the influence of the medium on the standard potentials.

IV. Complexes with molecular ligands

Ammonia is a classical ligand of the molecular type. The study of the formation of metal ammines in aqueous solutions by Bjerrum[104] determined the development of a large series of modern aspects of the chemistry of complex formation in condensed phases. However, in Bjerrum's studies the majority of problems concerning the formation of weak ammines in solutions were not solved. Until recent years, the very marked dependence of the formation constant of the complex $MgNH_3^{2+}$ on the type of magnesium salt[104] (p. 154) from the solubility of which in aqueous ammonia solutions the constant had been calculated was not understood. The solubilities at

291 K of magnesium naphthalene-β-sulphonate, cinnamate, and oxalate, led to $\lg\beta_1$ = 0.02, −0.13, and −0.66 respectively for the $MgNH_3^{2+}$ ion.

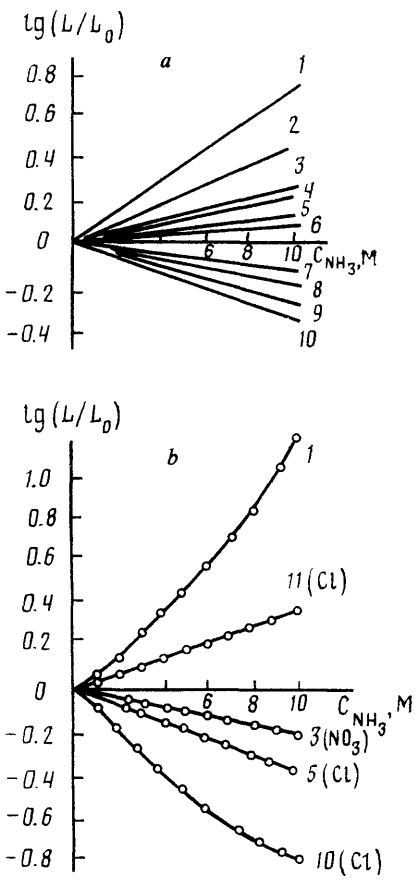


Figure 1. Dependences of the logarithms ($\lg L/L_0$) of the relative solubilities of thallium(I) salts (*a*) and hexamminecobalt(III) salts (*b*) on the ammonia concentration in 1.0 M aqueous solutions of ammonium perchlorate (nitrate (NO_3) or chloride (Cl)] at 298 K (L_0 represents the solubilities of the salts at c_{NH_3} = 0): *1*, perchlorates; *2*, iodides; *3*, nitrates; *4*, bromides; *5*, chlorides; *6*, bromates; *7*, carbonates; *8*, sulphates; *9*, oxalates; *10*, iodates; *11*, hexacyanoferrates.[25]

The decrease in the stability constant of the complex $TlNH_3^+$ with increase in ammonia concentration in aqueous solutions could not be explained[104] (p. 183). The value of this constant was unjustifiably included also among critically selected constants.[5] The marked increase in the solubility of $[Co(NH_3)_6](ClO_4)_3$ with increase in ammonia concentration in solution[105] in practical applications in the hydrometallurgy of non-ferrous metals[106,107] and the marked decrease in the solubility of $[Co(NH_3)_6]_2(SO_4)_3$ with increasing concentration of ammonia in water remain unexplained.

Systematic studies have been recently carried out[25,44–47,108–110] on the formation of weak ammines in relation to ammonia solutions of thallium(I) lithium, sodium, magnesium, calcium, strontium, barium, hexammine- and tris(ethylenediamine)cobalt(III), and a number of other simple and complex cations, which do not hydrolyse appreciably at pH < 11, in aqueous solutions with c_{NH_3} = 0–10 M. The principle standard state in the majority of these investigations consisted of 1.0 M solutions of ammonium perchlorate, nitrate, or chloride at 298 K. A number of experiments have also been carried out in 0.25, 0.50, 2.0, and 4.0 M solutions of ammonium salts at 293, 298, 303, and 308 K. A distinctive feature of the series of studies considered was the simultaneous measurement of the equilibrium concentrations or activities of the central cations, ammonia, the complexes, and water, i.e. the properties of all the reactants involved in type (1) equilibria. Electrodes reversible with respect to M and NH_3, measurements of the solubility of sparingly soluble salts, extraction, electronic spectroscopy, and NMR were used.

It is clear from the data in Fig. 1 and similar relations that the solubility of sparingly soluble salts in aqueous ammonia solutions at I = const. cannot be used to determine n and β_n^0 for type (1) reactions without taking into account the influence of the anion of the dissolved salt, although the anions considered are not appreciably associated with the cations M^{z+}.[3–6] Experiments designed to measure the vapour pressure of ammonia over aqueous salt solutions showed[44] that the potassium cation and the ClO_4^- anion do not influence appreciably the activity of ammonia in its aqueous salt solutions. Taking into account the fact that the potassium cation does not form ammines in aqueous solutions[3–5] while the solubility of $KClO_4$ in 1 M NH_4ClO_4 solutions with c_{NH_3} = 0–10 M is constant (0.040 M at 298 K),[47] a new extrathermodynamic assumption was introduced on the basis of the above postulate:

$$y_{K^+} = y_{ClO_4^-} = 1, \qquad (27)$$

where y_{K^+} and $y_{ClO_4^-}$ are the activity coefficients of the ions K^+ and ClO_4^- in aqueous ammonia solutions at 298 K. Assumption (27) served as the basis of a quantitative characterisation of the stepwise formation of weak ammines of a number of metals in aqueous solutions at c_{NH_3} = 0.1–10 M and also of the calculation of the activity coefficients of individual ions in aqueous-salt ammonia solutions. The calculation showed that the logarithms of these coefficients (Table 5) are positive for anions but negative for the majority of cations, including NH_4^+. Under these conditions, hydroxopentamminecobalt(III) has a zero value of the logarithm of the activity coefficient in 0.1–10 M ammonia solutions, i.e. ammonia is not appreciably bound by the cation, while the $Coen_2CO_3^+$ cation (en = ethylenediamine) actually salts out ammonia, like the anions.

A nearly zero value of the activity coefficient of the iodide ion combined with the similarity of the behaviour in aqueous ammonia solutions of potassium and caesium cations suggest that the extrathermodynamic assumption (27) is in many respects identical with the usual assumption[111,112] that the activity coefficients of the I^- and Cs^+ ions are equal. However, for the study of weak metal ammines in aqueous solutions, assumption (27) is better justified and more convenient[25,44] than the caesium iodide ionic scale.

On the basis of assumption (27), the composition and formation constants of thallium(I) ammines have been calculated[25] from the solubilities L of the salt $TlClO_4$ (Fig. 1) adjusted to a constant ionic strength of 1.0 based on the sum of the salts NH_4ClO_4 and $TlClO_4$.

The calculations were performed by the method of least squares on the basis of the equation

$$(L/L_0 - 1)\{H_2O\}\{NH_3\}^{-1} = K_1^0 + K_1^0 \cdot K_2^0\{NH_3\}\{H_2O\}^{-1}, \quad (28)$$

where L_0 and L are the solubilities of $TlClO_4$ in 1.0 M (NH_4 + Tl)ClO_4 solutions in the absence or presence of ammonia. The activities of water and ammonia (on the molarity) scale, required for the solution of Eqn. (28), were expressed in terms of the molarity scale.

Table 5. The logarithms of the activity coefficients of individual ions in 1.0 M aqueous ammonia solutions of NH_4A at c_{NH_3} = 10 M and 298 K.[25,44]

Ions	lg y	A^- in NH_4A	Ions	lg y	A^- in NH_4A
Tl^+	−0.95	ClO_4^-	NO_3^-	0.45	NO_3^-
$Co(NH_3)_6^{3+}$	−1.24	ClO_4^-	Cl^-	0.67	ClO_4^-
$Co(NH_3)_6^{3+}$	−0.94*	ClO_4^-	Br^-	0.53	ClO_4^-
$Co(NH_3)_6^{3+}$	−1.23**	ClO_4^-	I^-	0	ClO_4^-
$Co(NH_3)_5OH^{2+}$	0	ClO_4^-	IO_3^-	1.50	ClO_4^-
$Coen_2CO_3^+$	0.24	ClO_4^-	SO_4^{2-}	2.4	ClO_4^-
NH_4^+	−0.56	ClO_4^-	$Fe(CN)_6^{3-}$	0.51	NO_3^-

*At I = 0.50.
**At 309 K.

The potentiometric measurements of the activities of thallium(I) ions with the aid of the Tl(Hg) electrode in aqueous ammonia solutions led to values of K_n^0 for the thallium(I) ammines which agreed with those found for the solubility of $TlClO_4$ only after correcting the measured e.m.f.'s of the cells with transport for the liquid-junction potentials arising at the interfaces between the solutions: 1 M NH_4ClO_4|1M NH_4ClO_4 + x M NH_3. These potentials, determined with the aid of iodide and perchlorate membrane electrodes, were 3.0 mV for 1.0 M ammonia.

The Bjerrum formation functions $\bar{n}'$ of thallium(I) ammines were calculated by means of the following equation from the experimental values of $\{NH_3\}$ and y_{NH_3} in the studies under consideration:

$$\bar{n}' = (c_{NH_3} - \{NH_3\}/y_{NH_3})/c_{Tl^+}, \quad (29)$$

which led to negative values of $\bar{n}'$ for c_{NH_3} = 0.1 − 10 M. Additional measurements of $\{NH_3\}$ and y_{NH_3} were performed for aqueous ammonia solutions of the potassium salts KX. The corrections Δn were applied to $\bar{n}'$ on the basis of the above data in accordance with the equation

$$\Delta\bar{n} = (c_{NH_3} - \{NH_3\}/y_{NH_3})/c_{KX}. \quad (30)$$

The Bjerrum functions $\bar{n}$, from which the compositions and formation constants of the complexes $Tl(NH_3)_n^+$ were calculated, had been determined from the relation

$$\bar{n} = \bar{n}' - \Delta\bar{n}\ . \quad (31)$$

The values of $\Delta\bar{n}$ from Eqn. (30) were more negative than the values of $\bar{n}'$ found from Eqn. (29). Hence the values of $\bar{n}$ based on Eqn. (31) were positive and the least squares solution of the equation

$$\sum_n (\bar{n} - n)\{NH_3\}^n\{H_2O\}^{-n}\beta_n^0 = 0 \quad (32)$$

led to formation constants agreeing (Table 6) with the above parameters obtained with the aid of the $F(\{Tl^+\})$, $F([Tl^+])$, $F(\{NH_3\})$, and $F\left(\sum_n [Tl(NH_3)_n^+]\right)$ methods. ^{205}Tl NMR was employed as the last method. The constants K_n were calculated from the chemical shifts of the ^{205}Tl signal taking into account the influence of ammonia on σ_2' in accordance with the equation

$$\sigma_0 = \sigma_0' + \alpha_0 c_{NH_3} \quad (33)$$

where σ_0' and σ_0 are the chemical shifts in aqueous solutions without ammonia and at an ammonia concentration c_{NH_3}, while α_0 are coefficients taking into account the influence of ammonia on the chemical shift of ^{205}Tl present as the aquo-complex.

Table 6. Data on the compositions and stepwise stability constants of the complexes $Tl(NH_3)_n^+$ in 1.0 M NH_4ClO_4 solutions at 298 K.[25,44]

$\lg K_n \pm 3\sigma$		Experimental method	Type of method according to classification in Section III
n=1	n=2		
0.85±0.10	0.4±0.1	Solubility	$F([Tl^+])$
−0.89	−1.4	Ditto	Ditto with allowance for $[H_2O]$ on the mole fraction scale
1.2±0.3	0.3±0.1	Potentiometry with ammonia electrodes*	$F(\{NH_3\})$
1.2±0.3	0.3±0.1	Extraction of ammonia into chloroform*	$F(\{NH_3\})$
0.60±0.01	–	Potentiometry with a Tl(Hg) electrode	$F(\{Tl^+\})$
1.04±0.09	0.3±0.1	Ditto with a correction for the liquid junction potential	Ditto
−0.70±0.09	−1.3±0.1	Ditto	Ditto with allowance for $[H_2O]$ on the mole fraction scale
0.98±0.08	0.3±0.1	^{205}Tl NMR	$F([MA_n])$
0.4±0.2	–	Electronic spectra**	$F([MA_n])$

*$I \simeq$ 1.2 M NH_4ClO_4 + $TlClO_4$.
**At $c_{NH_3} \leqslant$ 5.0 M.

The low accuracy of the measurement of small changes in the optical density ($\Delta\overline{D}$) of Tl^+ solutions due to added ammonia precluded the determination of K_n for $Tl(NH_3)_n^+$ from electronic spectra in agreement with data produced by other methods (Table 6). This finding has already been explained.[113] The contribution of the formation of $Tl(NH_3)_2^+$ to $\Delta\overline{D}$ led to a low value of K_1 calculated from $\Delta\overline{D} = F(\{NH_3\})$.

The study of the influence of the ionic strength I of the solutions on the formation constant of the complex $TlNH_3^+$ afforded[44] the equation

$$\lg K_1^0 = \lg K_1 - 0.065I, \quad (34)$$

where K_1^0 is the constant at 298 K and $I \to 0$.

Tests of the possibility of determining the composition and stability of weak inner-sphere ammines of thallium(I) and a number of other metals with the aid of a wide range of experimental methods have made it possible to apply a similar approach to the study of the outer-sphere interaction of ammonia with coordinatively saturated inert cobalt(III) complexes. The calculations showed (Table 7) that hexammine- and tris(ethylenediamine)cobalt(III) combined with up to four ammonia molecules in the outer sphere in aqueous solutions. The binding strength of each succeeding molecule compared with the previous one diminishes in conformity with the statistical effects $S_{n,n+1}$ [104] for the limiting coordination number $N = 4$.

Table 7. The logarithms of the stepwise stability constants of the outer-sphere ammonia complexes of cobalt(III) in aqueous solutions at I = const. and 298 K and the statistical and average general effects.[25,44]

n	$\lg K_n^0 \pm 3\sigma$		$n, n+1$	$T_{n,n+1}$	$S_{n,n+1}$	
	$[Co(NH_3)_6](NH_3)_n^{3+}$	$[Coen_3](NH_3)_n^{3+}$			$N=4$	$N=8$
1	0.95±0.09 *	1.46±0.09 **	–	–	–	–
1	0.84±0.10 ***	0.85±0.07 ***	–	–	–	–
2	0.53±0.08	1.00±0.08	1.2	0.41	0.43	0.36
3	0.28±0.12	0.64±0.07	2.3	0.35	0.35	0.34
4	–	0.20±0.06	3.4	0.44	0.43	0.21

*The values of $\lg K_n^0$ were obtained from the solubility of hexamminecobalt(III) perchlorate in 1.0 M ammonium perchlorate solutions.

**The values of $\lg K_n^0$ were obtained from the averaged data for the extraction of ammonia into chloroform and potentiometric data obtained using an ammonia electrode at $I \simeq 2$.

***From electronic spectra t $I = 1$.

The low solubility (3×10^{-4} M at 298 K) of hexamminecobalt(III) perchlorate in 1.0 M NH_4ClO_4 solutions made it possible to investigate the outer-sphere ammonia derivatives of this complex only by the $F(\{M\})$, $F\{[M]\}$, and $F\{[MA]\}$ methods. The high solubility of tris(ethylenediamine)cobalt(III) perchlorate made it possible to investigate its ammonia derivatives in terms of the activity of ammonia, i.e. by the $F(\{A\})$ method, at $I \simeq 2$. In the study of hexamminecobalt(III) derivatives, it was observed[25,44] that the influence of ionic strength in the range 0.1–1.0 is represented by the relation

$$\lg K_1^0 = \lg K_1 + 0.54I. \quad (35)$$

Extrapolation in terms of Eqn. (35) to $I = 2$ yielded $\lg K_1 = 1.49$. Within the limits of error, this value agrees with that (Table 7) found for the outersphere complex $[Coen_3](NH_3)^{3+}$. This finding suggests that the $Coen_3^{3+}$ and $Co(NH_3)_6^{3+}$ ions have approximately the same ability to combine with ammonia in aqueous solutions.

The formation constants of the outer-sphere ammonia derivatives of hexamminecobalt(III) and the ionic activity coefficients in aqueous ammonia solutions (Table 7) provide a quantitative idea[106] about the increase in the solubility of $[Co(NH_3)_6](ClO_4)_3$ and the decrease in the solubility of $[Co(NH_3)_6]_2(SO_4)_3$ [107] in aqueous solutions with increase in the concentration of ammonia.

The method for the study of ammonia derivatives of metals considered above was extended to weak methylamine, pyridine, ethylenediamine and other relatively unstable complexes of cations with molecules in aqueous solutions.[25,44,48–50]

V. Acido-complexes

Careful studies of the stepwise formation reactions of weak acido-complexes of metals in aqueous solutions by different methods indicate the impossibility of obtaining a single set of stepwise stability constants with the representation of the experimental data obtained by different experimental methods. This situation has been demonstrated recently in relation to zinc chloride complexes.[114] It is entirely reasonable because the values of K_n^0 for these complexes leads to values of $\Delta_r G_n^0$ comparable to $1.5RT$, while reliable unambiguous isolation of the small contribution of the specific interaction of Zn^{2+} with Cl^- against the background of inevitable significant changes in the ionic acitivity coefficients is virtually impossible. However, only allowance for the changes in the activity coefficients in 3.0 M aqueous $(Na \to H)ClO_4$ solutions with the aid of an equation of type (11) led to the possibility of describing the complex form of the solubility curve for molybdenum(VI) oxide.[32] Other conceivable ways of explaining this curve with a complex shape did not lead to its quantitative representation in terms of the constants of the Law of Mass Action.

Data obtained solely by thermodynamic methods for the investigation of weak stepwise formation of acido-complexes without extrathermodynamic assumptions usually do not permit an unambiguous differentiation between the changes in the activity coefficients and the formation of the complex MA_{n+1} after the real formation of the associated species MA_n. Under favourable conditions, such differentiation can be achieved[31] on the basis of spectroscopic measurements at several wavelengths but that too is not unambiguous because no account is taken of the influence of the composition of the ionic medium on the molar extinction coefficients of the reactants.

Many weak inner-sphere and outer-sphere acido-complexes have been investigated[3–6] by the potentiometric method with the aid of electrodes reversible with respect to the proton or the central ion of the complex using cells with transport. In studies of this type, corrections were frequently introduced for the liquid junction potentials.[115] The correct application of such corrections led to the experimental determination of the activities or equilibrium concentrations of individual ions, M. The liquid junction potentials have been usually assumed to be proportional to the ligand concentrations and the proportionality coefficients b_A have been determined from experimental data. Such calculations have been carried out, for example, in the study of weak hydroxo-complexes of calcium, strontium, and barium in 3 M $Na(ClO_4 \to OH)$ solutions[116]

and of lead(II) and cadmium acetate and benzoate complexes in 1.0 M (Na, H)(ClO_4→A) solutions, where A represents acetate or benzoate ions,[117] and in a number of other systems.[3-5] The changes in the e.m.f.'s of the cells investigated as a function of the ligand concentration were attributed in the above studies to the contributions by β_n^0 and b_A. The calculations showed (Table 8) that variation of the coefficients b_A alters appreciably the calculated values of β_n^0 and even the values of n. The scale of the influence of the liquid junction potentials increases sharply[118] with decrease in the association constants determined. When an unreliable correction is applied for the liquid junction potentials, the constants have the significance of only semiquantitative characteristics of weak complex formation equilibria,[117] although they represent satisfactorily [with the differences $\sigma(E) \leqslant 0.1$ mV] the experimental data. A combination of different values and different corrections for diffusion potentials does not influence appreciably $\sigma(E)$, which hinders the selection of reliable information about the systems investigated.

Table 8. The compositions and stability constants of $Pb(Ac)_n^{2-n}$ in 1.0 M aqueous $Na(ClO_4 \rightarrow Ac)$ solutions at $c_{Ac^-} \leqslant 0.2$ M.[117]

method used to take into account E_d^*, mV	$\beta_1^0 \cdot 10^{-2}$	$\beta_2^0 \cdot 10^{-3}$	$\beta_3^0 \cdot 10^{-3}$	$\sigma(E)$, mV
No allowance for E_d^*	0.95±0.04	1.37±0.06	–	0.36
2.6 [HAc] – 7.2 [Ac$^-$]	0.99±0.02	1.23±0.03	–	0.17
2.6 [HAc] – 7.2 [Ac$^-$]	1.03±0.02	1.06±0.05	1.1±0.3	0.10
1.4 [HAc] – 13.6 [Ac$^-$]	1.00±0.01	1.11±0.01	–	0.09
1.4 [HAc] – 13.5 [Ac$^-$]	1.02±0.01	1.05±0.04	0.38±0.02	0.08
(2) [HAc_2^-] + [H_2Ac_2]	1.01±0.01	1.28±0.02	–	0.10
(6) + [HAc_2^-]	0.996±0.01	1.27±0.01	–	0.08
5.4 [HAc] – 13.6 [Ac$^-$]	1.029±0.004	1.11±0.02	–	0.03

*E_d = diffusion potential.

Vierling[34,69] studied the equilibria

$$Pb^{2+} + nA^- \rightleftarrows PbA_n^{2-n} \qquad (36)$$

where A are chloride and bromide ions and $n_{max} \geqslant 4$ according to the e.m.f.'s of cells with transport [containing Pb(Hg) electrodes] on the basis of Eqn. (11) without corrections for liquid function potentials. In the calculations of n, β_n^0, and λ_n, use was made of up to a thousand experimental e.m.f.'s at different ligand concentrations. The system (36) was investigated in 4.0 M $Na(ClO_4 \rightarrow A)$ solutions at $c_{A^-} = 0-4.0$ M.

The traditional expression for the complex formation function Φ is

$$\Phi = c_{Pb^{2+}}/[Pb^{2+}] = 1 + \sum_{n=1}^{N} \beta_n [A]^n \qquad (37)$$

and includes β_n standardised by variable composition $Na(ClO_4 \rightarrow A)$ solutions. Vierling replaced it by the relation

$$\Phi = 1 + \sum_{n=1}^{N} \beta_n^0 [A]^n \exp(\lambda_n [A]), \qquad (38)$$

where β_n^0 were standardised with 4.0 M $NaClO_4$ solutions and the quantities β_n, β_n^0, and λ_n were linked by relations (11). The contributions of the diffusion potentials in such calculations enter into the quantities λ_n. The parameters of Eqns. (37) and (38) were calculated from the dependences of ΔE on [A] using at $T = 298$ K the equation $\Delta E = 59.2 \lg \Phi$, where ΔE is the experimental e.m.f. The method of least squares with the minimisation of $\delta(E)$ led Vierling[34] to the data compiled in Table 9. It was found that the employment of a gigantic set of accurate experimental data makes it possible to represent the latter (within the limits of the error of the determination of ΔE) both by Eqn. (37) and by Eqn. (38) with different variations of β_n and λ_n. However, the application of Eqn. (38) yielded a series of values of β_n^0 for all the values of n equal to 1, 2, ..., N, while the application of Eqn. (37) frequently led to zero values of β_n for certain values of n. The λ_n found had different signs and did not depend regularly on the values of n. Only when the potentiometric study of equilibrium (36) was supplemented by solubility and spectrophotometric data did Vierling arrive at the unambiguous, from his point of view, conclusion[34] that in 4.0 M $Na(ClO_4 \rightarrow A)$ solutions with [A] = 0–4.0 and at $T = 298$ K, all the complexes PbA_n^{2-n} with $N = 4$ for A = Cl^- and $N = 5$ for A = Br^- are formed in succession. However, the very high values $\lambda_n = 0.232$, 0.244, 0.151, 0.399, and 0.309 for $n = 1-5$ were obtained for $PbBr_n^{2-n}$ from the measurements of the solubility of lead(II) bromide, in contrast to the potentiometric data (Table 9).

Table 9. Data for the formation of the complexes $PbCl_n^{2-n}$ and $PbBr_n^{2-n}$ obtained with the aid of Hg(Pb) electrodes in 4.0 M $Na(ClO_4 \rightarrow Cl)$ and $Na(ClO_4 \rightarrow Br)$ solutions at 298 K.[34,39]

n	Version (1)*			Version (2)*		
	lg β_n without λ_n	lg β_n^0 with λ_n	λ_n	lg β_n without λ_n	lg β_n^0 with λ_n	λ_n
Chloride complexes						
1	1.14	1.277	0.002	1.31	1.294	−0.006
2	1.93	1.574	0.001	1.34	1.473	−0.003
3	1.97	2.285	−0.036	2.37	2.330	−0.038
4	1.84	1.433	0.096	**	1.134	0.038
5	–	–	–	1.20	0.959	0.021
$\sigma(E)$, mV	0.37	0.15	–	0.12	0.14	–
Bromide complexes						
1	1.56	1.431	−0.021	1.53	1.505	−0.019
2	**	2.000	−0.050	**	1.443	−0.002
3	3.01	2.885	−0.237	3.03	2.996	−0.096
4	**	2.987	0.159	2.36	2.692	0.054
5	2.94	–	–	2.69	2.653	0.064
6	–	–	–	2.01	–	–
$\sigma(E)$, mV	0.55	0.21	–	0.15	0.16	–

*Versions (1) and (2) differ by the maximum values of n.
**$\beta_n \leqslant 0$ were obtained.

The system of thiocyanate complexes $(Nibipy_3)(SCN)_n^{2-n}$, investigated on the basis of the solubility of tris(2,2'-bipyridyl)-nickel(II) in 4.0 K (F→SCN) solutions, was analysed[63] in terms of Eqns. (37) and (38) using 12, 40, and 86 experimental solubilities.

The picture observed for the complexes PbA_n^{2-n} (Table 9) was in many respects repeated (Table 10) for the tris(2,2'-bipyridyl)nickel(II) thiocyanate complexes but, in contrast to the $PbBr_n^{2-n}$, the values of λ_n found were comparatively low, amounting to 0.04 ± 0.01 for all the values of n. Calculations for this system showed that a small set of comparatively accurate (errors of about ±1%) data, usually provided by the solubility method, does not permit the determination of reliable values of stepwise stability constants equal to 1.0 and below for $n \geqslant 3$ in combination with λ_n. The errors in the determination of the values of K_n^0 in Table 10 for $n \geqslant 3$ are comparable to the constants themselves. The high correlation of the quantities n, β_n^0, and λ_n with one another in equations of type (38) hinders an unambiguous and reliable calculation of all these functions from smooth $\Phi\{[A]\}$ curves for $n \geqslant 3$. Detailed analysis of the methods for the calculation of all the parameters of Eqn. (38) in systems of relatively unstable complexes has been correctly referred to as estimation of these parameters.[35] A reliable determination of β_n^0 and λ_n is possible only for $n = 1$; when $n \geqslant 3$, it is difficult to hope (Table 8) for the selection of a single reliable series of values of β_n^0 and λ_n with low errors of the determination of these functions. The validity of this conclusion has been confirmed by careful investigation.[35] However, the use of the values of λ_n found in independent experiments or calculations can increase the accuracy of the determination of the stepwise stability constants of the complexes by Eqn. (38).

Table 10. Data for the formation of the outer-sphere complexes $[Nibipy_3](CNS)_n^{2-n}$ obtained by the solubility method in 4.0 M K(F→SCN) solutions at 298 K.[63]

n	$\lg \beta_n$		$\lg \beta_n^0$	$\lg K_n^0$	λ_n
	r*=12	r=40	r=86		
0	−9.13±0.03**	−9.061±0.026**	−9.02**	–	0.05
1	1.98±0.11	1.445±0.13	1.50	1.50	0.04
2	***	3.045±0.032	2.98	1.48	0.03
3	2.97±0.19	2.544±0.19	2.34	−0.64	0.04
4	***	***	2.18	−0.16	0.03
5	2.23±0.12	2.419±0.036	2.02	−0.16	0.04

*r is the number of experimental values of the solubility used in the calculations.

**The logarithms of the solubility product of tris(2,2'-bipyridyl)-nickel(II) thiocyanate.

***$\beta_n \leqslant 0$.

The application of Eqn. (38) to a series of systems investigated previously demonstrated convincingly the conventional significance of many of the values of β_n for weak complexes with $n > 1$, which was noted in previous studies.[68] For example, the results of potentiometric measurements with the $Coen_3^{2+}$, $Coen_3^{3+}|Pt$ electrode in $NaClO_4 + Na_2SO_4$ solutions at constant ionic strengths, which were interpreted previously in terms of the hypothesis of the formation of a series of outer-sphere complexes $[Coen_3](SO_4)_n^{3-2n}$ (n = 1, 2, 3), were reproduced by means of the quantities β_1^0 and λ_1 with a high correlation coefficient (>0.995).[98] The validity of this treatment of potentiometric data has been confirmed by measurements of the activity of the sulphate ion and by thermochemical studies. A similar situation has been noted for other weak acido-complexes.[37,98,119]

The linear relation between $\lg\Phi$ and [A] in systems with formation of the acido-complexes MA_n in the absence of appreciable changes in the slopes of the above straight lines as a function of constant ionic strengths has been suggested[40,79] as proof of the absence of complex formation. This proof is based on the identification of the virial coefficients $b_{i,1}$ and $b_{i,1}^*$ in Eqn. (5) and on the claim that they are not influenced by the variation of constant ionic strengths in the range 0.5–4.0. Numerical data similar to those in Tables 3 and 11 were used by the authors[40,79] as a basis for such identification. In reality, for linear relations between $\lg\Phi_M$ and [A] or between $\lg y_M$ and [A], it is not permissible to differentiate on the basis of the data considered the effect of non-ideality and complex formation[31] without resorting to extrathermodynamic assumptions or additional experimental studies.

Table 11. The changes in the conventional diffusion potentials (E_d') and the contribution to the latter of the hydrogen ion activity coefficients (y_{H^+}) at 298 K.[115]

I	Composition of medium	$E_d'[H^+]$, mV mol litre^{-1}	$y_{H^+}[H^+]$, mV mol litre^{-1}
1.0	(Na → H)ClO_4	686	6
0.5	(Na → H)ClO_4	133	4
1.0	(Na → H)ClO_4	69	4
3.0	(Li → H)ClO_4	16	0.45
3.0	(Na → H)ClO_4	18	3
3.0	(K → H)Cl	10	4
1.0	(K → H)Cl	66	3
0.5	(K → H)Cl	123	5
0.5	Na(ClO_4 → OH)	615*	0.9*
3.0	Na(ClO_4 → OH)	8*	1.2*
0.5	Na(Cl → OH)	41*	0.2*

*Per 1.0 mol of OH^- litre^{-1}.

However, re-examination[120] of the Debye–Hückel theory taking into account the shielding of ions by water molecules leads to the possibility of partitioning the experimental values of the second virial coefficient. Such partitioning has already been achieved[121] in relation to a large set of experimental data for aqueous magnesium sulphate solutions with variable ionic strengths in the temperature range 273–423 K. The forces of attraction between the Mg^{2+} and SO_4^{2-} ions were expressed in terms of their association constants and only the effects of repulsive forces were included in the second virial coefficient. Unfortunately the subdivision was based on mean ionic activity coefficients which consist of unequal contributions by cations and anions, even in dilute solutions of ions with very similar electrostatic properties, for example, NH_4^+ and Cl^-.[15] Furthermore, it has been shown that $y_{M^{z+}}$ and y_{Cl^-} vary in fundamentally different ways with increase in the concentrations of aqueous solutions of

ammonium, nickel, and cadmium chlorides. This fact is associated with the increase in the stability of MCl_n^{2-n} in this series of M^{z+}. In view of the need for the summation of $\lg y_{M^{z+}}$ and $\lg y_{Cl^-}$ in order to find $\lg y_{\pm}$, it is difficult to find from the values of the latter the real values of n and β_n for weak acido-complexes. The linear relations between $\lg y_{\pm}$ and for example, concentrations in solutions of alkali metal or alkaline earth metal chlorides are replaced by non-linear relations for y_{H^+} and y_{Cl^-}. This usual phenomenon[54] indicates the desirability of determining n and β_n^0 for equilibrium (1) from the activities of individual ions, the specific features of the behaviour of which are obliterated in the mean ionic functions.

It is frequently forgotten[7,102] that the vast majority of modern data on equilibria of type (1) have been obtained from the activities of the cations and not from the mean ionic parameters. About 40% of the known values of β_n [3-6] have been calculated from the e.m.f.'s of cells with transport incorporating M^{z+}/M^0 indicator electrodes. The changes in the e.m.f.'s (ΔE, mV) of such cells after the introduction of ligands into the test solutions at 298 K are expressed by the equation

$$\Delta E = E_d + 59.2/z \lg C_u/\{M^{z+}\}, \quad (39)$$

where E_d is the liquid junction potential. The relative activities of the ions M^{z+} enter into Eqn. (39) within the quantity E_d.[54] These ionic activities are standardised by solutions in relation to which the values of ΔE have been measured.

The data in Table 11 show how the activity coefficients y_{H^+} vary in aqueous solutions at constant ionic strengths. These changes have been calculated from conventional diffusion potentials (E'_d), which are related to E_d in Eqn. (38) by the expression

$$E'_d = E_d + 59.2/z \lg y_{M_{z+}}.$$

Judging from Table 11, the variation of the constant ionic strengths from 0.5 to 3.0 does not affect appreciably the changes in y_{H^+} as well as the changes in λ_n (Table 3). The transition from 3.0 M (Na→H)ClO_4 solutions to 3.0 M (Li→H)ClO_4 solutions alters y_{H^+} by 4.5 $[H^+]$ mV mol litre^{-1}, i.e. $\lg y_{H^+}$ changes by 0.065, which agrees with λ_1 for the protonation of the acetate ion in 3.0 M (Na→Li)ClO_4. It has been recommended[115] that the numerical y_{H^+} data in Table 11 be used for the selection of ionic media, the variation of the composition of which causes minimal changes in the activity coefficients of the individual ions. The effect of these changes for y_{H^+} in (Li→H)ClO_4 media is much smaller than in (Na→H)ClO_4. The replacement of Cl^- or ClO_4^- by OH^- affects y_{H^+} less than the replacement of Na^+ by H^+, etc.

The need to use the ionic activities, and not mean ionic parameters, to characterise weak acdio-complex formation has been recently demonstrated by Yagodin, Solovkin, and co-workers.[122,123] Equations were proposed for the calculation of the activity coefficients of individual ions in media at constant ionic strengths and the errors in the extrapolation of β_n to I→0 on the basis of the Debye–Hückel theory were estimated. It must be emphasised that in systems with highly charged cations, for example Zr^{4+}, the detection of a whole series of weak complexes having the composition $Zr(NO_3)_n^{4-n}$ was a consequence only of the neglect of the changes in the ionic activity coefficients following the change in the composition of the salt medium.[123] It may be that the detection of stepwise acido-complex formation in M^{5+} solutions[124] is also associated with the contributions by the inconstancy of the activity coefficients like part of the experimentally determined effect described by the β_1 in similar systems.[125]

Bjerrum compared the available information about β_n and n for weak acido-complexes in 10 M H(ClO_4→Cl) and 1–10 M Cl^- solutions. The constancy of the activity coefficients of the Cl^- ions is taken into account with the aid of second virial coefficients. Spectrophotometric and extraction data, which make it possible to measure the MA_n concentrations, were used by Bjerrum in the study of weak acido-complexes,[18,20,26] but the influence of the salt media on the partition coefficients and the molar extinction coefficients of the complexes MA_n was not taken into account. Studies on weak acido-complexes based on the Bjerrum approach merit further expansion but it would be desirable to base future research on Eqn. (11) or on allowance for the second and third virial coefficients. The Storonkin–Lagunov rule[72] suggests that the applicability of Eqn. (11) extends over a wide range of variable concentrations (from 0.1–1 to 5 M) of the anions in aqueous solutions. The activity of water in the test solutions with $I \neq$ const. can be sometimes more usefully employed in equations of type (11) [126] rather than the concentrations of the ligand anions.

VI. Conclusion

The properties of aqueous solutions involving the formation of weak complexes of metal ions are characterised by formal activity coefficients (the conventional physical model) or the contribution due to the occurrence of complex formation reactions is isolated from the latter[121] (the conventional chemical model). The physical model alone frequently reproduces more accurately the properties of the solutions than does allowance for its chemical component, but one must remember that the initial model is based on several empirical parameters. The results obtained by thermodynamic methods do not provide procedures for the unambiguous separation of the experimental properties into the "physical" and "chemical" components when the stability of the complexes MA_n is low without resorting to extrathermodynamic assumptions. However, when account is taken of the two components of the second virial coefficient,[121] such separation is sometimes possible. The simplest assumption involves the attribution of the entire weak interaction in accordance with the type (1) equation to the physical model if the latter can be reproduced by the second virial coefficient alone.

However, on the basis of the determination of the activities of all the individual ions and molecules involved in the equilibria investigated and also with the aid of standard isotherms,[1] the second virial coefficient of the activity can be sub-divided into contributions due to the changes in the activity coefficients and the formation of complexes with a definite composition. A similar subdivision is possible when account is taken of the shielding of ions by water molecules[120] for complex formation in aqueous solution.

The attempts to isolate the contribution of chemical interactions on the basis of spectroscopic data are frequently unreliable because they are based on the assumption of the constancy of the spectroscopic molar parameters in solutions with very different compositions. A reliable separation of the effect of changes in these parameters from the effect of the formation of complexes is hardly possible, which has been demonstrated in the determination of the association constants of ions in aqueous solutions of strong acids.[103] Only the unitary stepwise association constants in excess of 1–5 can serve as reliable thermodynamic indicators of the formation of weak complexes subject to the condition that these constants have been determined from data obtained by a fundamentally different experimental method in accordance with the classification in

Section III of the present review. The information about the formation of weak complexes based on low values of K_n^0, presented in the new international handbooks as critically selective,[5] is frequently unreliable.

Naturally a property of systems with very weak complexes ($k_n < 0.1$) cannot be considered in isolation from the kinetics and mechanisms of the formation of the complexes[127,128] because the formation reactions of such complexes do not obey the principle of the minimisation energy and the Law of Mass Action is not applicable to them. The fluctuation theory, the thermodynamics of non-equilibrium systems, and molecular-kinetic models should be used more widely in the future for the study of systems of this kind, typical examples of which are aqueous solutions of alkali metal halides, nitrates, sulphates, and a number of other salts. The empirical and extrapolation methods for the determination of the stabilities of weak complexes in such systems[129] cannot be regarded as reliable. Furthermore very large errors in the determination of low formation constants are inevitable (for example, $\lg K_5$ for $AuCl_5^{2-}$ is -2.0 ± 1.0).[130]

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Translated from *Uspekhi Khimii* 60 1155–1189 (1991) U.D.C. 539.233;241.183.022;541.64

Polymer monolayers and Langmuir–Blodgett films. Polymerisation reactions in organised molecular ensembles; structural transformations and properties

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ABSTRACT. The method of preparation, structure, and properties of monolayers on the surface of a liquid and of Langmuir–Blodgett films on surface-active monomers are discussed. The influence of the chemical composition and structure of monomer molecules, the conditions for the preparation of organised ensembles, and the conditions in polymerisation reactions for the structural-morphological transformations in monolayers and Langmuir–Blodgett films are considered.

The bibliography includes 128 references.

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I. Introduction

Polymer monolayers and Langmuir–Blodgett films (LBF) should occupy in the next few years a position in the problem of multilayer two-dimensional structures consistent with their scientific and applied importance. This refers both to the unique possibilities of the assembly and study of two-dimensional polymer systems with controlled orientation and distances between the chains and their elements and to the prospects for the application of Langmuir–Blodgett (LB) ensembles in modern technology. The study of the specific characteristics of the behaviour of organised ensembles of macromolecules at interfaces between two fluids or at a solid/fluid interface makes it possible not only to achieve in practice the advantages of polymeric LBF already recognised (thermal and mechanical stability, resistance to the action of corrosive media) but also to construct new generation superstructures taking into account the chain structure of the polymers.

Polymeric LBF are nowadays obtained by three procedures which provide for (1) the formation of polymer monolayers on the surface of a liquid (usually water) and their transfer to a solid support, (2) the formation of monolayers made up of monomers, their polymerisation, and their transfer to a solid support, and (3) the formation of monomer monolayers, their transfer to a solid support, and their polymerisation in the LBF.

It is important to emphasise that, for compounds having the same chemical composition, LBF differing in structural organisation can be obtained depending on the method of formation. This is associated, for example, with different conditions in the polymerisation reactions carried out on liquid and solid surfaces, with the rotation of the monomer molecules in the preparation of the LBF, etc. For this reason, the current stage (in many respects, the initial stage) of the development of studies in the field of polymer LBF should include in the first place the comparative analysis of the three procedures for their formation indicated above. In the first case, attention should be concentrated on the study of the thermodynamic, structural-morphological, and molecular-kinetic features of the behaviour of polymer monolayers on the surface of a liquid which distinguish them from low-molecular weight analogues. A striking example of the existence of such differences is the possibility of obtaining stable monolayers from water-soluble polymers.

The regulation of the structure and properties of LBF during their preparation by the second method reduces mainly to the selection of known or the construction of new diphilic monomer molecules with a definite disposition of hydrophilic and hydrophobic fragments and their polymerisation, which is achieved preferentially with the aid of UV irradiation. Here so far little attention has been devoted to the use of the possibilities of a liquid support, the variation of the composition of which makes it possible to influence both the structure of the monolayer and the polymerisation process.

The third procedure for the formation of LBF has become most widely known in connection with the wide-scale employment of diacetylene derivatives. Photopolymerisation is carried out in two ways: either each transferred monolayer or the multilayer LBF as a whole is polymerised. The first method leads to the breakdown of the correlation between neighbouring LBF layers, while the second involves the retention of the three-dimensional crystal lattice of the monomer. The main problem arising in this method for the preparation of LBF is associated with the shrinking of the polymer which leads to the formation of defects (cracks, cavities, and folds).

Together with the increase in the thermal and mechanical stability of polymer LBF noted above, it is possible to realise with their aid also other, hitherto unused, possibilities of molecular architecture: the controlled phase separation in a mixed monolayer with immobilisation of the low-molecular-weight compound carrying a definite functional group; the fixation of additives introduced into the support; the formation of stable multilayers of polymers on a liquid surface and their transfer to a solid support, etc.

Polymer LBF are nowadays used in microelectronics as resistors and insulating layers with high specific characteristics. There are good prospects for the application of polar and alternating non-centrosymmetrical LBF in non-linear optics. Conducting polymers (for example, polyalkylthiophenes) are not inferior as regards their parameters to the known LBF consisting of charge-transfer complexes. Photochromic transformations (reversible *cis–trans* isomerisation and aggregation) can be used in the recording and representation of information. Molecular electronics, different types of sensors, multilayer selective membranes, and many other self-evident and merely predicted applications of polymer LBF require a significantly more vigorous investigation of these unique objects.

Langmuir's brilliant studies on the chemistry surfaces, for which he was awarded the Nobel Prize in 1932, served as a basis for the current spurt in the research into the monolayers (ML) and multilayer films obtained by the method also proposed by Langmuir (1920) and developed by his colleague Blodgett (1935). A historical survey of the studies on these unique objects has been given by Tredgold.[1] The present interest of physicists in the LBF was initiated by the elegant studies of Kuhn and his school on molecular architecture.[2] By virtue of Blinov's reviews,[3,4] the Soviet reader was able to become acquainted with the latest advances in the physics of LBF. Problems of the physical chemistry and mechanics of monolayers of low-molecular-weight surfactants and polymers have been described by Trapeznikov[5] and his students. The methodological problems of the formation of monolayers and LBF have been dealt with in reviews[1–4] and in the monographs of Adam,[6] Harkins,[7] Izmailova et al.,[8] and Gaines[9] and also in other communications.[10–12]

It is surprising that, despite the wide-scale research into monomer and polymer monolayers and LBF, reviews devoted to the present state of this problem are still lacking. The only exception is the publication by Tieke,[13] in which the properties of films of butadiynes and butadienes on the surfaces of water and solids are discussed.

In connection with the differences in the behaviour of polymer and monomer monolayers mentioned above and also with the abundance of data on this problem, the present review is devoted solely to the analysis of the polymerisation reactions of monomers on the surface of a liquid and in a LBF and the phase and structural-morphological transformations in these systems caused by these reactions. In addition, owing to the existence of a sufficient number of publications describing the methodological aspects of the problem under discussion, the latter have been excluded from the present review together with studies in the field of organised protein structures, which require independent analysis.

II. The preparation of monolayers on the surface of a liquid and of Langmuir–Blodgett films

The monolayers on the surface of a liquid (water, glycerol, dioxane, mercury, and gallium) consist of films of usually diphilic compounds one molecule thick. The monolayer is formed when a dilute solution of the surfactant in a volatile solvent spreads. In many instances, such films can be produced by the spreading of the bulk phase of the given substance. The phase state of the monolayer is recorded with the aid of compression isotherms: the dependence of the surface pressure (π) on the area per molecule or the monomer residue (A). In the general case, when the area is diminished, the gaseous, liquid, and solid states of the monolayer are produced. Each state of the monolayer is characterised by a definite orientation (thickness) of the molecules, which depends on the available area and the cohesive and adhesive properties of the system.

When the solid support is moved slowly through the surface of the liquid with the monolayer, the latter is deposited on the support. Successive upward and downward movements of the support lead to the formation of a Y-type centrosymmetrical LBF. Polar X- and Z-type LBF are obtained with the aid of special procedures. In X-type layers, the hydrophobic components of the molecule are directed towards the support, while in the Z-type layers they are turned in the opposite direction. Alternating LBF consist of layers of two and more compounds alternating in a specified sequence. They were obtained using several Langmuir baths. The LBF are usually formed from the monolayer in the liquid state. Solid monolayers are transferred by Shaefer's method, bringing into contact the surfaces of the solid support and the monolayer (horizontal transfer). In the course of the deposition of the monolayer, a specified surface pressure is maintained.

III. Polymerisation reactions in monolayers

One of the causes of the wide-scale interest in LBF is the possibility of reproducing the structure of the monolayer when it is transferred from the surface of the liquid to a solid support. The construction of a monolayer with the required structure on the surface of a liquid is a simpler problem than its construction on the surface of a solid. Indeed, slight changes in the chemical composition or structure of the molecules (increase in chain length, introduction of multiple bonds, change from single-chain to multichain lipids, change from an alcohol to an acid or ester, etc.) are instantly reflected in the compression isotherm. The structure of the monolayer is also extremely sensitive to changes in the pH and the temperature of the support, the introduction into the latter of electrolytes or other special additives, and the presence of slight admixtures of surfactants in the monolayer. Since the influence of these factors on the structure and properties of monolayers of low-molecular-weight compounds, such as the monomers, has been studied in fair detail, we are able to devote more attention to the characteristics of the behaviour of these systems associated with polymerisation reactions in monolayers.

1. Polymerisation of diphilic monomers containing multiple bonds in the polar component

Systematic studies on the influence of the chemical composition and structure of monomer molecules on the properties of monolayers and polymerisation reactions have been carried out recently by Ringsdorf and co-workers.[14–18]

The aim of the polymerisation of monomeric lipids (models of biomembranes) in organised systems (monolayers, bilayer lipid membranes, vesicles) is to increase their stability. However, polymerisation frequently leads to such an increase in the rigidity of the system that the formation of liquid phases is ruled out. To prevent this and to make sure that the main chains do not hinder the self-organisation of the side groups, flexible hydrophilic spacers are introduced into the monomer molecules. This leads to the formation of polymers of three types containing a spacer in the side chain (Fig. 1*a*), the main chain (Fig. 1*b*), and in both chains (Fig. 1*c*).[19,20] Such architecture makes it possible to achieve in the polymerised lipid an adequate degree of independence of the movements of the side chains. It is essential to note that a flexible spacer, leading

normally to the expansion of the monolayers, does not always increase their stability and hence the possibility of their transfer to a solid support.

The length of the spacer introduced between the lipid component and the polymer chain (Fig. 1*a*) influences the properties of the monolayer of not only the monomer but also of the polymerised system.

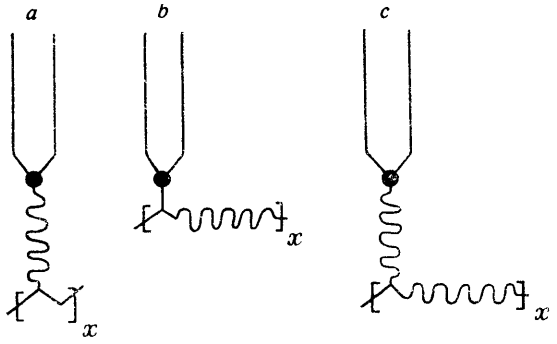
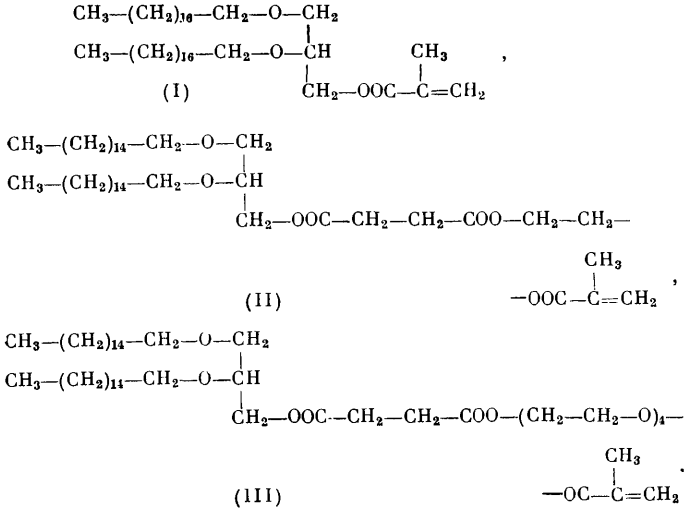


Figure 1. Three types of polymers containing a hydrophilic spacer in the side chain (*a*), the main chain (*b*), and the side and main chains (*c*).[20]

Fig. 2 illustrates the $\pi-A$ relations for the monolayers of two-chain methacrylate lipids (I), (II), and (III) with an increasing length of the spacer.[19,20]



An increase in the length of the hydrophilic spacer leads to the expansion of the monolayers: regions of expanded liquid and transition states appear for compounds (II) and (III). Nevertheless the monolayers of all the monomers retain a solid state with identical limiting areas and high decomposition pressures.

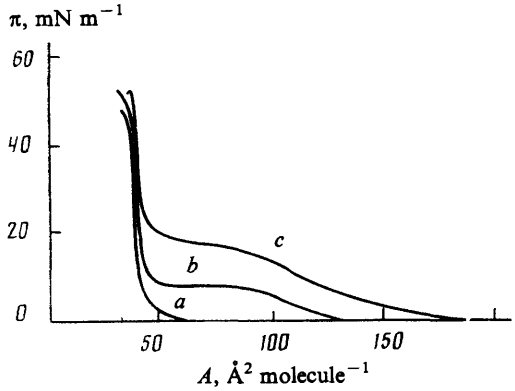


Figure 2. Surface pressure (π)/area (A) isotherms for monomeric lipids: *a*, (I), 20 °C; *b*, (II), 30 °C, *c*, (III), 30 °C.[19,20]

The compression isotherm for compound (I) photopolymerised in the monolayer virtually repeats the $\pi-A$ relation for the monomer,[20] i.e. the highly organised structure of the monolayer is retained during polymerisation (Figs. 3*a* and 3*b*). However, for the polymer obtained by the homopolymerisation of the lipid (I) in solution and then deposited on the surface of water, the $\pi-A$ relation (Fig. 3*c*) has a different form: there is no solid state and the monolayer decomposes at low surface pressures. This indicates a low capacity of the monomer without a spacer for self-organisation. In the presence of even a short spacer [the monomer (II)], the picture changes (Fig. 3*d*). The $\pi-A$ isotherm for the homopolymer obtained in solution from the lipid (II) is characterised by the presence of only the solid state, which indicates a high capacity of the macromolecules for self-organisation in the monolayer.

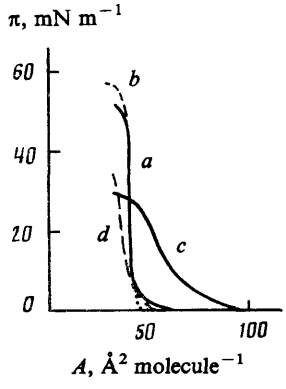
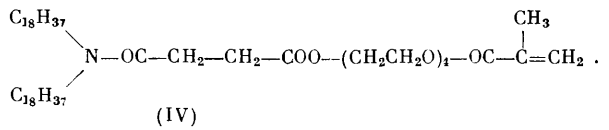


Figure 3. Surface pressure/area isotherms for monomeric (*a*) and polymeric (*b*–*d*) lipids: *a*, (I); *b*, (I), polymerised in the monolayer; *c*, (I), polymerised in solution; *d*, (II), polymerised in solution.[20]

Evidently, on polymerisation of the lipid (II) in the monolayer, the $\pi-A$ relation has a similar form. Finally, in the polymerisation of a monomer containing a fairly long spacer [the lipids (III) and (IV)] the condensation of the monolayer is much less marked (Fig. 4): the

isotherms for the polymers obtained by polymerisation in the monolayer (Fig. 4*b*) and in solution (Fig. 4*c*) have an expanded state region:[19]



(IV)

The incorporation of a flexible spacer in the main chain (Figs. 1*b* and 1*c*) is achieved as a rule by the copolymerisation of the corresponding monomers in solution. For example, the monomer (II) and 2-hydroxyethyl acrylate have been used for this purpose.[20]

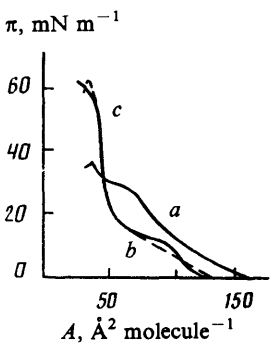
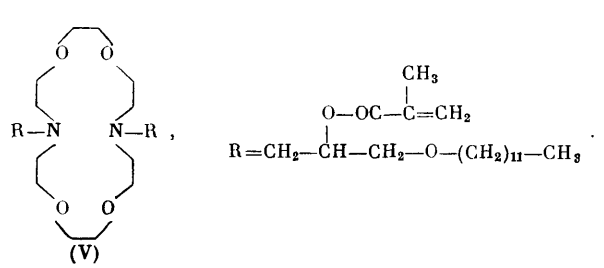


Figure 4. Surface pressure/area isomers for monomeric (*a*) and polymeric (*b*, *c*) lipids: *a*, (IV); *b*, (IV), polymerised in the monolayer; *c*, (IV), polymerised in solution.[19]

Thus the introduction of a flexible spacer with a definite link between the main chain and the lipid group intensifies the tendency of the polymers to undergo self-organisation in the monolayer and provides a possibility of choice: the formation of monolayers from the monomer and its subsequent polymerisation or the formation of the monolayer from the homopolymer.

The first steps have been taken in the study of polymerisation processes in monolayers of crown-ethers, which are important compounds.[21] Fig. 5*a* illustrates the compression isotherm for the monolayer of 1,10-bis(3-dodecyloxy-2-methacryloyloxypropyl)-1,10-diaza-18-crown-6 (V).



(V)

The isotherm, which is typical for the liquid state, is characterised by low decomposition pressures. The photopolymerisation of the crown-ether (V) under a nitrogen atmosphere leads to the shrinkage of the monolayer (Figs. 5*a* and 5*b*) and to a steeper $\pi-A$ relation.

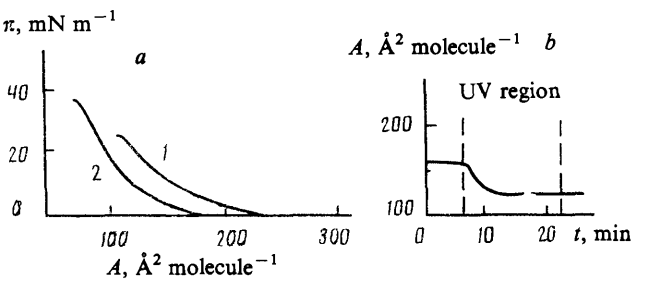
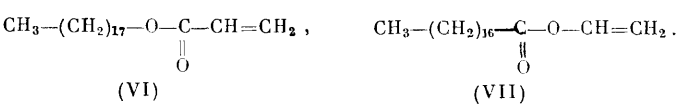


Figure 5. Surface pressure/area (*a*) isotherms for monomeric (curve *1*) and polymeric (curve *2*) crown-ether (V) and the dependence of the area of the monolayer of compound (V) on the duration of UV irradiation (*b*).[21]

The preparation of stable monolayers of LBF from polymerised crown-ethers leads to prospects for a more effective utilisation of these compounds as selective membranes and also as models of biomembranes. The success in the development of the latter aspect of this field is guaranteed by the fact that crown-ethers [for example, the monomer (V)] form bilayer lipid membranes and stable vesicular solutions.[21]

Generally speaking, a decrease in the area of the monolayer on polymerisation is not obligatory. As a result of the polymerisation of classical systems such as octadecyl acrylate (VI) and vinyl stearate (VII), the area of the monolayer increases, the degree of expansion depending on the area over which polymerisation has been carried out.



(VI) (VII)

Fig. 6 presents the $\pi-A$ relations for the octadecyl acrylate monolayer at a water/nitrogen interface before its irradiation with electrons and after exposure to an electron beam (30 s, 70% conversion). Evidently an increase in the area over which polymerisation has been carried out leads to an increase in the limiting area A_0.[22] Two facts are also of interest: the degeneracy of the point of inflection corresponding to the transition from the liquid state of the monolayer to the solid state and the possibility of polymerisation for large areas (42 Å^2 molecule^{-1}, π = 0). The first result reflects the structural changes in the monolayer associated with the fact that the polymerisation of the heat groups prevents close packing of the hydrocarbon chain and the second indicates a domain structure of the monolayer for large areas. Comparison of the data obtained for the water/air and water/nitrogen interfaces permits the conclusion that the polymerisation reaction is initiated by the products formed in the aqueous phase on irradiation of the system:[22] the reaction does not occur (remains unchanged during

irradiation) in the first case owing to the presence of atmospheric oxygen, which suppresses the activity of the hydrated electron, while in the second it does not occur when a compound (*N,N'*-dimethyl-*p*-nitrosoaniline), binding these products, is introduced into the aqueous support. Since the nitrosoaniline reacts with both water radiolysis products—the hydrated electon and the OH radical—it is so far not clear which of these species initiates the polymerisation.[22]

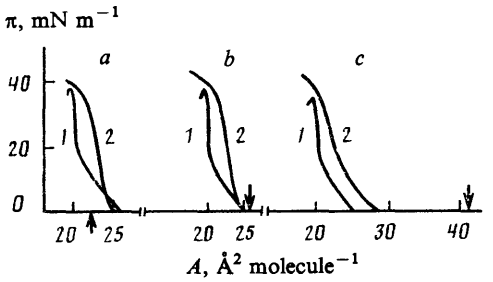


Figure 6. Surface pressure/area isotherms for the octadecyl acrylate (VII) monolayer on the water/nitrogen interface before (curve *1*) and after (curve *2*) 30 s UV irradiation; area for which the polymerisation was carried out (indicated by arrows (Å^2 molecule^{-1}): *a*, 22; *b*, 26; *c*, 42.[22]

The expansion of the monolayer is observed in the photopolymerisation of vinyl stearate.[23] The polymerisation reaction does not take place in air owing to the formation of ozone, which converts vinyl stearate into stearic acid. However, in circulating air, which reduces the time of contact between ozone and the monolayer, it is possible to achieve 50% conversion (in nitrogen, the conversion is 80%). The rate constant for the polymerisation reaction of vinyl stearate in the monolayer (N_2) for large areas (40 Å^2 molecule^{-1}) exceeds by a factor of 3 the rate constant for the polymerisation of the monolayer having an area of 22 Å^2 molecule^{-1}. This is apparently associated with the higher self-organisation of the monomer molecules in the domains[24] on the surface of water compared with the close-packed monolayer subjected to forced compression. However, the polymerisation of vinyl stearate on the surface of water leads in all cases to a more regular structure of the polymer and to a less effective monolayer than for the polymer obtained in solution.

Beredjick and Burlant,[25] who investigated the polymerisation of octadecyl methacrylate (VIII) in the monolayer on the surface of water, arrived at a similar conclusion.

$$CH_3-(CH_2)_{17}-O-\underset{\underset{O}{\|}}{C}-\underset{\underset{CH_3}{|}}{C}=CH_2 \quad .$$

(VIII)

It is of interest that the photopolymerisation occurring at the interface with argon and air can be accompanied both by the shrinkage (argon) and expansion (air) of the monolayer (Fig. 7). Fig. 8 illustrates the compression isotherms for octadecyl methacrylate and its polymers obtained under various conditions. Evidently, in contrast to the isotherm for the compression of the octadecyl acrylate monolayer (Fig. 6), the $\pi-A$ relation for the octadecyl methacrylate monolayer has no break point corresponding to the transition to the solid state. Furthermore, the decrease in the slope of the isotherm beyond A = 25 Å^2 molecule^{-1} indicates the onset of the decomposition of the true monolayer[26] in this range of areas. Such behaviour is associated not only with the steric hindrance to the formation of a close-packed monolayer[25] but also with its low stability. The bulk-phase or two-dimensional polymerisation of the monomer alters sharply the properties of the monolayer. The expansion of the monomer monolayer in the polymerisation reaction in air can be explained by the formation of a polymeric peroxide (copolymerisation with oxygen). The rate of this reaction is three times higher than the rate of polymerisation of the monomer in the monolayer at the water/argon interface.

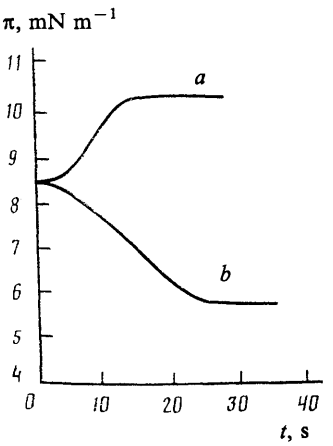


Figure 7. Dependence of the surface pressure on the duration of UV irradiation of the octadecyl methacrylate monolayer on the water/air (*a*) and water/argon (*b*) interfaces.[25]

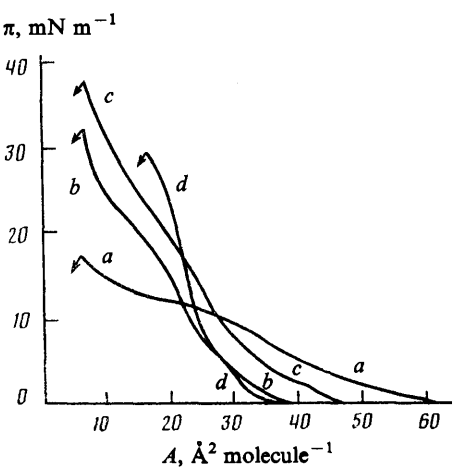


Figure 8. Surface pressure/area isotherms for octadecyl methacrylate (*a*) and poly(octadecyl methacrylate) (*b*–*d*) obtained by polymerising the monomer in the monolayer on the water/argon (*b*) and water/air (*c*) interfaces and in solution (*d*).[25]

Thus inappreciable changes in the structure and composition of the monomers [position of the oxygen bridge in the polar part of the molecules of the monomers (VI) and (VII), transition from the acrylic to the methacrylic monomer] lead to a significant alteration of the structural organisation of the monomer monolayers and induce differences in their response to the polymerisation conditions.

The results of studies on the monolayers of the two isomeric monooctadecyl esters of fumaric (ODF) and maleic (ODM) acids reflect in a clear-cut form the high susceptibility of the monolayers to the molecular structure. The isotherms for the cadmium salts of ODF and ODM, illustrated in Fig. 9, are clearly distinguishable.[27,28] The larger areas of the *cis*-isomer (ODM) compared with the *trans*-compound (ODF) reflect the fact that the head group of the ODM molecule occupies a larger area. The polymerisation induced by UV irradiation on the surface of water increases the area of the monolayer for ODF and decreases it for ODM, but the compression isotherms are identical for both polymers (Fig. 9).

$$CH_3-(CH_2)_{17}-OCOCH=CHCOOH.$$
(IX)

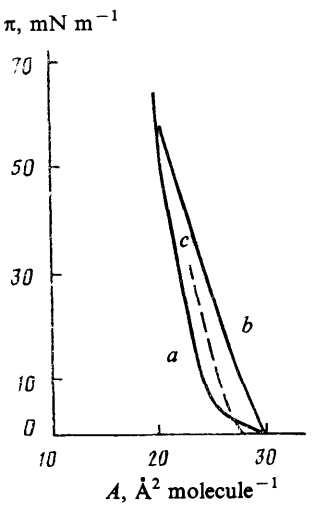


Figure 9. Surface pressure/area isotherms for the cadmium salts of octadecyl fumarate (*a*), octadecyl maleate (*b*), and the polymer (*c*) obtained by polymerising the salts in the monolayer.[27]

By varying the ratio of the components in mixed monolayers, it is possible to achieve a definite change or constancy (for a 25% content of ODF) of the area in polymerisation which gives rise to the hope that LBF free from cracks may be prepared. We may note that, whereas the structures of the films of polymeric ODF and ODM differ both on the surface of water and in the LBF, the polymeric monolayers and the LBF (subjected to UV and thermal polymerisation) have identical organisations and a higher thermal stability. The dimerisation of ODM and ODF with formation of cyclobutane rings was not observed.[27,28] Nevertheless, a cyclisation process, leading to the formation of an extremely unusual polymer structure, takes place in monolayers starting with compounds analogous to compound (IX) but containing a more complex central group: aliphatic monoesters of phenylenediacrylic acid:

$$C_nH_{2n+1}OCOCH=CHC_6H_4CH=CHCOOH,$$
(X)

$n=7$, 10, 12, 14, and 18.

A characteristic feature of the behaviour of these compounds on the surface of water is that an increase in the length of the hydrocarbon group leads not to the condensation but to the expansion of the monolayer.[29] Thus the limiting area of the monolayer of compound (X) with n = 14 is 27 Å^2 molecule^{-1}, which corresponds to A_0 for unsaturated aliphatic acids: A_0 = 24 Å^2 molecule^{-1} for n = 12 and A_0 = 34 Å^2 molecule^{-1} for n = 18. On photopolymerisation in the monolayer (π = 20 mN m^{-1}), the area of the latter (n = 12) increases by 20% and the surface pressure increases from 20 to 50 mN m^{-1} for A = const. Such appreciable changes of the parameters of the monolayer are due to the alteration of its structure during polymerisation, which leads to the breakdown of the parallel orientation of the benzene rings and the formation of chains of cyclobutane rings with mirror symmetry (Fig. 10).

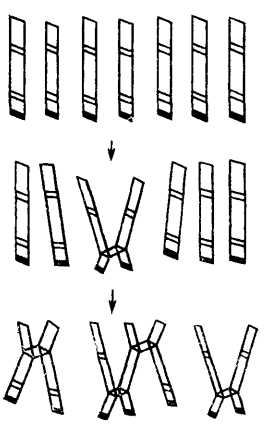


Figure 10. The change in the structure of the monolayer on photopolymerisation of an aliphatic monoester of phenylenediacrylic acid (X).[29]

A similar structure is formed also on polymerisation of these monoesters in the LBF (Z-type, 20 layers), It has been shown by UV spectroscopy[29] that the organisations of the molecules in the LBF and in the bulk-phase crystal differ significantly: in the bulk phase, the molecular packing resembles that in a Y-type LBF. As a result of these differences, the monoesters (X) with n = 14 and 18, which are photostable in the crystalline state, readily polymerise in the monolayer under the influence of UV radiation. The latter fact demonstrates the notable possibilities of monolayers and LBF in molecular engineering.

The degree of shrinkage or expansion of the monolayer as a result of polymerisation, which is a function of many parameters, depends also on the area of the monolayer for which the process takes place. For example, in the photopolymerisation of a two-chain lipid, as in

that of compound (X), containing the styrene group (XI), the shrinkage of the monolayer diminishes with increase in the area over which the polymerisation reaction takes place and disappears altogether when a close-packed monomer monolayer is polymerised.[30]

$$(C_{18}H_{37})_2\overset{+}{N}(CH_3)(CH_2C_6H_4{=}CH_2)Cl^- .$$
(XI)

This factor complicates in many respects the studies of the kinetics of polymerisation reactions in monolayers which are in any case not simple and therefore not popular. Evidently, the most reliable data on the rate of consumption of the monomer can be obtained with the aid of optical spectroscopy. In their absence, the reaction order and rate constant are found from the change in the area of the monolayer[30] or the surface potential,[23] specifying at the same time the type of function describing the variation of the surface concentration of the monomer.

2. Polymerisation of diphilic monomers containing multiple bonds in the hydrophobic component. Diacetylenes

Among the surface-active monomers investigated in monolayers and in LBF, diacetylene derivatives have firmly retained leading positions. This is explained by the interest in the study of two-dimensional solid-phase photopolymerisation and by the prospects for the application of thin layers made up of macromolecules with long chains of conjugated bonds oriented in the plane of the monolayer.

Tieke's review,[13] published in 1985, on the monolayers and LBF of diacetylene surfactants summarises the brief but extremely vigorous periods of their investigation. In recent years, there has been a significant expansion of the geography of these studies, the ideas concerning the behaviour of traditional diacetylene monomers and polymers have been deepened, and new compounds have been synthesised.

The properties of the monomer monolayers examined above are characteristic also of diacetylene surfactants on the surface of water. The interest in compounds of this class and in particular in the diynoic acid (XII), encouraged by the synthesis of homologous series of the latter,[31,32] is due to the possibility of studying the influence of the chain length and of the position of the diacetylene group relative to the carboxy-group on the stability[33] and other properties of the monolayers.

$$CH_3{-}(CH_2)_{m-1}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_n{-}COOH \text{ or } C_mC_n .$$
(XII)

Fig. 11 illustrates the dependence of the decomposition pressure of the monolayers of long-chain diynoic acids on the surface of water as a function of the overall chain length $L = m + n + 5$.[34] The parameter m, with increase of which (or with increase in L) the decomposition pressure π_c increases linearly, plays an important role in increasing the stability of the monolayers. For low values of n, this increase is steeper and the influence of n on the variation of the stability is manifested to a lesser extent than the influence of m. With decrease in n, i.e. as the diyne group approaches the head group, the stability increases appreciably both as a consequence of the decrease in the perturbation of the packing of the hydrocarbon chains of the diyne group[33] and by virtue of the activation of the carboxy-group by the diyne group. The stability of the monolayer increases greatly after the introduction of $CdCl_2$ (10^{-3} M) into the aqueous subphase.[35] The acid $C_{12}C_0$ forms a condensed film only on a support of this kind. The increase in stability can be explained in this instance by the formation of a salt which is controlled by the pH of the support. According to IR spectroscopic data, the transfer of the acid to the cadmium salt is completed at pH 6.5.[36] The concentration of Cd^{2+} ions in the support influences the stability of the monolayer in two ways.[33,37] High $CdCl_2$ concentrations greatly increase the decomposition pressure of the monolayer and diminish A_0 while low ones promote a decrease in stability owing to the formation in the monolayer of small amounts of a polymer, this effect intensifying when other divalent ions are employed (Ba^{2+}, Ca^{2+}, Cu^{2+}, Zn^{2+}, and Mn^{2+}). On the other hand Collins[38] showed that, compared with the stability of the monolayers of $C_{16}C_8$ and $C_{16}C_0$ acids on different supports, the first monomer forms more stable monolayers on the surface of water while the second forms them on the surface of an aqueous $CdCl_2$ solution.

In this instance one must emphasise that inadequate attention has

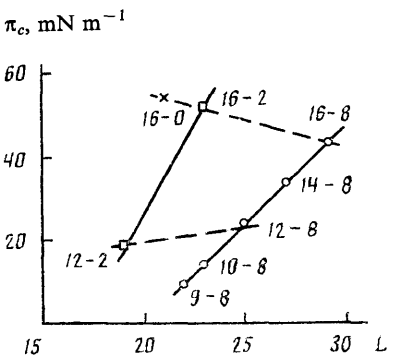


Figure 11. Dependence of the decomposition pressure (π_c) of solid monolayers of diynoic acids C_mC_n on the overall chain length L (T = 12 °C).[34]

In this instance one must emphasise that inadequate attention has been devoted to problems of stability in modern studies on monomer monolayers and the very concept is treated in a narrow sense, although more than 40 years ago Cris[39] proposed reliable criteria for the determination of this important characteristic of the monolayer. We may note the results of studies by Owens et al.,[33] who investigated the influence of the rate of compression of the monolayer of the $C_{12}C_8$ acid on the $\pi-A$ relations. At a rate of compression of the monolayer of 1.3 Å^2 molecule^{-1} min^{-1}, the isotherms hardly differ from relations obtained by other workers and have values of π_c reaching 30 mN m^{-1}. When the rate of compression is reduced by a factor of 4, π_c diminishes to 1 mN m^{-1}. The authors[33] attribute such behaviour to the loss of molecules from the monolayer. The cause of this effect, observed for diynoic acids also in other investigations,[38,40] still remains unexplained. However, if one assumes that the molecules cannot pass from the monolayer to the support, the only cause of such low values of the surface pressure may be a high rate of three-dimensional crystallisation. In order to elucidate the mechanism of the instability of the monolayer, it is essential to carry out more detailed investigations: the determination of the equilibrium pressure of the spreading and hysteresis of the compression isotherm at different temperatures and rates of compression. The high rigidity of the monolayers of diacetylenes gives rise also to other problems associated with the

measurement of the surface pressure of Wilhelmy's method. In this case, and also for rigid monolayers of other monomers and especially polymers, important information can be obtained from data for the viscoelastic behaviour of the monolayer.

Polymerisation of diacetylenic carboxylic acids in monolayers on the surface of water has been studied in greatest detail by Tieke[13] and Day and Ringsdorf.[41] The architecture of the acid molecule influences the course of the photopolymerisation reaction in the following way. Monomers with L from 25 to 29 (m = 12, 14, and 16) polymerise at 20 °C in nitrogen; for L = 23 and m = 10, polymerisation occurs at 2 °C and for m = 5 and 8 the acids in the monolayer do not polymerise at all.[41] If polymerisation occurs, then it proceeds at any surface pressure from 0 to π_c. Consequently the degree of orientation is higher even at π = 0. In the latter case, domains, formed on spreading of the acid as a result of the interaction between the hydrocarbon chains, are present on the surface of water. Clearly, despite the low values of π, fragments of the monolayer are in the solid state because in the liquid state of the monolayer, as in solution, in a melt, and in the liquid crystal state, the polymerisation of diynoic acids is impossible.[42,43] The polymerisation of the acid $C_{12}C_8$ at π = 0 leads to a decrease in area by 10% and at π = 10 mN m^{-1} the decrease is by 15%. The degree of conversion of the monomer can be judged from the degree of shrinkage. However, kinetic studies are difficult owing to the lack of reliable calibration methods. It is believed[38,41] that the degree of conversion of diyne surfactants in the monolayer reaches 100%.

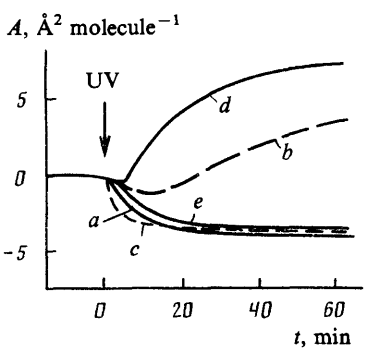


Figure 12. Dependence of the area per molecule of the monolayer of the acid $C_{12}C_8$ on the duration of UV irradiation; polymerisation conditions: π = 10 mN m^{-1}, T = 0–2 °C: *a*, water, pH 6.0, N_2; *b*, water, pH 6.0, air; *c*, 3 × 10^{-4} M M^+, pH 10.5, N_2; *d*, 3 × 10^{-1} M M^{2+}, pH 10.5, N_2; 3 × 10^{-4} M dM^{2+}, pH 5.5, N_2.[41]

other hand, for all the divalent ions (Be^{2+}, Mg^{2+}, Ca^{2+}, Ba^{2+}, and Cd^{2+}) at high pH (10.5) a perturbation of the packing is observed. Under these conditions, there is a possibility of the occurrence of side reactions, for example, the formation of carbenes by reaction with water. The decrease of the pH to below 6 restores the ability of the salts to polymerise with topochemical control.

Following the procedure of Day and Ringsdorf,[41] we shall compare the compression isotherms for polymer monolayers obtained from the acid $C_{14}C_8$ under different conditions. As can be seen from Fig. 13, the polymerisation in the monolayer at π = 10 mN m^{-1} leads to a system which is rigid to the maximum extent. A less rigid monolayer is formed when the polymerisation is carried out at π = 0 and A = 60 Å^2 molecule^{-1}. These differences are understandable since close packing of the monomer domains is observed in the polymerisation of the first system, while in the polymerisation of the second the domains are distributed over a larger area and regions with a free water surface are present between them. On compression of the smaller layer, close packing cannot be achieved. The monolayer of a specimen polymerised in block, dissolved and deposited on the surface of water, is unstable and has a low decomposition pressure (Fig. 12). Evidently, the self-organisation of the monomer molecules on the surface of water is more effective than that of the molecules linked to one another into a long chain.

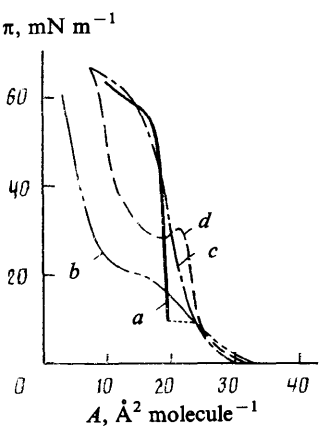


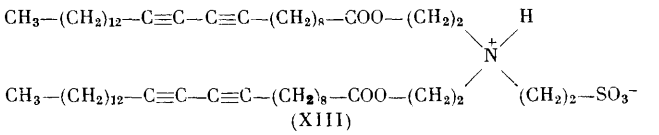
Figure 13. Compression isotherms for the $C_{14}C_8$ polymer at 20 °C: *a*, polymerisation at π = 10 mN m^{-1}; *b*, polymer obtained in block; *c*, polymerisation at π = 0 and A = 60 Å^2 molecule^{-1}; *d*, monomer.[41]

Fig. 12 illustrates the kinetics of the shrinkage of the monolayers for different polymerisation conditions.[41] Polymerisation in the presence of O_2 leads initially to a slight shrinkage, after which appreciable expansion is observed. Evidently, the formation of the polymer is followed by the ozonolysis of the conjugated bonds with formation of hydrophilic groups. This is shown by IR spectroscopic data indicating the appearance of bands at 1255, 1020, and 800 cm^{-1}. As can be seen from Fig. 12, the polymerisation is influenced by the ionic charge and the pH of the subphase. The salts of singly charged ions (Li^+, Na^+, and K^+) polymerise at high pH with shrinkage, by analogy with acids on the surface of water. On the

Consequently, the highly organised rigid two-dimensional structure of polydiacetylenes can be obtained only by the polymerisation of the monomer on the surface of the liquid.

The topochemical control of the polymerisation reaction in the monolayer imposes fairly rigid conditions of the packing of the monomer molecules.[14,44,45] It would appear that, if diynoic acids polymerise in the monolayer and at π = 0, then the photopolymerisation of the monolayer in the solid state should be achieved without obstacles. However, the acid $C_{12}C_8$ does not exhibit photoreactivity at high degrees of compression (A_0 = 23 Å^2 molecule^{-1}, pH 6.8),[44] while the two-chain diyne lipid (XIII)

polymerises only in one of two solid phases, namely in the less condensed phase A at $\pi \leqslant 20$ mN m^{-1} (Fig. 14).[14,43]



(XIII)

The causes of such behaviour are revealed by the schematic disposition of the lipid molecules in phases A and B illustrated in Fig. 14. The vertical displacement of the molecules relative to one another prevents the topochemical polymerisation reaction. By varying the composition of the support and temperature, it is possible to influence the region corresponding to the existence of each phase. The data of Tamura et al.,[44] who established the decrease of the reactivity of the acid $C_{12}C_8$ with decrease in the area of the monolayer, are consistent with these ideas. However, in his study of the behaviour of the two acids with different positions of the diyne group ($C_{16}C_8$ and $C_{16}C_0$), Collins[38] arrived at the opposite conclusion. The acid containing the unsaturated bonds in the centre of the chain was distinguished by a much lower reactivity in the monolayer.

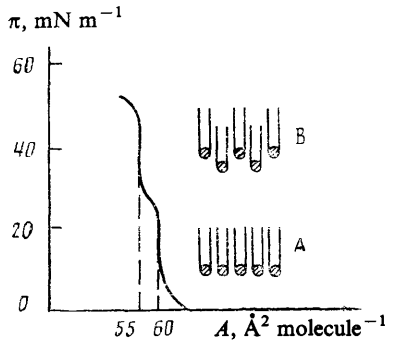


Figure 14. The surface pressure–area relation for the monolayer of the diyne lipid (XIII) at 41 °C at pH 2.[43]

The combination of data obtained by means of the Langmuir balance with UV spectroscopic data,[46] which presents no serious technical difficulties, makes it possible to follow *in situ* the polymerisation in the monolayer on the surface of water. In contrast to monomer monolayers, the polymerised monolayers of diacetylenes strongly adsorb in the visible region. For this reason, the observation of the variation of the optical density with increase in the duration of UV irradiation yields information about the degree of conversion of the monomer. Differences between the reflection spectra of the monolayer of the acid $C_{14}C_8$ on the surface of pure water and on that of an aqueous $CdCl_2$ solution have been recently established.[47] In the former case (254 nm; 0.4 mW cm^{-2}; 15 °C; 20 mN m^{-1}; 26.5 Å^2 molecule^{-1}; N_2) (Fig. 15*a*), the blue form of the acid (610 nm), formed in the initial stages of the polymerisation reaction, is converted into the red form (529 nm) with increase in the duration of UV irradiation. Similar spectra have been published in another communication,[46] where it is noted that the red form can be obtained also after prolonged heating of the blue form at temperatures above that of the phase transition of the monomer. In the polymerisation of the monomer on the surface of the $CdCl_2$ solution (4×10^{-4} M; pH 6.5; 20 mN m^{-1}; 22.3 Å^2 molecule^{-1}) on which it is more close-packed, only the red form can be detected (Fig. 15*b*). This effect can be explained by the differences between the mechanical stresses arising in the polymerisation of monolayers having different limiting areas. Indeed, as can be seen from Fig. 16, an increase in surface pressure is accompanied by an increase in the intensity of the band corresponding to the red form of the partly polymerised monolayer of the acid $C_{14}C_8$ on the surface of water and a decrease in the intensity of the band due to the blue form.[47] These stages are reversible and are reproduced in a large number of cycles (Fig. 17).

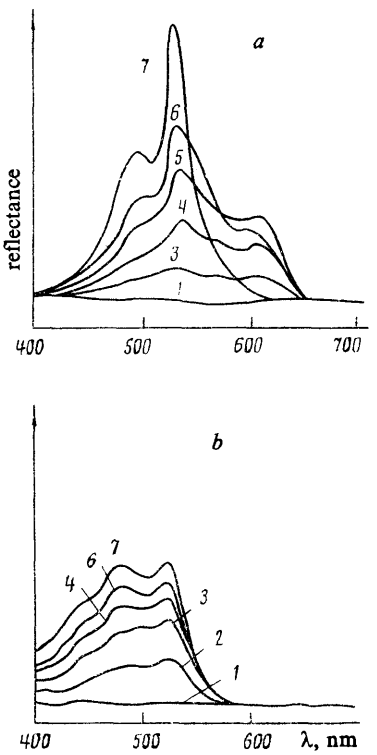


Figure 15. The reflectance spectra of monolayers of the diynoic acid $C_{14}C_8$ on the surface of water (*a*) and of an aqueous $CdCl_2$ solution (*b*); UV irradiation time (min): *1*, 0; *2*, 10; *3*, 20; *4*, 30; *5*, 40; *6*, 50; *7*, 100.[47]

The reversibility of the photochromism is based on the deformation of the monomer monolayer lattice, i.e. is determined by the phase transition induced by the change in surface pressure. It has been noted[44] that the reversible transition between the red and blue forms of the acid $C_{12}C_8$ in the monolayer, observed when the pH of the support is varied between 5 and 6, is not associated with the

isomeric changes in the main polymer chain (transformation of the diacetylene bonds into butatriene bonds) but is related to the structural disordering of the side chain. For the monolayer of the symmetrical diacetylene containing urethane groups [compound (XIV)], reversible photochromism is not observed owing to the strong interactions between the side chains.[47]

$$R{-}C{\equiv}C{-}C{\equiv}C{-}R,$$

(XIV)

$$R = -(CH_2)_4-O-\overset{\overset{O}{\|}}{C}-NH-CH_2-\overset{\overset{O}{\|}}{C}-O-(CH_2)_3-CH_3 .$$

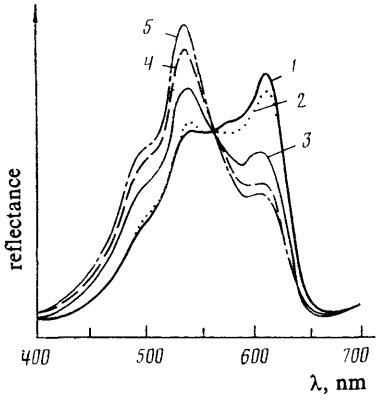


Figure 16. Reflectance spectra of a partly polymerised monolayer of the diynoic acid $C_{14}C_8$ at the nitrogen/water interface for different surface pressures (mN m^{-1}): *1*, 3; *2*, 14; *3*, 20; *4*, 24; *5*, 25.[47]

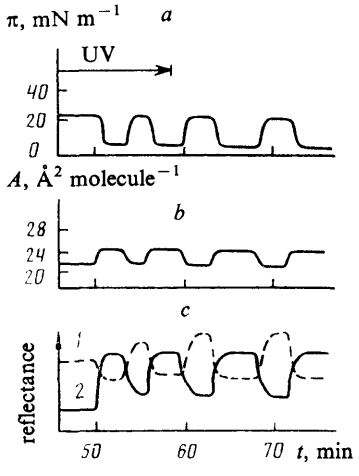
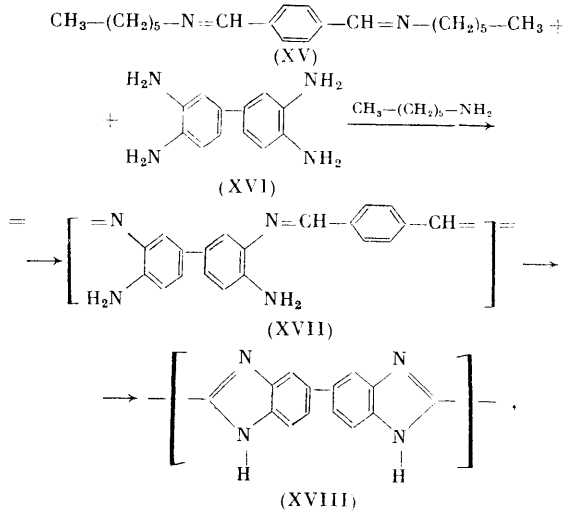


Figure 17. Reversibility of the photochromism of the partly polymerised monolayer of the diynoic acid $C_{14}C_8$ at the nitrogen/water interface in compression–expansion cycles: *a*, surface pressure; *b*, area per molecule of the monolayer; *c*, reflectance at the band maxima with different λ (nm); *1*, 535; *2*, 610.[47]

3. Polycondensation reactions and polymer-analogue transformation.

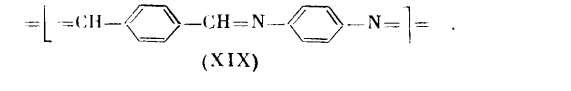
The polycondensation reactions in monolayers have not so far become very common owing to the more rigid requirements as regards the reacting compounds and the conditions of the synthesis: the compatibility of the components in the binary monolayer, the solubility in the support of one of the reactants and its adsorption on the monolayer of the other, desorption of low-molecular-weight reaction products from the monolayer, etc. One can state confidently that much more attention will be devoted to these reactions in the immediate future because with their aid it is possible to obtain two-dimensional ensembles with unique properties.

The synthesis of aromatic polybenzimidazoles in accordance with the scheme[48]

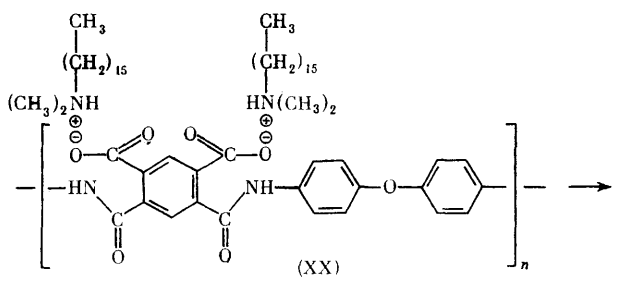


is instructive in this respect. The monolayer of dialkylterephthalaldimine (XV), which, as can be seen from the scheme above, contains no long alkyl chain, is formed on an acidified aqueous support containing the tetramine (XVI). The polyanil (XVII) formed, is converted into the polybenzimidazole (XVIII) as a result of the oxidative cyclodehydrogenation reaction. The latter reaction, controlled by the transport of oxygen and occurring in the monolayer on the surface of water at room temperature, does not occur in a LBF (21 layers) even at 120 °C. This can be readily demonstrated by the absence of changes in the colour of the LBF and is confirmed by optical spectroscopic data. The complete conversion in the LBF is attained at temperatures above 220 °C and such films are stable in air at 420 °C.

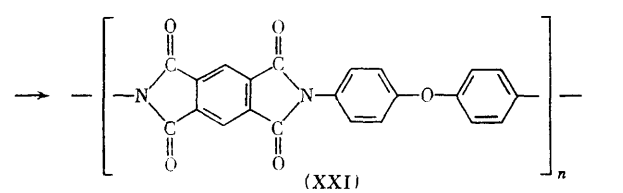
A similar approach has been used in the synthesis of thermostable aromatic Schiff bases from dioctadecylterephthalaldimine, forming the monolayer, and *p*-phenylenediamine introduced into the support.[49] The polycondensation reaction leads to a significant expansion of the monolayer and, with increase in the concentration of the diamine in the support, this effect intensifies and the resulting polymer [polyphenylterephthalaldimine (XIX)] has a higher molecular weight.



It is of interest to note that this synthesis cannot be carried out in solution owing to the rapid crystallisation of terephthalaldimines, while the polymer (XIX), synthesised by an alternative procedure from the corresponding aldehyde and the diamine, does not dissolve in solvents suitable for deposition and does not form a monolayer on the surface of water. Consequently, the polycondensation in the monolayer and subsequent formation of the LBF (Z-type, 25 layers) is the only procedure for the preparation of organised ensembles of the polymeric aromatic azomethine (XIX), whose thermal stability is high. The foregoing refers to ultrathin films of polyimides. Hitherto, the minimum attainable thickness of such films, obtained on a rotating support from solutions of a polyamidoacid with subsequent conversion into the imide form (thermal at 300 °C or chemical in a mixture of acetic anhydride and pyridine) was 0.1 μm.[50] Films with a thickness corresponding to between one and two hundred layers can be obtained with the aid of monolayers and LBF. For this purpose, one obtains initially monolayers of the alkylamine salt of the polyimidoacid (XX) on the surface of water and then, after the transfer to a solid support, the chemical conversion into the imide form is carried out:[50,51]



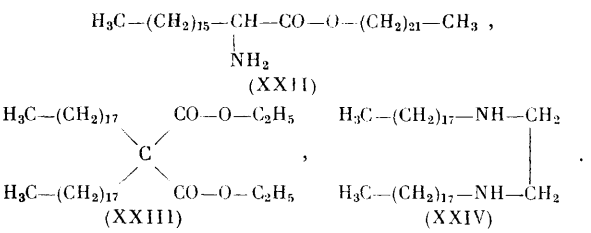
(XX)



(XXI)

The structure and electrical and mechanical properties of the LBF of poly *N,N'*-bis(phenoxyphenyl)pyromellitimide (XXI) have been investigated,[52] while in another study[53] it was demonstrated by scanning tunnel microscopy that the structural organisation of the monolayer on the surface of water is retained also after its transfer to the surface of highly oriented pyrolytic graphite.

Polycondensation in monolayers of long-chain α-aminoacids, diamines, and diesters has been described.[14,54] Naturally, together with the head group and the alkyl chain, the pH of the support exerts a major influence on the structure of the monolayer. The ionisation of the amino-group on an acid subphase leads to a more expanded state of the monolayer with a lower decomposition pressure than on an alkaline subphase. In the polycondensation of docosyl 2-aminooctadecanoate (XXII), the expansion of the monolayer was observed, while the monolayer of the polymer formed on reaction of diethyl 2,2-dioctadecylmalonate (XXIII) with *N,N'*-dioctadecylethylenediamine (XXIV) occupies a smaller area than the initial 1 : 1 mixture of compatible monomers.



(XXII)

(XXIII) (XXIV)

The oriented polypeptide films thus formed served as models of biomembranes.[54]

One of the effective ways of constructing new macromolecules and their organised ensembles with various functions involves carrying out polymer-analogue reactions in monolayers. However, with the exception of the elegant studies by Fariss et al.,[55] there have been virtually no studies on this aspect of the field. This confirms yet again the considerations put forward above concerning the low degree of utilisation of the possibilities of the subphase for reactions in monolayers.

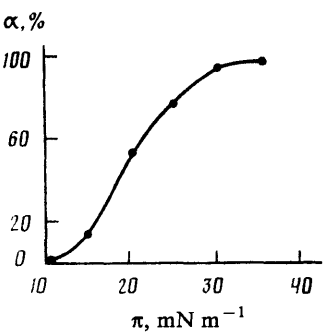


Figure 18. Dependence on surface pressure of the degree of conversion (α) of octadecyl acrylic acid in the monolayer on the surface of water.[55]

The aim of the study mentioned above was to increase the resulting capacity of an electronic resistor based on polyoctadecylacrylic acid by grafting aromatic ester groups to it. Since monomeric esters do not polymerise in the monolayer, a monolayer of octadecylacrylic acid (XXV) was formed initially on the surface of water and photopolymerised. Next benzyl alcohol (XXVI) was introduced into the support and a polymer-analogue reaction (esterification) was carried out. The degree of conversion α of the polymeric acid depends on the degree of polymerisation, the unpolymerised acid being apparently incapable of esterification. The degree of conversion of the monomer (XXV) is in its turn determined by the surface pressure at which it is polymerised in the monolayer, reaching 100% at $\pi = 35$ mN m^{-1} (Fig. 18). The degree of conversion of the acid groups of the polymer depends in a

complex manner on the pH of the subphase and varies from 0 to 70% with decrease in pH (Fig. 19), the degree of conversion of the monolayer greatly exceeding the maximum degree of conversion attained in aqueous solution. The linear resolution achieved by Schaefer's method of the 20 layer LBF of the polyester (electron-beam resistor) reaches 80 nm.

$CH_3-(CH_2)_{17}-C(=CH_2)-COOH$ (XXV); $HO-CH_2-C_6H_5$ (XXVI).

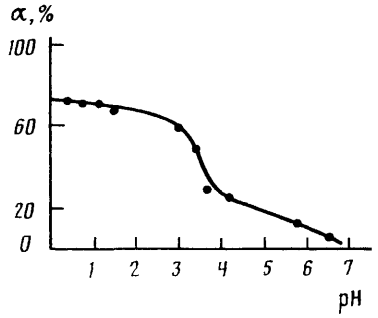


Figure 19. Dependence of the degree of conversion of the acid groups into ester groups of poly(octadecylacrylic acid) in the monolayer on the surface of water on the pH of the support.[55]

The high sensitivity of the organisation of the monolayer to changes in a large number of system parameters facilitates the control of their assembly and can be used for molecular switching. We shall consider the switching mechanism based on a phase transition in monolayers of silane lipids containing different numbers of hydrocarbon chains:[56] [γ-(*N*-octadecylsuccinylamino)-propyl]-triethoxysilane (XXVII), [γ-(*N*, *N*-dioctadecylsuccinylamino)-propyl]-triethoxysilane (XXVIII), and tris(octadecanoyloxy-methoxy)({[γ-(triethoxysilyl)propyl]succinyl}amino)methane (XXIX).

$CH_3(CH_2)_{17}-NHCO-CH_2-CH_2-CONH-(CH_2)_3-Si(OC_2H_5)_3$ (XXVII).

$(CH_3(CH_2)_{17})_2N-CO-CH_2-CH_2-CONH-(CH_2)_3-Si(OC_2H_5)_3$ (XXVIII).

$(CH_3(CH_2)_{16}COO-CH_2)_3C-NHCO-CH_2-CH_2-CONH-(CH_2)_3-Si(OC_2H_5)_3$ (XXIX).

Fig. 20 demonstrates the influence of the number of chains and of the pH of the support on the state of the monolayers of silane lipids. On an acid support (pH 2), all lipids form solid monolayers. At pH 5.8, the monolayers of compounds (XXVII) and (XXVIII) expand, while the monolayer of the three-chain lipid (XXIX) remains in the solid state. According to IR Fourier spectroscopic data,[56] at these pH the monolayers of the monomers do not hydrolyse. The lipids are therefore subjected to polycondensation at pH 2. The polymerisation on the surface of water leads to the formation of a brittle monolayer of the single-chain silane (XXVII) and of an elastic monolayer, suitable for transfer to a solid support, of the two-chain lipid (XXVIII). The three-chain lipid (XXIX) does not polymerise on the surface of water due to steric hindrance. The monolayer method makes it possible to determine directly the molecular weight of the polymer during the reaction. The molecular weights of the silane lipids, calculated by the equation

$$M_w = RT/(\pi A)_{\pi \to 0},$$

for $\pi < 0.2$ mN m^{-1} amounted to $(6-15) \times 10^4$ after 60 min from the start of the polymerisation. On heating the monolayer of the polymerised compound (XXVIII), a phase transition is observed from the solid to the liquid-crystal state, whose temperature (T = 44 °C) agrees with the transition temperature found by differential scanning calorimetry for an aqueous solution of this lipid. At this temperature, the permeability of the monolayer of the polymerised lipid (XXVIII), deposited on the surface of porous glass by the Langmuir–Blodgett method, to NaCl and a fluorescent probe charges by an order of magnitude.[56]

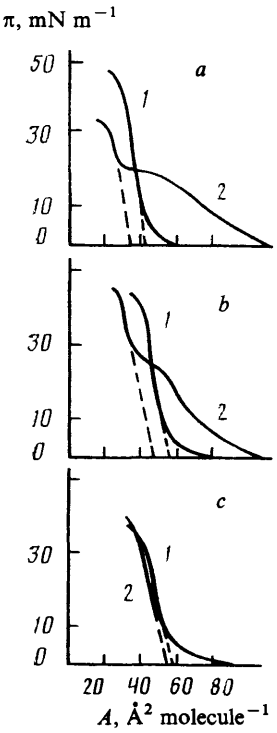


Figure 20. The surface pressure/area isotherms for the monolayers of single-chain (*a*), two-chain (*b*), and three-chain (*c*) silane lipids: *1*, pH 2; *2*, pH 5.8.[56]

Evidently, the possibilities of molecular switching based on a phase transition, predicted to occur in the stage involving the formation of the polymer monolayer, are not restricted by permeability. Another important aspect of the studies of monolayers and LBF of silane compounds is the modelling of decorative layers (of γ-aminopropyltriethoxysilane, etc.) for adhesion polymer systems,[57] the mechanism of the action of which still remains unexplained[58] despite vigorous investigations.

IV. Polymerisation reactions in Langmuir–Blodgett films

1. Diacetylenes

The structure of the LBF of monomers is determined by the transfer conditions, the organisation of the monolayers on the surface of water, and the properties of the solid support.

On the geometrically and energetically uniform surface of water, it is impossible to create an extended monolayer of diacetylenes with identical orientation of the monomer molecules. The attempts to increase the area of the domains in the monolayer, which are of great practical interest, have been at the centre of attention of investigators. The reported formation of regions in the monolayer with a uniform orientation having an area of several square centimetres[59] on spreading a 1:1 mixture of diacetylenic acid and hexadecane from a solution in chloroform was checked.[40] The author also used benzene as the solvent and together with hexadecane applied octadecane (from 1 to 33 mol%) for the formation of the binary monolayer. The largest domains (100 × 500 μm) are formed in a monolayer of the pure acid $C_{12}C_8$, deposited from benzene, and the smallest (from 1 × 1 to 1 × 10 μm) are produced in the system subjected to the test. The morphology of the monolayer on the surface of water is appreciably influenced by the solvent, admixtures and additives, the temperature and composition of the support, and the surface pressure.[40] Impurities in chloroform (ethanol) diminish the size of the domains.[60] The use of hexane, octane, cyclohexane, or aromatic hydrocarbons as the solvent instead of chloroform increases the size of the domains by a factor of 10. The dynamic annealing of the monolayer of the acid $C_{14}C_8$ leads to the transformation of the structure of the monolayer and the formation of domains whose size amounts to several square millimetres.[61]

As in the monolayer on the surface of water, the polymerisation of diacetylenes in the LBF is topochemically controlled. This type of reaction takes place without diffusion and with minimal movements of the molecules forming the crystal lattice.[62] Since the reaction zone is characterised by a definite size and form, which depend on the structure of the lattice, the topochemical control presupposes minimal changes in the form and size of the zone (minimal deformation of the surface zone) during and at the end of the polymerisation reaction.[63,64]

Fig. 21 illustrates schematically the topochemical polymerisation reaction.[64] The transformation from the monomeric to the polymeric single crystal is accompanied by the concerted rotation of the monomer units. This transformation can be regarded as a special case of a phase transition. Bubeck[64] divided topochemical reactions into two subtypes—homogeneous and heterogeneous. In the former case (Fig. 22*a*), the products form a solid solution with a statistical distribution in the lattice of the initial material. This case occurs in the absence of causes increasing the reactivity of the monomer (lattice defects, traps, etc.). With increase in the degree of conversion and with a significant difference between the lattice parameters of the monomer and the polymer, the limit of solubility may be reached. This leads to the formation of a new phase, which may induce perturbations in the structure of the initial lattice and hence arrest further polymerisation.

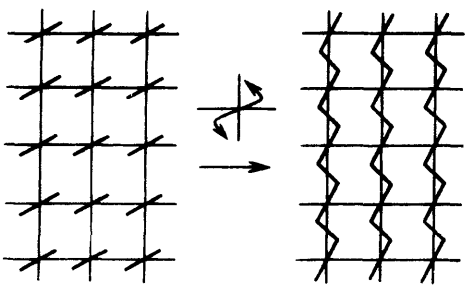


Figure 21. Schematic illustration of topochemical polymerisation.[64]

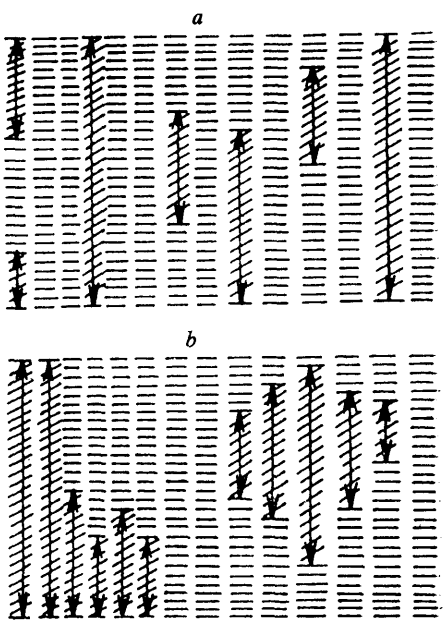


Figure 22. Schematic illustration of homogeneous (*a*) and heterogeneous (*b*) topochemical polymerisation.[64]

The heterogeneous subtype of the reaction (Fig. 22*b*) presupposes the presence of a phase structure in the reaction products within the monomer matrix already in the initial stages of conversion. It occurs when the product formed is capable of increasing the reactivity of the monomer. Evidently, the nucleation of the phase regions can also be induced by the presence of random impurities or special additives in the monomer lattice.

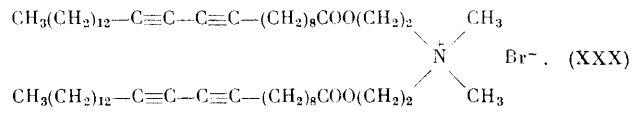
The high transparency of the LBF of diacetylenes and the change in their colour on polymerisation make it possible to monitor visually the course of the polymerisation and quantitative studies of photochemical processes. Significant differences in the photochemistry of the polymerisation of diyne surfactants on the surface of water and in the LBF are not usually observed. Admittedly, differences in the behaviour of these two systems have been inferred[13,65] from the fact that the absorption spectra of the monolayer on the surface of water have an isosbestic point, in contrast to the LBF. This point reflects the presence of a direct transition between the electronic structures of the blue and red forms of the polymers without passage through any intermediate states. Its existence in the spectra of the monolayers might be associated with the greater mobility and capacity for reorganisation of the molecules on the surface of the liquid.[13] However, the latest data for the acids $C_{14}C_8$ (Fig. 15)[47] and $C_{12}C_8$[44] do not confirm the presence of an isosbestic point in the spectra of monolayers on the surface of water. The incomplete clarity of the picture as regards photochromic transitions in monolayers and LBF is also indicated by the wide variety of interpretations of these transitions. Among the causes responsible for the photochromic transformations, the following have been discussed: the influence of the isomerisation of bonds,[66] the conformational transformations,[67] aggregation effects,[68] disordering of the side chains,[44] and the stresses arising in the polymerisation process.[69] Probably the above effects make different contributions to the photochromic transformations of polyacetylenes in monolayers and LBF. Here it is necessary to take into account the fact that in the case of LBF oxygen hardly affects the polymerisation reaction and also data[44] indicating the reversibility of the photochromic transitions in monolayers and their irreversibility in LBF.

Monochromatic light with the wavelength $\lambda = 254$ nm is usually employed for polymerisation of LBF of diacetylenic surfactants. The absorption band of the monomer is located in precisely this region of the spectrum and the polymerisation reaction is therefore initiated by the absorption of a photon by the diyne group, the quantum yield ($\Phi = 10$) showing that the absorption of one photon initiates the formation of the entire polymer chain.[70] If the specimen is subjected to preliminary pulsed irradiation by monochromatic light with a short wavelength, then the subsequent polymerisation proceeds on exposure to light with $\lambda \leqslant 500$ nm. Since the photopolymerisation should not occur under these conditions, it has been assumed[13,64] that the oligomer formed on UV irradiation induces the self-sensitised polymerisation. Sensitised polymerisation in the visible region is observed when the LBF of diacetylenes are doped with dye molecules. This process has been investigated in detail by Bubeck et al.[71] in relation to electron-donating and electron-accepting dyes. The quantum yield of this type of polymerisation is extremely low: the dye molecules must absorb a thousand photons for one monomer molecule to react.

The examples of photochemical reactions examined refer to two subtypes of topochemical polymerisation reactions: homogeneous and heterogeneous.[64] When LBF are irradiated with monochromatic light at $\lambda = 254$ nm, the excitation of the monomers and hence the initiation of the reactions assume a statistical character and lead to the homogeneous growth of polymer chains in the lattice. For longer wavelengths at which the sensitisation or self-sensitisation of polymerisation takes place, the reactions involve primarily monomers present near the dye or oligomer molecules. This leads to the heterogeneous growth of the polymer phase in the monomer matrix and to a less perfect morphology of the film.

Annealing exerts an appreciable influence on the structure, the spectroscopic properties, and the polymerisation of diyne surfactants in LBF.[40,44,72] Heating of the LBF of the $C_{10}C_8$ acid at 40–80 °C and the subsequent photopolymerisation result in the appearance of a new intense band in the absorption spectra at $\lambda = 704$ nm (blue form) and also increase the degree of order in the layers (X-ray diffraction). Annealing at $T > 90$ °C leads to the breakdown of orientation in the LBF and precludes its polymerisation.[72] Under these conditions, the band at 704 nm vanishes, which indicates its relation with the organisational structure of the LBF. On the other hand, breakdown of order has been observed[40] in the LBF of $C_{12}C_8$ together with a decrease in reactivity at an annealing temperature exceeding only 59 °C. If one bears in mind that the melting points of these monomers differ by only 4 K,[13] then the differences in the behaviour of the acids cannot be explained from the standpoint of the given phase transition.

The degree of conversion of the monomer and the rates of the polymerisation reactions, which determine their effectiveness, have remained little investigated and there are no reliable data for the molecular weights of the polymers obtained in LBF. For example, the M_w for diyne surfactants, obtained from viscosity data,[73] proved to be 200 000, while according to the view of Göbel et al.,[45] based on diffraction studies, in the polymerisation of dimethylbis(2-hexacosa-10,12-diynoyloxyethyl)ammonium bromide (XXX) the chain length does not exceed 50 units.



(XXX)

Evidently these parameters are affected by the same factors which determine the photochemistry of the polymerisation reactions described above and the morphology of the LBF considered below. The complete conversion in the LBF is not attained in photopolymerisation with topochemical control and the approach to the maximum degree of conversion is asymptotic.[16] This is associated with the fact that either the packing of only some of the molecules in the layers corresponds to the topochemical control, or that the structural organisation of the layers breaks down in the course of the reaction, or is caused by both factors. The complete conversion is attained on irradiation of diacetylenes with X-rays or γ-rays,[74] whereupon the quantum yield is 10^{12} [sic. (Ed. of Translation)].

The polymerisation of diynes containing a second functional group [for example, compound (XXXI)] is of interest because it can be carried out in two stages by irradiating the LBF with light at different wavelengths characteristic of each type of reactive group.[16] By alternating the irradiation, it is possible to vary the architecture of the change in the LBF at will.

$$CH_3(CH_2)_{13}—C\equiv C—C\equiv C—(CH_2)_8—CH_2—OOC—CH=$$
$$= CH—COOH.$$
(XXXI)

Structural-morphological studies on LBF are carried out by X-ray diffraction (small angle scattering, fine structural analysis in the vicinity of the edge of the X-ray absorption), electron diffraction,

different versions of optical spectroscopy, electron and polarisation-optical microscopy, scanning tunnel microscopy, X-ray photoelectron spectroscopy, surface plasma resonance, etc.

LBF made up of diacetylenes have as a rule a Y-structure with hydrocarbon chains inclined relative to the normal to the support at an angle of 30–50°.[16,65,75] The preparation of polar LBF of diacetylenes (X- and Z-types) requires special procedures.[76] Like the sublayers of aliphatic acids, diacetylenic LBF can crystallise spontaneously with formation of a three-dimensional lattice.[13] This tendency intensifies with decrease in the overall length of the acid chain.[77] The crystal structures of the monomeric and polymeric LBF of diynoic acids and the alcohol $C_{10}C_2$ are identical with the structures of these specimens in bulk-phase crystals.[78]

The polymerisation of diyne surfactants leads to an increase in the repeat period and to a decrease in the angle of inclination of the chains to the normal. The increments in the repeat period depend on the surfactant structure and reach 30% for the acid $C_{16}C_0$.[65] However, comparison of the structures of the LBF and a sputtered film of the acid $C_{10}C_8$ [79] led to the unexpected conclusion that the degree of order in the LBF is smaller and that on polymerisation the angle of inclination to the normal increases for the LBF and diminishes for the sputtered films. These differences may be caused by the instability of the polymerisation LBF on exposure to X-rays: in the determination of the structures of the films by fine structural analysis near the edge of the X-ray absorption (EXAFS), the blue form of the LBF is converted into the red form, whereas the sputtered films remains unaltered in the visible part of the spectrum. Polymerisation takes place in each layer (with the exception of ω-derivatives) and the macromolecular chain is arranged parallel to the support. The cations distributed between the head groups of neighbouring monolayers do not form an intrinsic lattice. As a result of the polymerisation, the initial domain texture of the monomeric LBF is established. In the domains, the macromolecular chains are packed parallel to one another but the orientations of the chains in different domains differ. The shrinkage accompanying the polymerisation of the LBF predicates the appearance and growth of cracks and cavities. The sharp difference between the changes in the volume of the unit cell on polymerisation, found[78] for the acid $C_{10}C_2$ and the alcohol $C_{10}C_2$ (388 and 217 Å^3 respectively) is reflected in the texture of the LBF: in contrast to the polymeric acid, the diyne polymeric alcohol forms significantly less effective polymer structures. The thickness of the LBF, the number of layers, and the changes in the repeat period also influence the degree of defectiveness of the polymeric LBF.[76] The mechanical properties of the LBF are determined on the basis of their ability to cover the pores of solid supports without being ruptured.[16]

In conclusion it must be emphasised that at the present time a fairly detailed analysis of the behaviour of monolayers and LBF of diphilic monomers can be achieved only for diacetylenic surfactants because none of the monomers of other classes have been subjected to such intensive and comprehensive studies in organised systems.

2. Polymerisation of diphilic monomers containing multiple bonds in the ω-position

The bias in the studies on the polymerisation of monomeric surfactants in LBF is in many respects due to their use as resistors. This applies fully to ω-tricosenoic acid (XXXII) and its salts.

$$CH_2=CH-(CH_2)_{20}-COOH\,.$$
(XXXII)

The polymerisation of ω-tricosenoic acid in Y-type LBF (electron beam) takes place via an ionic mechanism, which is indicated by the low activation energies, the insensitivity to the presence of free radicals and oxygen, and the first order of the reaction.[80] The angle of inclination of the aliphatic chains to the normal for the monomeric LBF depends on the surface pressure at which the monolayer is transferred to a solid support (π_{tr}). According to X-ray diffraction data,[81] this angle is 33°, 30°, and 27° for π_{tr} = 20, 25, and 30 mN m^{-1}. During polymerisation, the angle of inclination increases by 4° and the film itself becomes less ordered.[80] There is a close relation between the structure of the LBF of the polymerised acid (XXXII) and the characteristics of its multilayer ensembles used as electronic resistors in microlithography. The high contrast and sensitivity of the negative resistors based on the acid are due to the monodispersity of the polymer and the coherence of the LBF. The first fact can be explained by the appearance of mechanical stresses in the solid-phase polymerisation of the monomer, which limits the growth of the chains, and the second is caused by the high packing density of the hydrocarbon chains.[82,83] It is of interest to compare the properties of multilayers of ω-tricosenoic acid obtained by the Langmuir–Blodgett method and vacuum sputtering. The larger repeat period for the LBF (56.3 Å at π_{tr} = 30 mN m^{-1} compared with 49.6 Å) and the smaller angle of inclination of the chains (27° and 38° respectively) indicate a more organised structure of the acid in the LBF.[81] Peterson and Russell[84] do not rule out the possibility of the epitaxial growth of the multilayers when ω-tricosenoic acid is deposited on a solid support.

The high interlayer adhesion in the LBF of ω-tricosenoic acid shows that polymerisation is possible not only in the plane of the layers but also between them. It is of interest[85] that the solid-phase polymerisation is initiated by the defects of the crystallites in the vicinity of which the orientation of the atoms readily changes. The interface between the layers of the LBF can be regarded as a controlled defect.[86] Therefore in this particular region with a low structural organisation the initiation and growth of the chains are most likely. Furthermore, the interlayer polymerisation in Y-type LBF of ω-compounds can be facilitated by the penetration of the ends of the chains into neighbouring layers. This feature is apparently characteristic of all ω-monomers forming Y-type LBF and, depending on the purpose of the LBF, the high interlayer adhesion can play both a positive and a negative role. In order to eliminate polymerisation between the layers, it is useful to generate polar X- or Z-structures, although this can be by no means always achieved, or to obtain alternating LBF separating the monomer monolayers by inert (for example, aliphatic acid) intervening layers.[80,86] In order to prevent the interlayer polymerisation of the diynoic ω-acid C_0C_{20} in a LBF (Y-type, 135 monolayers), alternating polymeric structures with arachidonic acid have been obtained.[87]

3. Polymerisation of monomers containing multiple bonds in the polar component

The study of the monolayers and LBF of vinyl stearate and octadecyl acrylate has a long history.[88] Nevertheless, these classical subjects still remain within the range of interests of investigators.

In the radiation-induced polymerisation (^{60}Co) of vinyl stearate, there is no interlayer poymerisation problem because, regardless of the method of preparation of the LBF (Y- or X-transfer), only X-type multilayers are formed. The irradiation is carried out at low temperatures ($T \leqslant 0$ °C) at which the degree of conversion is low and then, after the removal of the radiation source, the post-polymerisation is carried out and its kinetics are investigated.[89] The

reaction proceeds via a free-radical mechanism, oxygen inhibiting the process as in polymerisation in a monolayer. At low pressures π_{tr} = 10–12 mN m^{-1}, the degree of conversion is low, which can be explained by the low packing density of the molecules. The increase of π_{tr} to 17–19 mN m^{-1} makes it possible to achieve 100% conversion of the monomer, which depends in its turn on temperature, the irradiation time and dose, and the temperature and duration of the post-polymerisation reaction. As a result of the polymerisation reaction, the orthorhombic structure of the monomer in the LBF is converted into the hexagonal structure of poly(vinyl stearate).[90] Mixed monolayers of vinyl and ethyl stearate are solid solutions for any component ratio.[88,90] These systems can be used to construct fairly thick (1000 layers) polar (X-type) skeletised LBF.

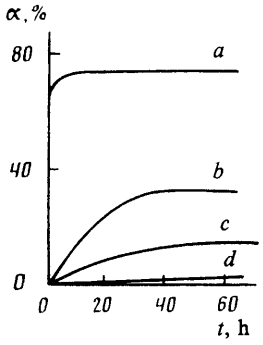


Figure 23. Dependence of the degree of conversion on the duration of the radiation-induced post-polymerisation of octadecyl acrylate in block (*a*, *d*) and in LBF (*b*, *c*): *a*, hexagonal lattice; *d*, triclinic lattice; *b*, X-type LBF; *c*, Y-type LBF; T = 20 °C.[91]

The slight differences between the chemical structures of the vinyl stearate (VII) and octadecyl acrylate (VI) molecules influence significantly the behaviour of these monomers in the LBF. Fig. 23 illustrates the dependence of the degree of conversion on the post-polymerisation time at 20 °C (^{60}Co irradiation at −196 °C) for X- and Y-type octadecyl acrylate LBF and also a block monomer in the hexagonal and triclinic crystal forms. Evidently the rate and limiting conversion depend on the type of LBF, the parameters assuming intermediate values between those for bulk-phase crystals of the two modifications.[91] The less dense packing of the X-type LBF obtained at low π_{tr} promotes higher rates of polymerisation and higher degree of conversion compared with Y-type LBF. The relative disposition of the curves in Fig. 23 of Ref. 91 led to the conclusion that hexagonal and triclinic packing corresponds to the X-type and Y-type LBF respectively. On comparing these results with the data presented above for vinyl stearate, it can be seen that the degree of conversion of the acrylic monomer is appreciably lower for the same X-type LBF and, in contrast to vinyl stearate, a higher rate and a higher degree of conversion correspond to smaller values of π_{tr}, affording LBF with less dense packing. However, the picture changes sharply in the photopolymerisation of octadecyl acrylate and vinyl stearate and the copolymerisation of their mixtures (Fig. 24). The rate of polymerisation and the degree of conversion of vinyl stearate in X-type LBF are much lower than for octadecyl acrylate in the same vinyl stearate LBF subjected to radiation-induced polymerisation.[92] With increase in the content of octadecyl acrylate in the mixture with vinyl stearate, the degree of conversion rises and reaches 95% for the LBF of the acrylic monomer (Fig. 24). The differences in the behaviour of these monomers have been explained[92] by differences between their structures, ensuring, in the case of octadecyl acrylate, the conjugation of the C=C and C=O bonds, which increases the reactivity of the monomer.

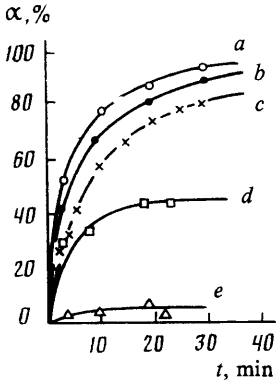


Figure 24. Dependence of the degree of conversion on the duration of the photopolymerisation of octadecyl acrylate (*a*), vinyl stearate (*e*), and their mixtures (*b*–*d*) in X-type LBF: *b*, 8:2; *c*, 1:1; *d*, 2:8; T = 10 °C, N_2.[92]

An exceptionally large increase (30%) in the repeat period has been observed[93] in the photopolymerisation of 2-eicosenoic acid (XXXIII) in a LBF (Y-type, up to 30 layers).

$$CH_3-(CH_2)_{16}-CH=CH-COOH\,.$$
(XXXIII)

The increase in this parameter during polymerisation reaction is accompanied by a phase transition between the monomer and polymer matrices. Since the phase separation in the concluding stage of the polymerisation reaction takes place via the migration of the monomer molecules and the formation of their clusters in the polymer matrix, it has been suggested[93] that the molecules in the layers possess a much higher mobility than has been assumed hitherto. The question of the possible involvement of the molecules of neighbouring layers of the LBF in the phase separation therefore requires elucidation.

An important difference between the photopolymerisation of 2-eicosenoic acid and vinyl monomers, examined above, is the absence of the influence of atmospheric oxygen on the polymerisation reaction, which is explained by the close packing of the hydrocarbon chains, preventing the diffusion of oxygen.[93] Although in our view this conclusion conflicts with the author's claim that the monomer molecules possess a high mobility, the fact itself is of undoubted practical interest.

The radiation-induced polymerisation[94] or photopolymerisation[95,96] of octadecylacrylamide (XXXIV) results in the formation of high-quality Y-type LBF which can be used as negative resistors.

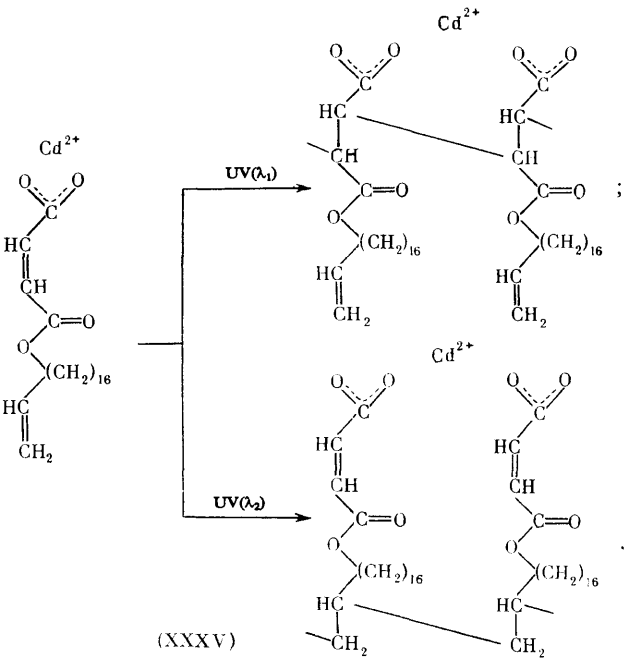
$$CH_3-(CH_2)_{17}-NH-CO-CH=CH_2\,.$$
(XXXIV)

According to X-ray diffraction, electron diffraction, and IR spectroscopic data,[94] phase transitions are not observed in the polymerisation process and the side chains retain their orientation.

A convenient object for the study of the influence of the configuration of the double bond or the organisation of monomers in the LBF and their polymerisation is provided by the isomers octadecyl fumarate (ODF) and octadecyl maleate (ODM) (IX). A thorough analysis was carried out by the low-angle IR transmittance and reflectance spectroscopy of the structures of the LBF (Y-type, 9 and 20 layers) obtained by transferring the ODF and ODM monomers from the surface of water onto a KRS-5 prism and an aluminium support and then polymerised, and of the LBF of polymers transferred from an aqueous support.[27] It was established that the molecular structure of the LBF is independent of the support on which the polymerisation has been carried out. The molecules of the cadmium salt of ODF are oriented along the normal to the surface of the support, whereas the molecules of its analogue have an appreciable angle of inclination, which is associated with the conformational limitations of the *cis*-configuration of the double bond of ODM. On polymerisation, a profound reorganisation of the molecules of the *cis*-isomer in the LBF takes place, as a result of which the aliphatic chains are arranged along the normal to the surface. Both monomers ultimately give rise to polymers whose IR spectra are indistinguishable. Two important features distinguish the LBF of these compounds. Firstly, there is a possibility of thermopolymerisation (up to 145 °C). Although it leads to a less ordered structure (thermally induced disorder accompanying polymerisation) compared with photopolymerisation, it has definite prospects. Secondly, the formation of non-shrinking LBF for a 1 : 3 ratio of ODF and ODM prevents the appearance of cracks and stresses in the multilayer structure. For these systems, it is of interest to determine the molecular weight of the polymer obtained in the LBF. It was noted above that the cessation of chain growth on polymerisation in two-dimensional structures and the formation of monodisperse polymers are associated with the appearance of stresses. If this mechanism is valid, then the molecular weights of the polymers obtained in the LBF from individual compounds and their mixture should differ.

4. Polymerisation of certain other diphilic monomers

The introduction of the double bond in the ω-position in octadecyl fumarate increases the ease of controlling the structure and properties of the LBF. Irradiation of ω-octadecenyl fumarate (XXXV) by UV light at different wavelengths leads to selective polymerisation:[97]



(XXXV)

If we recall that reaction between neighbouring layers is possible in polymerisation of monomers containing terminal double bonds (ω-tricosenoic acid) in Y-type LBF, then one can readily foresee the prospects for such bifunctional surfactants in the preparation of systems with high interlayer and intralayer adhesion. In alternating and polar LBF, compounds of this type are capable of forming polymer networks.

Long-chain derivatives of dienes also polymerise in two stages.[13] When the LBF of docosyl penta-2,4-dienoate (XXXVI), a monobasic dienoic acid ester, is irradiated with UV light (λ = 250 nm), the dimerisation reaction takes place initially in the first stage. It is rapid, the conversion is complete, and it involves only the C(3)=C(4) bonds. The second stage (polymerisation at λ = 210 nm) occurs at low rates and the degree of conversion does not exceed 80%:

$$CH_3-(CH_2)_{21}-O-\overset{\overset{O}{\|}}{C}-CH=CH-CH=CH_2\,,$$
(XXXVI)

$$CH_2=CH-(CH_2)_{21}-O-\overset{\overset{O}{\|}}{C}-CH=CH-CH=CH_2\,.$$
(XXXVII)

It is believed[98] that the differences between the reactivities of the C(3)=C(4) and C(1)=C(2) bonds are due to the different dispositions of these groups relative to the interlayer plane. The end groups have a greater freedom to change their conformation compared with the C(1)=C(2) groups located deeper within the lattice. In the analogous compound ω-tricosenyl penta-2,4-dienoate (XXXVII), containing a third double bond in the ω-position, there is

a possibility of a third polymerisation stage. Despite the fact that the vinyl groups in the ω-position are at the interface between the layers, polymerisation under the influence of the electron beam proceeds with difficulty.[98]

The monoesters of dibasic dienoic acids polymerise in LBF with 100% conversion.[16] Although the rate of the photopolymerisation reaction and the degree of conversion of hydrocarbon [compound (XXXVIII)] and fluorocarbon [compound (XXXIX)] derivatives of muconic acid are identical, their UV absorption spectra differ significantly.

$$CH_3(CH_2)_{16}CH_2-O-\overset{\overset{O}{\|}}{C}-CH=CH-CH=CH-COOH\ ,$$

(XXXVIII)

$$H(CF_2)_{10}-CH_2-O-\overset{\overset{O}{\|}}{C}-CH=CH-CH=CH-COOH\ .$$

(XXXIX)

This shows that the orientation environments of identical chromophoric groups in the LBF of these compounds are not the same. Evidently, the differences are established in the Y-type LBF formation stage: the fluorine-containing surfactants are transferred to a solid support for areas greater by a factor of 1.5 than the hydrocarbon muconates. The stability of the LBF of these compounds was estimated from their ability to cover pores (0.2 μm) in a polypropylene membrane. The monomeric and polymeric LBF (2–6 layers) of compound (XXXVIII) cover the pores without disrupting the coherence of the film. The LBF of compound (XXXIX) in any form are incapable of covering the pores. Such behaviour of the fluorocarbon muconic monoesters can be explained by the small chain length and by the weak interchain interactions.[16] On the other hand, tridecylpentadienoic acid, a hydrocarbon analogue of compound (XXXIX), does not form a LBF at all.[99]

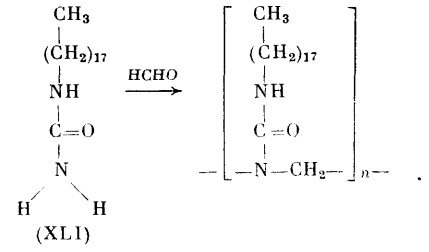
In contrast to diacetylenic derivatives, surfactants of the diene series, containing an unsaturated group at the edge or in the middle of the hydrocarbon chain, have remained uninvestigated. By analogy with diyne and ethylene surfactants, one may claim that the migration of the diene group along the chain in the direction of the polar group can initially reduce the stability of the monolayer and the quality of the LBF and then increase these characteristics of the system. The results of studies on the structure of the LBF made up of mixed monolayers of β-parinaric acid (XL) and stearic acid then lend a definite support to these considerations.[100]

$$trans\text{-}C_2H_5(CH=CH)_4(CH_2)_7COOH\ .$$

(XL)

According to X-ray diffraction data the LBF consisting of the individual acid (XL) are amorphous and do not have a layered structure. With increase in the concentration of stearic acid, the degree of order in the LBF increases but polymerisation again disrupts the organised structure of the LBF.

A novel example of a polymerisation reaction in the LBF, leading to the formation of a network polymer, is provided by the polycondensation of octadecylurea (XLI) with formaldehyde, which diffuses into the LBF from the vapour phase:[86,101]



(XLI)

The methylene bridges connecting the polar head groups, do not prevent the close packing of the molecules in the layers. On raising the temperature, a network polymer is formed as a result of the interaction of formaldehyde with the NH groups.[102] Here we again encounter the situation where the reaction is possible only in the organised ensembles but not in the bulk phase.

V. Prospects for the application of polymeric Langmuir–Blodgett films

The prospects for the application of LBF may well satisfy those who indulge in the wildest fantasies. Fairly complete information has been published[1–4,12,103–107] about the possible applications of LBF, low-molecular-weight surfactants, and partly, polymeric surfactants. The majority of the applications of LBF comprising small molecules hold also for polymer systems. The molecular groups carrying a definite functional group are immobilised in the polymer (a network polymer is best) matrix by forming a mixed monolayer with the matrix or are grafted via a spacer of definite length in the side chain or the main chain of the polymer (polymer-analogue transformations, copolymerisation). An important advantage of such systems is that the "guest" molecules may not in fact possess pronounced surface-active properties and may not form their own stable monolayer on the surface of the liquid.

In any case, the application of LBF in both fundamental and applied research is based on the possibility of assembling uniform two-dimensional structures with a controllable thickness and orientation of the molecules in the layers. The controllable structural organisation of monomers in monolayers and LBF (the inclination of the molecules, the distances between them, the influence of the environment, the positions of the functional groups, isomerisation, etc.) make it possible not only to investigate the theoretical questions concerning polymerisation reactions in these systems but also to synthesise new materials, whose preparation is impossible under other conditions (in the melt, in solution, and in the solid phase).

The phase transitions in individual and mixed monomer monolayers, the thermodynamics and kinetics of polymerisation, copolymerisation, polycondensation, and grafting reactions, carried out under different physical influences (UV irradiation, electron beam, radiation, temperature) or under the influence of initiators and cross-linking agents introduced into the aqueous (monolayer) or gaseous (monolayer and LBF) phases, represent the range of

problems requiring nowadays an appreciably greater attention of investigators.

The molecular weights and molecular weight distributions of polymers, obtained when they are synthesised in monolayers, the mechanism of the termination of chain growth and of the formation of monodisperse polymers in LBF, and sensitised and self-sensitised photopolymerisation effects await a more detailed development.

Langmuir–Blodgett films provide a unique possibility of constructing models of boundary layers comprising combined (with polymers) materials, which constitute the basis of modern materials science.[57,108,109] The regulation of intralayer and interlayer polymerisation make it possible to generate gradient boundary structures with different levels and ratios of adhesive and cohesive strengths and a specified free volume, sorption-diffusion properties, stresses within cracks, etc. Consequently, the mechanism of the of adhesion interactions in polymer/metal and polymer/finishing agent/metal systems and the principles governing the protection of metals against corrosion by organic coatings associated with it may not only be comprehended at a deeper level but can also be used to create a new generation of polymeric protective coatings.[58,105,110] After considering reactions at the support/first LBF layer interface, Barraud et al.[86] identified the adhesion problem as the main one. When acids are deposited on an aluminium support coated by the oxide, salts are formed (for example, aluminium stearate) which ensure an effective adhesion to the support. The intensification of adhesion interactions with supports made of noble metals, germanium, and silicon constitute a more complex problem. Studies designed to devise gradient transition zones in polymer/adhesion junctions are being prosecuted at the Institute of Physical Chemistry of the USSR Academy of Sciences.

An important advantage of the organised layered structure of monomers is that certain polymers can be obtained only by polymerising monomers in the monolayer on the surface of a liquid or in a LBF or the formation of the LBF by them is possible only via the stage involving the synthesis of the polymer in the monolayer. In the former case, one is dealing with monomers polymerising under the conditions of a topochemical reaction, while in the latter the problem concerns polymers from which monolayers cannot be formed on the surface of water in view of their negligible solubility (polyimides, dense network polymers).

A wide range of compounds, polymerising in monolayers and in LBF, have been synthesised and used to devise models for biological membranes by Ringsdorf and co-workers.[14–20] The "architects" from Mainz (Federal Republic of Germany) have successively improved lipid molecules by introducing polarisable groups into the hydrophobic and/or hydrophilic parts of the molecules and by altering the length of the spacer in the side chain and/or the main chain. Ultimately the biomembrane models stabilised by photopolymerisation became very similar to the original.

Together with the use of polymer monolayers and LBF in fundamental research, polymers are used nowadays in modern engineering and in the first place as calibrated insulating and active layers in metal–dielectric–metal and metal–dielectric–semiconductor systems and also as optical and electron beam resistors in high-resolution microlithography.[1,76,81–83,95,96,111]

Much attention has been devoted recently to the study of non-linear optical effects in both centrosymmetrical and polar and alternating polymeric LBF.[1,3,4,103,112] The high non-linear susceptibilities in polydiacetylenes are due to the presence of chains of conjugated bonds. The influence of the length of the chain of conjugated bonds on the cubic magnetic susceptibility has been investigated[113] for LBF comprising mixed monolayers of arylbutadienes and hexatriyne with poly(isobutyl methacrylate). The introduction of hexatriyne into LBF makes it possible to obtain a longer chain of conjugated bonds compared with diyne derivatives and hence a greater intensity of the third harmonic signal.[113] The effects associated with the doubling of the frequency of the light (generation of the second optical harmonic) are being investigated using polar and alternating as well as centrosymmetric LBF in an electric field which eliminates the centre of inversion. Together with thin (several bilayers) films, LBF containing hundreds of bilayers began to be used.[114,115] The combination of non-linear optical properties of the LBF with the possibility of using them as light guides [optic fibres?][112,116] has opened up prospects for the application of these systems in integrated optics, in recording devices, and in information storage and reproduction devices.

The iodine-doped diacetylene LBF have a fairly high electrical conductivity. For example, whereas the specific conductances of LBF comprising diacetylenic acids containing a diyne group in the centre of the chain ($C_{16}C_8$)[117] and in the ω-position (C_0C_{20})[87] do not exceed 10^{-2} and 5×10^{-8} Ω^{-1} cm^{-1} respectively, after doping with iodine the specific conductance increases by 3–4 orders of magnitude. However, LBF comprising polythiophenes, whose electrical conductivity and stability are greater, are of major interest nowadays from this point of view.[118,119]

The possibilities of polymeric LBF as partition membranes have perhaps still not been utilised. The regulation of the thickness, structure, and composition of the LBF deposited on a porous support makes it possible to vary within wide limits the productivity and selectivity of membranes. Membrane gas-separation processes and processes involving the reverse-osmotic separation of solutions have been investigated using LBF comprising diacetylenes[120] and organosilicon[56] and other polymers.[121] An appreciable increase in the number of publications on this field is to be expected soon. They will discuss the properties of LBF partition membranes consisting of interesting compounds such as derivatives of cyclodextrins,[122–125] calixarenes,[126,127] crown-ethers,[21] and macrocyclic polyamides.[128]

* * *

In conclusion, it must be emphasised that the monomer polymerisation processes in monolayers and LBF examined in this part of the review together with the associated changes in the structural organisation and properties of these planar systems represent one aspect of the general problem of Langmuir–Blodgett polymer films. The second aspect involves analysis of the behaviour of monolayers and LBF of polymers synthesised by traditional methods. Although studies on the polymer monolayers, which are only part of this aspect, have long been prosecuted, much less attention is devoted nowadays to problems of the preparation of LBF and the relation between the properties of monolayers and LBF comprising macromolecules than to monolayers and Langmuir–Blodgett films comprising monomers. On the other hand, polymer monolayers have a series of specific features. These include the possibility of obtaining stable monomolecular films from water-soluble polymers and polymers without pronounced diphilic properties, a broad relaxation spectrum, and a high kinetic stability of monolayers. The above features of polymer monolayers will apparently attract in the immediate future the attention of specialists using LBF for the solution of applied problems. The author plans to devote his next review to the analysis of these systems.

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Translated from *Uspekhi Khimii* **60** 1190–1228 (1991) U.D.C. 547+546+541

Oxidation of phosphine and arsine by metal complexes and free and bound oxygen

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ABSTRACT. Data on the oxidation of PH_3 and AsH_3 by metal complexes and oxygen compounds of metals and non-metals and on their catalytic and coupled oxidation by dioxygen, ozone, and peroxide compounds are analysed. The methods for the activation of oxidants, phosphine, and arsine, ensuring the acceleration of the oxidative reactions in processes involving the elimination of the extremely harmful impurities PH_3 and AsH_3 from gases, are examined.

The bibliography includes 176 references.

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I. Introduction

Reactions involving oxidation by metal complexes and free and bound oxygen are used widely to remove the extremely toxic impurities AsH_3 and PH_3 from gases.[1–4] These impurities are present in the effluent gases from phosphorus, carbide, metallurgical, phosphide, hypophosphite, and other industries and are evolved in the processing of phosphorus slags.[1–5] Reactions involving the oxidation of PH_3 and AsH_3 by dioxygen are used to purify oxygen-containing gases while oxidation of phosphine and arsine by bound oxygen is employed for the detoxification of oxygen-free gases.[1–4] However, there are no reviews in the literature of the oxidation reactions of PH_3 and AsH_3. Certain reactions of PH_3 and AsH_3 have been described.[6–12]

The present review discusses the principal features of the kinetics and mechanisms of the majority of the known reactions involving the oxidation of PH_3 and AsH_3 by metal complexes and the oxygen compounds of metals and non-metals as well as their catalytic and chemical oxidation by dioxygen, ozone, and peroxide compounds.

In the analysis of the oxidation reaction PH_3 and AsH_3, it was observed that a common feature of the fast reactions is the many-electron nature of the rate-limiting stage involving an even number of electrons in the case of PH_3 and an odd number of electrons in the case of AsH_3. On the other hand, in processes where an odd number of electrons is transferred in the rate-limiting stage of the oxidation of the PH_3 and an odd number of electrons is transferred in the corresponding stage in the oxidation of AsH_3 are slow. The observed effect made it possible to divide the PH_3 and AsH_3 oxidation reactions into two groups: complementary and non-complementary reactions.[13] The number of electrons involved in the oxidation-reduction reactions depends on the type of stable valence states of the oxidant and their redox potentials.[14] The rate of reaction increases with increase in the number of electrons participating in the rate-limiting stage. Four methods for the acceleration of the PH_3 and AsH_3 oxidation reactions are most common: (1) the use of solvents or carriers which stimulate the formation of polynuclear complexes ensuring the transfer of the necessary number of electrons: (2) the use of catalysts which are capable of being reduced by PH_3 and AsH_3 in the presence of an oxidant with participation of the required number of electrons and which are rapidly regenerated by the oxidant to the initial state; (3) the application of catalysts which permit the separation of the rate-limiting stage into two slow stages: the reduction of the catalyst by PH_3 or AsH_3 with participation of the required number of electrons and the reoxidation of the catalyst by the oxidant; (4) the introduction of additives (activators) which ensure the coupled oxenoid oxidation of PH_3 and the non-oxenoid oxidation of AsH_3. In a number of instances, several methods are used simultaneously to accelerate the reduction of metal complexes and free and bound oxygen by phosphine and arsine.[11,12]

II. The many-electron rate-limiting stage

The oxidation of PH_3 and AsH_3 to the phosphate and arsenate respectively, i.e.

$$PH_3 - 8e + 4O^{2-} \rightarrow PO_4^{3-} + 3H^+, \quad (1)$$

$$AsH_3 - 8e + 4O^{2-} \rightarrow AsO_4^{3-} + 3H^+, \quad (2)$$

proceeds with participation of eight electrons and can occur in principle as a multistage process. We shall consider the thermodynamics of such successive oxidation. The oxidation of PH_3 and AsH_3 reduces the electron density of the P and As atoms and converts them into electron acceptors. As a result, phosphate and arsenate as well as the intermediate and final products of the

oxidation of PH_3 (phosphinite, phosphonite, phosphite, and phosphate) and AsH_3 (arsenite and arsenate) are stabilised in basic media owing to the formation of bonds with the bases. Presumably the rate constants for the oxidation of PH_3 and AsH_3 by bound and free oxygen are higher, other conditions being equal, in alkaline media than in acid media as a consequence of the formation of a donor–acceptor bond with the bases in the transition state. Thus for identical oxidising capacities of the reactants, alkaline media are more favourable for the oxidation of PH_3 and AsH_3. Since at high pH many oxidants are sparingly soluble and have a low redox potential, the oxidation-reduction reactions of PH_3 and AsH_3 were investigated in greater detail at low pH.[11,12]

Fig. 1 illustrates the distribution of energy in the successive oxidation of PH_3 in two-, four-, six-, and eight-electron processes. The redox potentials of the two-, four-, six-, and eight-electron oxidation of PH_3 in acid and alkaline media were calculated from data in handbooks using the law of the conservation of energy.[15] It is possible to use weaker oxidants for the oxidation of PH_3 in an alkaline medium than in the acid medium (see Table 1 at the end of the review). Since in most cases the oxidation reactions of PH_3 were investigated in the presence of an acid, which ensured the homogeneous occurrence of the process, we shall consider the distribution of energy among different stages in an acid medium. Phosphorus gives rise to stable compounds of the following oxidation states: P^{-3}(PH_3, PR_3); P^{-1}(PH, R_3PO, H_3PO); P^{+}[$R_2(RO)PO$, $H_2(HO)PO$, HPO, R_2P_2, R_4P_4]; P^{+3}[$R(RO)_2PO$, P_2O_3, $P(RO)_3$, PCl_3, $H(HO)_2PO$]; P^{+5}[$(RO)_3PO$, $P(RO)_5$, $(HO)_3PO$, P_2O_5, PCl_3O, PCl_5].[16]

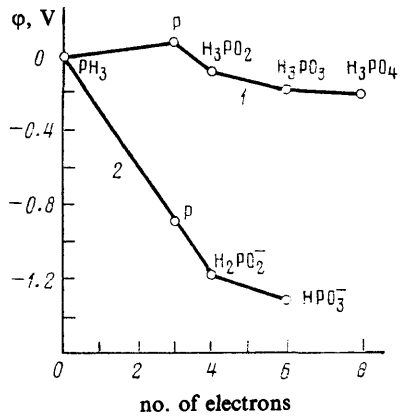


Figure 1. The oxidation-reduction potentials of three-, four-, six-, and eight-electron oxidation of phosphine to phosphorus, hypophosphorus, phosphorus, and phosphoric acids respectively in acid (curve *1*) and alkali (curve *2*) media.

The oxidation state varies in the above series in steps corresponding to an even number of electrons.[17] Other valence states of the P atom, differing from P^{-3} by an odd number of electrons (P^{-2}, P^{0}, P^{+2}, and P^{+4}), are unstable.[17] The stability of the P^{-2}, P^{0}, P^{+2}, and P^{+4} valence states increases somewhat in the presence of the P–P bond [P_2H_4, P_2R_4, P_4R_6, P_4, $P_2H_2(O)_2(OH)$, $P_2(RO)_4$, P_2Cl_4, $P_2(HO)(O)_2$].[18] However, diphosphorus compounds are obtained either from substances already containing P–P bonds or by the reaction of the P^{+3} acid chlorides with P^{-3} compounds (secondary phosphines, alkyl phosphides, alkali metals).[18] In the oxidation of PH_3, the formation of diphosphorus products is hindered by the necessity for the involvement of two PH_3 molecules in the rate-limiting stage.

One-, three-, five-, and seven-electron oxidation of PH_3, leading to the regeneration of unstable intermediates, is thermodynamically less viable than the two-, four-, six-, and eight-electron oxidation leading to the formation of stable intermediate or final products. Bearing in mind the rules stating that the variation of free energies is linear,[14] one can assume that the non-complementary oxidation of PH_3 should be appreciably slower and should require a higher activation energy than the complementary oxidation.[13] Similar rules are characteristic of the complementary and non-complementary transitions also in other oxidation-reduction reactions.[13,14,19,20]

The thermodynamic, activation, and kinetic parameters of the rate-limiting stage of the oxidation of PH_3 depend not only on the complementarity but also on the total number of participating electrons. Fig. 1 shows that, in the successive complementary oxidation of PH_3, the energy is distributed non-uniformly among different stages. If P^{-1} compounds are formed in the interaction as intermediates (two-electron rate-limiting stage), then the first stage can be carried out only using oxidants with a redox potential in excess of 0.06 V. If P^{+1} compounds are generated as intermediates (four-electron rate-limiting stage), then weaker oxidants with redox poentials in excess of −0.08 V are suitable for the initial step. The six- and eight-electron reactions can occur using oxidants having redox potentials in excess of −0.14 and −0.15 V respectively. Similar rules have been established also for the reduction reactions of many-electron reactants.[21–24].

The overall energy effect in the rate-limiting stage increases with increase in the number of active electrons and reaches a maximum when the process involves eight electrons of PH_3. Since a large number of molecules (phosphine, several oxidant and base molecules) usually participate in a many-electron rate-limiting stage, it follows that, with increase in the number of active electrons, the role of the entropy prohibition becomes more pronounced.[13] However, if the solvent or the carrier stimulate the formation of polynuclear complexes containing bases in the coordination sphere, the entropy barrier is lowered.[14] Positive changes in the activation entropy are observed when the polynuclear complex forms fairly stable compounds with PH_3. Metal complexes forming phosphides on interaction with PH_3 are especially effective. The phosphides generate the ions of d^8–d^{10} metals from CuCl, $AgNO_3$, $HgCl_2$, AuCl, $PdCl_2$, and $PtCl_2$.[16] The coordinated phosphide anion has more marked reducing properties than PH_3. The molecules deprotonated by the complex-forming agent are usually oxidised much faster than the initial molecules.[25] Polynuclear complexes can be detected by physical[26] and physicochemical methods.[27]

The formation of polynuclear metal complexes is promoted by solvents with a low dielectrical constant and mono- and poly-dentate ligands having at least two unshared electron pairs with similar energies (F^-, Cl^-, Br^-, I^-, O^{2-}, HO^-, S^{2-}, HS^-, Se^{2-}, Te^{2-}). The content of polynuclear complexes in solution increases in turn with increase in the total concentration of the metal.[26] As a rule, the amount of polynuclear complexes ($C_{Ox_iY_i}$) depends on the total

concentration of the oxidant ($C_{Ox\Sigma}$) and the ligands (C_Y) as described by the formula[26]

$$C_{Ox_jY_i} = \frac{C_{Ox\Sigma}\gamma C_{Ox}^{j-1} C_Y^i}{1 + \gamma C_{Ox}^{j-1} C_Y{}^i}.$$

When $\gamma C_{Ox}^{j-1} C_Y^i > 1$ and $C_{Ox_jY_i} = C_{Ox\Sigma}$, we have $\gamma = C_{Ox_jY_i}/C_{Ox}^j C_Y^i$.

Polynuclear metal complexes are reduced by phosphine in the following way: one of the metal ions of the polymeric complexes is bound to PH_3 and electrons are transferred from phosphine to other ions of the intermediate. This mechanism operates in the reduction of a many-electron oxidant.[21–24]

The stability of polynuclear oxygen-containing compounds depends on the acidity of the medium and usually increases as half the sum of the electronegativities of the central atom and oxygen approaches 2.5.[28] Since phosphine and arsine do not form complexes with high-valence forms of the metal, the oxygen compounds react with PH_3 and AsH_3 via an outer-sphere mechanism. Phosphine adds to an O atom of the polynuclear oxygen compound. The nearest central metal atom effects the transfer of electrons from PH_3 to the remaining ions of the intermediate and transfers non-bridging O atoms to phosphine. The loss of oxygen atoms by this centre is made good by the oxygen atoms from other oxygen compounds of the polynuclear ensemble.

Iodide and bromide ions are most often used as catalysts ensuring the oxidation of PH_3 and AsH_3 by metal complexes and bound oxygen via separate mechanisms. In order to estimate their catalytic properties in the reduction of various oxidants, a correlation equation has been proposed.[29] The oxidation reaction usually begins with the stage involving the formation of a complex of PH_3 with the oxidant. It follows from data on the mechanisms of the oxidative reactions of PH_3 that metal complexes form intermediates with a central atom–phosphorus bond, while oxygen compounds of metals and non-metals give rise to products with an O–P bond:

$$PH_3 + Ox_j \overset{K_1}{\rightleftarrows} Ox_j(PH_3). \quad (3)$$

Next comes the inner-sphere or outer-sphere redox reaction of the intermediate $Ox_j(PH_3)$. Coordinated bases (O^{2-}, OH^-, H_2O, ROH, RO^-, Cl^-, Br^-, I^-, etc.) add to phosphine:

$$(PH_3)Ox_j \overset{K_2}{\rightleftarrows} (PH_3O_m)\,Red_j. \quad (4)$$

The process terminates with the decomposition of the complex formed by the reduced form of the oxidant (Red_j) and the oxidised phosphine (PH_3O_m):

$$(PH_3O_m)\,Red_j \xrightarrow{k_0} PH_3O_m + j\,Red. \quad (5)$$

The equilibrium constant K_2 can be determined from the difference between the redox potentials φ_1 and φ_2:

$$\lg K_2 = \frac{(\varphi_1 - \varphi_2)\,RT}{nF}, \quad (6)$$

where n is the number of electrons which in the given instance are transferred from the reductant to the oxidant and F is the Faraday (96 500 coulomb mol^{-1}). According to this mechanism, the effective rate constant k is given by

$$k = k_0 K_1 K_2. \quad (7)$$

It follows from Eqns. (6) and (7) that

$$\lg k = \lg k_0 + \lg K_1 + \frac{RT}{nF}(\varphi_1 - \varphi_2). \quad (8)$$

The quantities φ_1 and φ_2 characterise the oxidation-reduction potentials of the oxidant and phosphine respectively in the intermediate complex.[30] On complex formation, the oxidation-reduction potentials of the reactants involved change and frequently in the opposite directions.[30] As K_1 varies, the effective rate constant k therefore passes through a maximum. The formation of a complex between Ox_j and PH_3 facilitates, on the one hand, the inner-sphere redox transfer of electrons and, on the other hand, lowers the redox potential of the oxidant φ_1. As a result of the formation of a stable complex with PH_3, the oxidant is converted into a reductant.[30] Metal phosphides [$(HgCl)_3P$, Cu_3P, Ag_3P, Au_3P] exhibit only reductive properties. It follows from Eqn. (8) that the rate constant for the reduction of the oxidant by phosphine increases with increase in the redox potential of the oxidant in the half-reaction involving an even number of electrons (n). Mononuclear and polynuclear complexes of the oxidant can participate in the rate-limiting stage. The transition state in the rate-limiting stage is stabilised if the system contains species capable of forming donor–acceptor and dative bonds with the oxidised P atom and the reduced oxidant. Since an increase and decrease in the positive charge on the P atom enhances the "hard" and "soft" properties respectively,[14] a combination of species of both types in the system is optimal. Since oxygen-containing molecules (H_2O, ROH) stabilise the positively charged states of the P atoms while iodide ions stabilise the reduced forms of the metal complexes, aqueous and alcoholic solutions of alkali metal iodides are most often employed as the solvent in PH_3 oxidation reactions.[11,12]

The concerted transfer of an appreciable number of electrons in the rate-limiting stage takes place stepwise via the formation and subsequent reactions of unstable intermediates which have definite albeit short lifetimes.[31] Such intermediates, formed as a result of one- or two-electron transfer, are present in shallow energy wells.[31] The energy profile of a many-electron rate-limiting stage involves several transition states. The saw-tooth form of the energy barrier in a many-electron rate-limiting stage is due to the fact that the simultaneous transfer of more than one electron is prohibited by the Franck–Condon principle.[13] The Franck–Condon barrier increases sharply in the transfer of two electrons.[13,14] The intermediate complex is rearranged in small energy wells, which makes it possible to overcome the Franck–Condon barrier. Other important limitations to the many-electron transfer in the rate-limiting stage arise from the rule of the conservation of electron spin[32] and of the symmetry of the interacting orbitals.[33,34] The energy wells are shallow if the successive transfer of a large number of electrons in the rate-limiting stage takes place without the infringement of these rules.

The main driving force of a many electron rate-limiting stage is the difference between the energies of the one-electron and many-electron stages [Eqn. (8)]. The greater this difference, the greater the probability of the many-electron transition. Exothermic reactions are preferred because a definite energy is required to rearrange the intermediates. Low activation energies are characteristic of all the steps in a many-electron rate-limiting stage owing to the high degree of utilisation of the energy of formation of new bonds in the dissociation of old ones.[35]

Eqn. (8) can be used to predict reactions with participation of other many electron-donors, since the known correlations (see, for example, Tobe[13] and Basolo and Pearson[14]) are used only for estimations relating to one-electron reactions. In conformity with Eqn. (8), a three-electron transfer in the rate-limiting stage is preferred in the oxidation of AsH_3. It can be seen from Fig. 2 that the redox potential $\varphi_{AsH_3 \rightarrow As} = -0.65$ V, while the redox potentials of the six- and eight-electron transfers reach -0.18 and 0.05 V respectively. Oxidants ensuring the energetically favourable three-electron oxidation of AsH_3 in the rate-limiting stage are therefore rapidly reduced by arsine.[6]

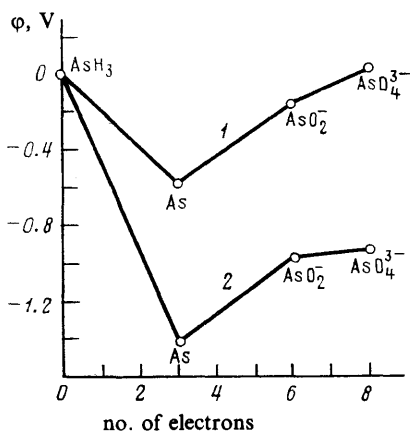


Figure 2. The oxidation-reduction potentials of three-, six-, and eight-electron oxidation of arsine to arsenic, arsenious, and arsenic acids in acid (curve *1*) and alkaline (curve *2*) media.

Oxidants capable of effecting the six- and eight-electron transfer (HIO_3 or H_5IO_6) convert AsH_3 directly into $HAsO_2$ or H_3AsO_4 without the preliminary liberation of As. The point is that the successive oxidation of AsH_3 to As and then of As to $HAsO_2$ or H_3AsO_4 is energetically less favourable than the direct transformation $AsH_3 \rightarrow HAsO_2$ (or H_3AsO_4). The $AsH_3 \rightarrow HAsO_2$ and $AsH_3 \rightarrow H_3AsO_4$ redox potentials are only -0.18 and 0.05 V respectively, while the $As \rightarrow HAsO_2$ and $As \rightarrow H_3AsO_4$ redox potentials are respectively 0.25 and 0.58 V. The rates of reduction of six- and eight-electron oxidants by AsH_3 and PH_3 are therefore similar. In reactions with oxidants promoting the transfer of an odd number of electrons, the reactivity of AsH_3 is appreciably higher than that of PH_3.

Other features are observed in the oxidation of ammonia. Nitrogen forms stable compounds when it exists in the following oxidation states: $N^{-3}(NH_3)$, $N^{-1}(NH_2OH, NH_2Cl)$, $N^0(N_2)$, $N^{+1}(NHCl_2)$, $N^{+3}(HNO_2)$, and $N^{+5}(HNO_3)$.[36] In contrast to the increase in the positive charge on As and P, its increase on nitrogen is accompanied by an increase in the redox potential (Fig. 3). It follows from Fig. 3 that, in the oxidation of NH_3 in an alkaline medium, two-, four-, six-, and eight-electron transfers take place preferentially in the rate-limiting stage. Similar transfers in an acid medium are distinguished by high redox potentials. The most favourable six-electron transfer is hindered by the necessity for the involvement of two NH_3 molecules in the slow stage. It follows from a comparison of Figs. 1–3 that concerted four-, six-, and eight-electron oxidation is preferred for PH_3, three- and six-electron oxidation is preferred for AsH_3 and two- and four-electron oxidation is preferred for NH_3. The above properties of PH_3, AsH_3, and NH_3 influence significantly the kinetics of the oxidation reactions of the hydrides. The different behaviour of the hydrides is due to the sharp decrease in the energies of the bonds formed by the heteroatoms with hydrogen in the sequence (energy in kJ mol^{-1}) N–H (380) > P–H (323) > As–H (281) > Sb–H (256) and in the heats of formation of the hydrides in the sequence (heats expressed in kJ mol^{-1}) NH_3 (−46.2) > PH_3 (9.6) > AsH_3 (67.0) > SbH_3 (144.6).[36] The probability of the concerted three-electron oxidation with abstraction of all the hydrogen atoms therefore increases in the same sequence and the tendency towards the synchronous two-electron oxidation, accompanied by the loss of only two hydrogen atoms, diminishes.

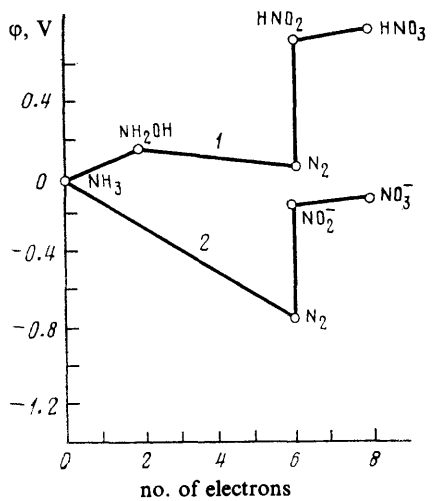


Figure 3. The oxidation-reduction potentials of two-, six-, and eight-electron oxidation of NH_3 to hydroxylamine, nitrogen, and nitrous and nitric acids respectively in acid (curve *1*) and alkaline (curve *2*) media.

The many electron single-state oxidation of PH_3 is facilitated by the fact that the intermediate phosphorus compounds (+1, −1, +3) are characterised by a much greater capacity for complex formation than phosphine. The intensification of the ligand properties of the phosphorus atom as it is oxidised lowers the entropy barrier in the multistep rate-limiting stage. On the other hand, the ligand properties of the nitrogen atom are rapidly weakened as ammonia is oxidised. This increases the energy barrier in the multistep rate-limiting stage and limits the number of electrons transferred simultaneously.

Thus oxidation mechanisms with many-electron rate-limiting stages are energetically favourable for PH_3 and AsH_3. The entropic obstacles are not so great if the intermediate complex is formed

before the rate-limiting stage. The barriers associated with the rules of the conservation of electron spin and the Franck–Condon principle are removed by virtue of the multistep nature of the slow stage where one or two electrons are transferred in each step.

III. PH_3 and AsH_3 oxidation reactions and orbital symmetry rules

In the analysis and prediction of the chemical properties of PH_3 and AsH_3, account is taken of the predominantly *s* character of the unshared electron pair,[37,38] of the relatively low ionisation potentials (10.5 and 9.8 eV respectively), of the high electron affinities (0.77 and 1.07 eV respectively), of the high polarisabilities and the large dimensions of the 3*s* and 3*p* orbitals,[39] of the presence of valence *d* levels,[10] and of the tendency of the diffuse σ*-bonds to effect the σ,*n*- and σ,π-coupling of these molecules.[40] In order to account for the mechanisms of the reactions of PH_3 and AsH_3, the orbital symmetry rules, which have found wide applications in organic and inorganic chemistry and catalysis,[32–43] will be used in the present review.

According to Hammond's postulate,[32] in exothermic reactions the energy and the structure of the transition state are close to those of the initial reactant while in endothermic reactions they are close to those of the product. In order to determine the nature of the activation, it is therefore necessary to have information about the nodal structures, energies, and populations of the frontier orbitals (HOMO and LUMO) of the reactants and products.[33,34] Data on the structures of PH_3, AsH_3 and their oxidation products, obtained by quantum-chemical,[34,41–52] photoelectron spectroscopic,[41,44] and X-ray spectroscopic[53–62] methods, are important. According to calculations,[34,42,43] the molecular orbitals of NH_3, PH_3, AsH_3 and SbH_3 have the following configurations:

$$\text{for } NH_3\text{: } (a_1)^2(e)^4(2a_1)^2(3a_1)^0(2e)^0,$$

$$\text{for } SbH_3,\ PH_3 \text{ and } AsH_3\text{: } (a_1)^2(e)^4(2a_1)^2(2e)^0(3a_1)^0.$$

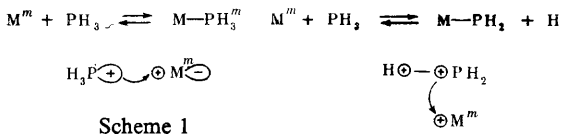
In contrast to NH_3, the 2*e* orbitals of the PH_3, SbH_3, and AsH_3 molecules occupy a lower energy level than the $3a_1$ orbitals, since the 2*e* molecular orbitals of stibine, phosphine, and arsine belong mainly to the 3*d* type.[34–41] The usual parallel decrease in the ionisation potentials of the molecule and atom are not observed in the series of hydrides NH_3, PH_3, AsH_3, and SbH_3:[41] the ionisation potentials of atoms diminish on passing from N to Sb and the ionisation potentials of the hydrides vary in the opposite sequence: $NH_3 < PH_3 < AsH_3 < SbH_3$.[34,41] This reversal of the sequence on passing from atoms to molecules of the hydride is induced by the increase in the contribution of the *s* orbital of the heteroatom to the occupied *n* orbital of the hydride with increase in the size of the heteroatom (E) and with decrease in the H–E–H bond angle.[34,41]

It follows from the data presented that, in contrast to NH_3, the PH_3 and AsH_3 molecules tend to form donor–acceptor and dative bonds with complex-forming agents. In contrast to the ammonia molecule, the HOMO and LUMO in phosphine and arsine form respectively P–H and As–H σ- and σ*-bonds. The frontier orbitals are predominantly of σ character and to a much lesser extent the n character, which is reflected, in our view, in the chemical properties of the hydrides PH_3 and AsH_3. Thus, the two-sided exchange reactions of PH_3 of the type [σ + σ], [σ + π], and [σ + ππ] are therefore symmetry-prohibited. Owing to the difference between the energies of the $2a_1$ and *e* orbitals, reactions of the type [σσ + σ], [σσ + π], and [σσ + ππ] are difficult for PH_3. The one-sided homolytic processes proceed at elevated temperatures or in the presence of radicals.[7] One-sided heterolytic reactions of the type [*n* + *n*] require the participation of (soft) electrophiles or nucleophiles.[8] Reactions involving the nucleophilic addition and the electrophilic substitution of H atoms are therefore typical for phosphines with a P–H bond.[8]

By virtue of the presence of valence *d* orbitals, phosphine exhibits a tendency to undergo both one-sided and two-sided exchange reactions with the reactants containing occupied *d* and π orbitals. Donor–acceptor electron transfer occurs on formation of complexes between phosphine and "hard" protic and aprotic acids (H_2SO_4, $TiCl_4$, $AlCl_3$, BCl_3).[6] Synchronous donor–acceptor and dative electron transfers are observed in the interaction of PH_3 with "soft" transition metal complexes having high redox potentials and low charges (Ag^I, Au^I, Cu^I, Hg^{II}, Pd^{II}, Pt^{II}) [16] and polar unsaturated molecules.[8]

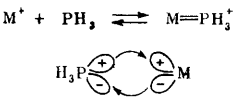
The donor–acceptor one-sided interaction of PH_3 with a metal cation (M^+) leads to the appearance of an unstabilised phosphonium ion, in contrast to the ammonium ion. The dative one-sided electron transfer from the cation M^+ to PH_3 is thermodynamically unfavourable, since it leads to the formation of unstable negatively charged phosphine. The two-sided exchange interaction, in which two close *d* and *s* orbitals of the cation interact in concert with the frontier orbitals of PH_3, is more favourable. The reverse transfer is not accompanied by an appreciable localisation of electrons on one of the fragments. Complexes with close *d* and *s* levels, populated overall by two electrons, are most suitable for such interaction.[33] This is indicated by the particular tendency of PH_3 to form complexes with ions of d^{10} metals (Ag^I, Cu^I, Hg^{II}, Au^I).[63]

The orbital diagrams of single bond formation (Scheme 1), electrophilic substitution (Scheme 2), and double bond formation (Scheme 3) reactions with participation of phosphine and a d^{10} metal ion are presented below:



Scheme 1

Scheme 2



Scheme 3

Scheme 1 illustrates the unshared orbital of PH_3 and an unoccupied orbital of the *p* metal cation, while Scheme 2 illustrates the nodal structures of the P–H σ-bond and the unoccupied orbital of the cation. It follows from the comparison of the orbitals that nucleophilic addition and electrophilic substitution reactions are symmetry-allowed for PH_3.[33] The mode of reaction depends on the redox potential of the complex. The higher the redox potential, the more likely the formation of metal phosphide complexes. Thus $AgNO_3$, $CuHSO_3$, $HgCl_2$, and $PdCl_2$ form phosphides on interaction with PH_3, while AgCl, AuCl, CuI, BCl_3, $TiCl_4$, $AlCl_3$, and SiF_4 give rise to phosphine complexes.[6,16]

Scheme 3 illustrates the orbital diagram for the appearance of the $H_3P{=}M^+$ double bond. The PH_3 orbitals are presented as five equivalent sp^3d orbitals. Three of these are used for bonds with H atoms, while in the other two the remaining electrons are accommodated in two ways depending on whether they are paired or not. In the singlet state the electrons are paired and occupy one of the accessible orbitals. This form participates in complex formation reactions with d^{10} metal ions, whose frontier orbital are constructed similarly (Scheme 3).[32,33] In the triplet state, the electrons are located in different orbitals. This form is preferable for reactions with radicals.[32,33]

It is seen from Scheme 1 that, on interaction with complexes of *s* and *p* elements, phosphine is hardly activated, since the hybridisation of the phosphorus atom is not altered. On the other hand, on coordination to complexes of *d* metals, phosphine is activated because the hybridisation of the phosphorus atom becomes significantly different (Scheme 3). A similar change in the hybridisation of the phosphorus atom occurs also on formation of complexes of *d* metal phosphides.

In order to assess the nature of the activation of the reactants needed for the occurrence of the reaction, one must have information about the electronic structure of the products.[14,32] The point is that the activation energy falls as the electronic configurations of the initial and final substances are approached.[14,32] The PH_3 oxidation products (oxygen compounds of phosphorus) have been thoroughly investigated by quantum-chemical[41] and UV and X-ray spectroscopic[41,61] methods. The main conclusion is that, with increase in the number of P–O bonds, the *d* character of the phosphorus atom becomes more pronounced.[61] In order to accelerate the PH_3 oxidation reactions, it is therefore necessary to intensify, by means of activation, the *d* character of the phosphorus atom. This is achieved by coordinating PH_3 to d^{10} metal ions which have close *d* and *s* levels (Cu^I, Au^I, Ag^I, Hg^{II}).

IV. Oxidation by the halogens

In contrast to NH_3 and AsH_3, gaseous PH_3 does not react with the halogens.[64] The interaction of NH_3 with the halogens leads to the formation of haloamines.[37] Arsine reacts vigorously with chlorine; it ignites even at the temperature of liquid nitrogen.[6] The reaction with bromine and iodine is rapid at room temperature with formation of arsenic halides.[6] Ammonia, which possesses a distinct unshared electron pair, as already mentioned, reacts with the halogens (X_2) via an S_N2 mechanism. Arsine, which has a weak unshared electron pair and is characterised by weak As–H bond energy, interacts with the halogens via homolytic mechanisms. The rate of the reaction of NH_3 with X_2 increases with increase in the redox potential of the halogens and the N–X bond energy (i.e. on passing from Br_2 to Cl_2).[37] The reactivity of arsine in this reaction is determined mainly by the As–X bond energy. In the liquid phase, all three hydrides are readily oxidised by the halogens.[65]

These reactions are widely used for the liquid-phase purification of gases.[2–4] Phosphine,[65,66] phosphine derivatives,[10] phosphites, and phosphorus halides[67] readily react with the halogens,[16,17] hypohalites,[68] and alkyl halides:[10,68]

$$PH_3 + 4Cl_2 + 4H_2O \rightarrow (HO)_3PO + 8HCl, \quad (9)$$

$$PH_3 + 4Br_2 + 4H_2O \rightarrow (HO)_3PO + 8HBr, \quad (10)$$

$$PH_3 + 2I_2 + 2H_2O \rightarrow (HO)H_2PO + 4HI, \quad (11)$$

$$PH_3 + 4HXO \rightarrow (HO)_3PO + 4HX, \quad (12)$$

$$R_3P + Cl_2 \rightarrow R_3PCl_2, \quad (13)$$

$$(RO)_3P + Cl_2 \rightarrow (RO)_2ClPO + RCl, \quad (14)$$

$$Cl_3P + Cl_2 \rightarrow PCl_5, \quad (15)$$

$$(PhO)_3P + Cl_2 \rightarrow (PhO)_3PCl_2. \quad (16)$$

Phosphorus(III) derivatives, which possess, in contrast to PH_3, a distinct unshared electron pair, react vigorously with the halogens,[68] forming nucleophilic addition or substitution products[68]—phosphonium salts and phosphoranes. The nucleophilic attack by the tertiary phosphine is directed to the atom with the highest LUMO coefficient (effective positive charge). Despite the fact that the P–O bond is much stronger than the P–Cl bond, tertiary phosphines attack the halogen atom in alkyl hypohalites in which the LUMO is localised. The halophosphonium salts, formed on interaction of PR_3 with hypochlorites, i.e.

$$R_3P + Cl{-}OR \rightarrow [R_3PCl]OR \rightarrow [R_3POR]Cl,$$

rearrange to the stable alkoxyphosphonium salts.[68] When the reaction is carried out in methanol, optically active phosphines are converted into phosphine oxides with the inverted configuration:

$$[R_3PCl]OR + MeOH \rightarrow R_3PO + MeCl + ROH.$$

Compounds with the RCO–Br, CCl_3–Cl, and Br–$CHArSO_2Ph$ bonds behave similarly. However, compounds with the Cl–CH_2R and Cl–COR bonds attack tertiary phosphines via the carbon atom.[68]

NH_3 behaves similarly to a tertiary phosphine. The oxidation of NH_3 to N_2H_4 and N_2 by sodium hypochlorite takes place in stages with the intermediate formation of chloramine:[36]

$$NH_3 + NaClO \rightarrow NH_2Cl + NaOH,$$

$$NH_2Cl + NH_3 + NaOH \rightarrow N_2H_4 + NaCl + H_2O,$$

$$N_2H_4 + 2NH_2Cl \rightarrow N_2 + 2NH_4Cl.$$

The interaction of coordinated ammonia with Cl_2 leads to the formation of the products of the electrophilic substitution of hydrogen atoms by chlorine atoms. The oxidation of platinum(II) ammines with chlorine results in the formation of dichloramineplatinum(IV).[37]

Since, in contrast to PR_3 and NH_3, PH_3 has weak nucleophilic properties, the driving force of the attack is to a large extent the energy of the bond formed.

The kinetics and mechanism of the oxidation of PH_3 by the halogens [reactions (9)–(12)] in solutions have been investigated.[65,66] The rates of reactions (9)–(12) increase with increasing concentrations of X_2 and PH_3 and of temperature and fall with increase in the content of X^- and in the pH. When the pH and C_{X^-} are varied, the ratios of the different forms of X^+ (X_2, X_3^-, XOH, XO^-) also vary:

$$X_2 + H_2O \rightleftarrows XOH + HX, \quad (17)$$

$$XOH + OH^- \rightleftarrows XO^- + H_2O, \quad (18)$$

$$X_2 + X^- \rightleftarrows X_3^-, \quad (19)$$

The above species are characterised by different reactivities in relation to PH_3.[12] The reactivity of the halogen compounds diminishes sharply in the sequence $X_2 > XOH > X_3^- > XO^-$ (see Table 1 at the end of the review).[11] Since the rate constants for the hydrolysis of X_2 [reaction (17)] and XOH [reaction (18)] decrease appreciably on passing from Cl_2 ($pK \simeq 4$) to Br_2 ($pK \simeq 9$) and I_2 ($pK \simeq 12$) and from ClOH ($pK \simeq 8$) to BrOH ($pK \simeq 9$) and IOH ($pK \simeq 13$),[36] iodine reacts with PH_3 in both acid and weakly alkaline solutions while chlorine reacts only in neutral and acid solutions.[12] In neutral and weakly alkaline solutions, the mixed systems $ClOH-Br_2-H_2O$, $ClOH-I_2-H_2O$, and $BrOH-I_2-H_2O$ exhibit a high reactivity.[12] In such systems, the halogen characterised by low hydrolysis rate constants plays the function of the catalyst, while the halogen which exhibits a higher tendency towards hydrolysis is the oxidant. Thus the interaction in the $PH_3-ClOH-I_2-H_2O$ system takes place via a separate mechanism in the following manner: phosphine is oxidised via Eqn. (11), while the I^- ion is reoxidised back to I_2 by hypochlorous acid:

$$2HI + ClOH \rightarrow I_2 + HCl + H_2O. \quad (20)$$

The catalytic effect is due to the fact that in neutral and weakly alkaline media, reactions (11) and (20) are faster than reaction (12).[11] The equilibrium constants of reaction (19) increase significantly in the sequence Cl_3^- ($pK \simeq 1$) < Br_3^- ($pK \simeq -1$) < I_3^- ($pK \simeq -4$).[36] Therefore the addition of I^- ions has a negative effect on reaction (11).

The facts listed above show that reactions (9)–(12) proceed via the formation and hydrolysis of phosphorus halides in accordance with the mechanism

$$PH_3 \xrightarrow[-H^+]{X^+} PH_2X \xrightarrow[-HX]{H_2O} PH_2(OH) \xrightarrow[-H^+]{X^+} PH(OH)X \xrightarrow[-HX]{H_2O}$$

$$\rightarrow PH(OH)_2 \rightarrow (HO)H_2PO \xrightarrow[-H^+]{X^+} (HO)XHPO \xrightarrow[-HX]{H_2O}$$

$$\rightarrow (HO)_2HPO \xrightarrow[-H^+]{X^+} (HO)_2XPO \xrightarrow[-HX]{H_2O} (HO)_3PO. \quad (21)$$

Since the P–X bond energy diminishes rapidly in the sequence F > Cl > Br > I, it follows that PI_5 does not exist, in contrast to PF_5, PCl_5, and PBr_5.[10] Therefore the oxidation of PH_3 by iodine in water terminates in a stage involving the formation of $(HO)_2HP$, which isomerises to $(HO)H_2PO$.[11]

The hydrogen atoms of PH_3 are substituted by X^+ in the rate-limiting stage in accordance with the S_N2 mechanism (see Scheme 2). The intermediate halo-derivatives of phosphorus(III) and phosphorus(V) hydrolyse immediately after their formation, so that it is impossible to detect them.[11] The high rate of hydrolysis is due to the fact that the energies of the P–O (86 kcal mol^{-1}) and P=O (146 kcal mol^{-1}) bonds are higher than the energy of the P–X bond (44–79 kcal mol^{-1}).[10]

The parallel variation of the reactivities of the halogens (Cl_2 > Br_2 > I_2 > HClO > HBrO > HIO) and the ionisation potentials [Cl (12.97 V) > Br (11.81 V) > I (10.45 V)] and of the oxidation-reduction potentials [Cl_2 (1.36 V) > Br_2 (1.07 V) > I_2 (0.54 V), ClOH (0.94 V) > BrOH (0.76 V) > IOH (0.49 V)] and the electron affinities [Cl (3.8 eV) > Br (3.54 eV) > I (3.29 eV)] is observed.[36] The active species X^+ is formed as a result of the reactions

$$H_2O + X_2 \rightleftarrows H_2OX^+ + X^-, \quad (22)$$

$$XOH \rightleftarrows X^+ + OH^-. \quad (23)$$

The X^+ formation constant increases in the sequences Cl_2 ($pK \simeq 30$) < Br_2 ($pK \simeq 20$) < I_2 ($pK \simeq 10$) and HClO ($pK \simeq 58$) < HBrO ($pK \simeq 53$) < HIO ($pK \simeq 39$).[69] Since the electrophilicity and the equilibrium concentration of X^+ vary in parallel as a function of its nature, its reactivity depends only slightly on the nature of X_2 and HXO.[12]

The tendency towards the formation of X^+ increases sharply in the sequence $F^+ \ll Cl^+ < Br^+ < I^+$,[69] since the metallic properties of the halogens intensify in the same sequence.[36] There is little evidence for the existence of Cl^+ or Br^+, but the I^+, I_3^+, and I_5^+ ions as well as I_2Cl^+, I_2Br^+, and ICl^+ have been thoroughly investigated.[36] The I^+ ion is highly electrophilic. It exists in media with weakly nucleophilic properties, for example in acid solutions.[36] The Cl_2, Br_2, and I_2 molecules, which have the $(\sigma)^2(\sigma^*)^2(\pi)^4(\sigma)(\pi^*)^4$ structure,[36] tend to exhibit the delocalisation of the antibonding π^* electrons. Thus the delocalisation of the π^* electrons over the unoccupied *d* orbitals tends to strengthen the X–X bond. Since, as already mentioned, PH_3 tends to form dative bonds with complex-forming agent (Cu^+, Ag^+, Au^+, Hg^{2+}, Pt^{2+}, Pd^{2+}), the unusual reactivity of the halogens in the PH_3 oxidation reaction becomes understandable. This reactivity is caused by the two-sided exchange interaction of the halogens with phosphine, which facilitates the formation of an intermediate complex. The fairly inert PH_3 molecule is activated in this complex as a result of the change in hybridisation $sp^3 \rightarrow sp^3d$. The latter structure is better prepared for oxidation than the initial sp^3 structure.

Another feature of the halogens is their tendency to polymerise in the presence of X^-.[36] The energetically favourable single-stage many-electron oxidation of phosphine is associated with this important property. Since the fraction of polyhalides increases with increase in the concentration of the halogens, the latter exhibit reactivity at elevated concentrations (10^{-3}–10^{-1} M).[11]

Different features are observed in the oxidation of AsH_3 by the halogens in an aqueous medium:[70]

$$AsH_3 + 3X_2 + 2H_2O \rightarrow HAsO_2 + 6HX. \quad (24)$$

The rate constants for the reactions of AsH_3 with the halogens (see Table 1) are higher than those for the analogous reactions of PH_3.[70] In constrast to PH_3, arsine is oxidised at low concentrations of the halogens (10^{-4}–10^{-5} M for I_2). The oxidation of AsH_3 in the mixed systems $ClOH-KI-H_2O$ and $ClOH-NaBr-H_2O$ takes place readily at KI concentrations higher by an order of magnitude than in the oxidation of PH_3.[70] The point is that, in contrast to

PH_3, AsH_3 is oxidised by the halogens homolytically. Such behaviour of AsH_3 is caused by its tendency to dissociate into the elements.[6]

Thus phosphine reacts with the halogens via a heterolytic mechanism, while arsine reacts via a homolytic mechanism.

V. Oxidation by oxygen compounds of the halogens

Phosphine and arsine are very readily oxidised by the oxygen compounds of bromine(V),[71-74] iodine(V),[75-78] and iodine(VII):[79-81]

$$PH_3 + HIO_3 \rightarrow (HO)_2HPO + HI, \quad (25)$$

$$PH_3 + H_5IO_6 \rightarrow (HO)_3PO + HI + 2H_2O. \quad (26)$$

PH_3 undergoes substitutional oxidative hydroxylation in reactions (25) and (26). Iodine(V) and iodine(VII) react similarly with AsH_3:

$$AsH_3 + HIO_3 \rightarrow HAsO_2 + HI + H_2O, \quad (27)$$

$$AsH_3 + H_5IO_6 \rightarrow H_3AsO_4 + HI + 2H_2O. \quad (28)$$

Since the IO_3^- and $H_4IO_6^-$ ions do not react with PH_3 and AsH_3, the rates of reactions (25)–(28) increase sharply after the addition of a very small amount of acid.[75-81] At pH 3–4, phosphine and arsine are rapidly oxidised by HIO_3 and H_5IO_6.[75-81]

Bromine(V) and especially chlorine(V) and chlorine(VII) compounds exhibit a very low reactivity in reactions of type (25)–(28).[71-74]

The appreciable reactivity of HIO_3 and H_5IO_6 in dilute acid solutions is caused by the relatively high proton affinity:

$$IO_3^- + H^+ \rightleftharpoons HIO_3, \quad K = 10 ,$$
$$H_2IO_6^{3-} + H^+ \rightleftharpoons H_3IO_6^{2-} \quad K = 10^{15} ,$$
$$H_3IO_6^{2-} + H^+ \rightleftharpoons H_4IO_6^-, \quad K = 2 \cdot 10^{10} ,$$
$$H_4IO_6^- + H^+ \rightleftharpoons H_5IO_6, \quad K = 3 \cdot 10^3 .$$

In contrast to $HClO_3$, $HBrO_3$, and $HClO_4$, the molecules of HIO_3 and H_5IO_6 exhibit "soft" properties, which are necessary for the formation of adducts with diphilic PH_3. Reactions (25)–(28) are characterised by the presence of an induction period, which diminishes after the introduction of KI or $HClO_4$.[75,78] Even at low KI or $HClO_4$ concentrations (10^{-4} M), the induction period disappears.[80] In terms of their effectiveness, the KI and $HClO_4$ additives are similar.[75-81] The optimum acid concentration is equal to the initial concentration of $H_4IO_6^-$ or IO_3^-.[78,80] Potentiometric study has shown that the redox potential of the reacting system gradually increases during the induction period.[78,80] The point is that the redox potentials of the IO_3^- and $H_4IO_6^-$ ions are respectively 0.26 and 0.70 V, while those of the HIO_3 and H_5IO_6 molecules are 1.20 and 1.64 V. The system begins to absorb PH_3 actively only after the attainment of the redox potential characteristic of HIO_3 or H_5IO_6. Hence one may conclude that H_3PO_3 accumulates and the HIO_3 and H_5IO_6 molecules, responsible for the reaction, are formed during the induction period.

The geometry of the oxy-anions XO_4^- and XO_3^- is determined by the sp^3 hybridisation of all the valence electrons of the halogen atom.[36] The O–X–O angles are in all cases close to the tetrahedral value. However, the *d* orbitals also definitely participate in the formation of X–O π-bonds.[36] Judging from the redox potential, compound (IX) with a potential of 1.1 V is formed under the influence of iodide ions. Compounds in which iodine is present in intermediate valence states are not produced in reactions (25)–(28).

The substitutional hydroxylation of PH_3 by iodine(V) and iodine(VII) compounds can be represented as follows:

$$PH_3 \xrightarrow[-H^+]{IO_3OH} [(IO_2)\,PH_2OH]^- \xrightarrow[-H^+]{H^+} [(IO)PH(OH)_2]^- \xrightarrow{H^+} \longrightarrow OP(OH)_2H + HI, \quad (29)$$

$$PH_3 \xrightarrow[-H^+]{IO_3OH} [(IO_3)PH_2OH]^- \xrightarrow[-H^+]{H^+} [(IO_2)PH(OH)_2]^- \xrightarrow[-H^+]{H^+} \longrightarrow [(IO)P(OH)_3]^- \xrightarrow{H^+} (HO)_3PO + HI. \quad (30)$$

The six- and eight-electron reactions (29) and (30) apparently take place in one stage via three or four two-electron steps with shallow energy wells in the course of the reaction. The driving force of the many-electron rate-limiting stage is the increase in the exothermic heat evolution with increase in the number of electrons participating in the reaction (Fig. 1). The entropy barrier of the many-electron type is lowered as a consequence of the tendency of the phosphorus atom to form intermediates containing iodine in all possible intermediate valence states. The analogous bromine and chlorine compounds do not have this property and are incapable of effecting the many-electron process in one stage because of entropic factors. Therefore, as X varies in the sequence HIO_3 (1.08 V) < $HBrO_3$ (1.44 V) < $HClO_3$ (1.47 V) [36] (see Table 1 at the end of the review), the reactivity and the redox potential vary in opposition.

Arsine is oxidised by oxygen compounds of iodine(V) similarly to phosphine and the rates of oxidation are also similar. The formation of arsenious acid as the product indicates the many-electron nature of the rate-limiting stage in which six electrons participate. The direct oxidation $AsH_3 \rightarrow HAsO_2$ is energetically more favourable than the multistage oxidation via the formation of As and its subsequent oxidation to $HAsO_2$. The redox potential of the reaction $AsH_3 \rightarrow HAsO_2$ is −0.18 V and that of the reaction $As \rightarrow HAsO_2$ is 0.25 V. AsH_3 and PH_3 therefore have similar reactivities in relation to iodine(V) (see Table 1).

The oxygen compounds of the halogens are activated by metal ions in a high oxidation state as a result of the increase in the redox potential and the polarity of the oxidant. Thus the reactions involving the oxidation of PH_3 by halates and perhalates are accelerated by molybdenum(VI) [71,76] and tungsten(VI) [77,81] complexes. Metal ions in the highest oxidation states are coordinated to the oxygen compounds of the halogens via the O atom. Halates and perhalates add to PH_3 via the other oxygen atom. The oxidant activated in this way gives up an O atom to phosphine more readily. In the presence of Cl^- ions, ICl, characterised by a potential of 1.1 V, participates in reactions (25) and (26).

VI. Oxidation by oxygen compounds of nitrogen

The oxygen compounds of nitrogen oxidise PH_3 and AsH_3 fairly readily via the reactions[11-12,82-86]

$$PH_3 + 2N_2O_4 \rightarrow 4NO + (HO)_3PO, \quad (31)$$

$$AsH_3 + HNO_3 \rightarrow As + NO + 2H_2O. \quad (32)$$

These compounds are used to remove PH_3 and AsH_3 from gases[2-4] (see Table 1 at the end of the review). Under these conditions, PH_3 interacts effectively only with concentrated HNO_3 solutions (above 25%),[2] while AsH_3 reacts rapidly also with dilute nitric acid.[6] The conversion curve for the oxidation of PH_3 by nitric acid (dependence of the rate of reaction on the amount of absorbed PH_3) passes through a maximum, which indicates the involvement of N_2O_4, and not HNO_3, in the reaction. N_2O_4 is formed by the reaction

$$HNO_3 + HNO_2 \rightarrow N_2O_4 + H_2O. \quad (33)$$

The remaining oxygen compounds of nitrogen (NO, N_2O, HNO_2, and HNO_3) are relatively inactive.[11,12] These data show that, in contrast to AsH_3, PH_3 is oxidised only by oxygen compounds of nitrogen(IV), in the presence of which there is a possibility of a many-electron rate-limiting stage with participation of an even number of electrons. Phosphorus(III) compounds exhibit a tendency to interact with the O atoms of the oxygen compounds of nitrogen[7,87] owing to the high P=O bond energy (611 kJ mol^{-1}).[10] The rate-limiting stage in the oxidation of organophosphines and phosphites by *N*-oxides (R_3NO) is the nucleophilic addition of an O atom to phosphorus(III). The rate of oxidation of phosphorus(III) derivatives by pyridine *N*-oxide diminishes in the sequence

$$PCl_3 > PhCl_2P > Ph_2PCl \gg (PhO)_3P > (EtO)_3P \gg Ph_3P > Bu_3P > Et_2PhP.$$

On the other hand, in the oxidation of phosphites by the oxide N_2O_4 the electrophilic addition of an O atom to the phosphorus(III) atom takes place in the rate-limiting stage. This is indicated by the series of reactivities of phosphorus(III) compounds in relation to N_2O_4: $P(RO)_3 \gg P(PhO)_3$.[10] When account is taken of the data presented, the mechanism of the oxidation of PH_3 by the oxide N_2O_4 can be represented as follows:

$$N_2O_4 + PH_3 \rightleftarrows (N_2O_4)PH_3 \xrightarrow[-NO]{} (NO_2)PH_2(OH) \xrightarrow[-NO]{} PH(OH)_2, \quad (34)$$

$$PH(OH)_2 + N_2O_4 \rightleftarrows (N_2O_4)PH(OH)_2 \xrightarrow[-NO]{} (NO_2)P(OH)_3 \xrightarrow[-NO]{} (HO)_3PO. \quad (35)$$

Reaction (31) includes two four-electron stages. In each stage there are in its turn two two-electron steps to which shallow energy wells correspond. The entropy barrier in the many-electron transition is overcome by virtue of the formation of a complex between N_2O_4 and PH_3 or, in the general case, between N_2O_4 and phosphorus(III). As a result of complex formation with participation of the O atoms of the oxygen compounds of nitrogen and the phosphorus(III) atom, the reactions involving the oxidation of phosphorus(III) derivatives by nitrogen oxides are very rapid.[7]

The oxidation of phosphine by nitrogen dioxide is accelerated by Ag^+ ions. A small amount of added $AgNO_3$ (10^{-4} M) ensures a high reactivity of these and dilute (<10%) solutions of nitric acid.[2,11] The kinetic equation for the oxidation of PH_3 by nitric acid does not then change.[11] Like other d^{10} ions (Cu^+, Au^+, Hg^{2+}), Ag^+ ions form phosphides on interaction with phosphine.[6] The deprotonation of phosphine on formation of the phosphide tends to reduce the redox potential of the electron donor. Furthermore, as already mentioned above, on formation of *d* metal phosphides, the hybridisation of the P atom changes ($sp^3 \rightarrow sp^3d$). In contrast to the initial phosphine, activated phosphine interacts more readily with an O atom in N_2O_4 as a result of the enhancement of the role of the $d_\pi - p_\pi$ interaction. Reaction (31) is also accelerated by mercury(II) chlorides, which form the phosphides $(HgCl)_3P$ (see Table 1).[11]

The iodide ion is also an effective catalyst of the oxidation of phosphine by the acids HNO_3 and HNO_2.[12] In the presence of I^-, the oxidation of phosphine by nitric acid proceeds via a stepwise mechanism:[82-86]

$$2HNO_3 + 6KI + 2H_2O \rightarrow 3I_2 + 2NO + 6KOH, \quad (38)$$

$$2I_2 + PH_3 + 2H_2O \rightarrow (HO)H_2PO + 4HI. \quad (39)$$

Reactions (38) and (39) are faster than the direct oxidation of PH_3 by HNO_3 (see Table 1).[11,12]

Consequently reaction (31) is accelerated following the enhancement of the electron-accepting properties of the phosphorus atom as a result of the replacement of hydrogen atoms by metals or if a strong nucleophile (the I^- ion) is used as the electron transferring agent. The point is that the oxides N_jO_i are ambident oxidants.[32-34] The LUMO and HOMO are located on the N and O atoms respectively. For this reason, the N atom reacts preferentially with nucleophiles and the O atom with electrophiles. Thus amines, in which there is a distinct unshared orbital, enter preferentially into diazotisation or nitrosation reactions.[36] Phosphine, which is characterised by the presence of a weak non-bonding level, reacts with the oxygen atoms of nitrogen oxides. Furthermore, in contrast to amines, PH_3 has a valence *d* orbital capable of $d_\pi - p_\pi$ conjugation with an oxygen atom in N_jO_i.

Thus, a characteristic feature of PH_3 is a tendency to undergo outer-sphere oxidation by oxygen compounds in which an O atom is present as a bridge.

VII. Oxidation by oxygen compounds of sulphur, selenium, and tellurium

The oxidation of PH_3 by concentrated H_2SO_4 is widely used in industry[2-4] (see Table 1 at the end of the review):

$$3H_2SO_4 + PH_3 \rightarrow 3SO_2 + (HO)_2HPO + 3H_2O, \quad (40)$$

$$H_2SO_4 + PH_3 \rightarrow S + (HO)_2HPO + H_2O, \quad (41)$$

$$H_2SO_4 + PH_3 \rightarrow H_2S + (HO)_3PO. \quad (42)$$

Reactions (40)–(42) take place at a high rate only at H_2SO_4 concentrations in excess of 90 wt.%.[2,3] At such a concentration, the monomeric and trimeric SO_3 molecules, responsible for the reaction, are formed:[36]

$$2H_2SO_4 \rightleftarrows SO_3 + H_3O^+ + HSO_4^-,$$

$$3SO_3 \rightleftarrows (SO_3)_3, \quad (43)$$

and the redox potential of SO_3 also increases. Sulphur trioxide oxidises PH_3 in accordance with the mechanism

$$PH_3 + SO_3 \rightleftarrows SO_3PH_3,$$

$$SO_3PH_3 \rightarrow S + (HO)_2HPO,$$

$$H_2O + SO_3PH_3 \rightarrow SH_2 + (HO)_3PO,$$

$$(SO_3)_3PH_3 \xrightarrow[-SO_2]{} PH_2(OH)(SO_3)_2 \xrightarrow[-SO_2]{} \longrightarrow PH(OH)_2(SO_3) \xrightarrow[-SO_2]{} OPH(OH)_2. \quad (44)$$

Reactions (40)–(42) are accelerated appreciably after the addition of a small amount of $HgSO_4$,[2] which forms phosphides with PH_3. As already mentioned, on passing to the phosphide state, the reduction potential increases and the phosphorus atom undergoes sp^3d hybridisation, which is convenient for the $d_\pi-p_\pi$ interaction with an oxygen atom of sulphur trioxide. The participation of monomeric and trimeric sulphur trioxide in the process is indicated by the high order of the reaction with respect to H_2SO_4. The occurrence of reactions (41) and (42) is direct evidence for the real occurrence of the eight-electron single-stage oxidation of PH_3, since in the intermediate valence states (SO_2 and S) sulphur does not oxidise PH_3 but does oxidise organophosphines.[68] The low redox potential of H_2SO_4 (only 0.2 V) and the high rate of reactions (40)–(42) indicate unambiguously that many-electron single-stage PH_3 oxidation processes are preferred. The many-electron rate-limiting stage takes place stepwise and there are small energy wells in the reaction pathway. The entropy barrier in reaction (44) is lowered by virtue of the involvement in it of the associated species $(SO_3)_3$ and the formation of a complex with participation of the phosphorus atom and an oyxgen atom of sulphur trioxide. The depth of the energy wells diminishes as the hydrogen atoms of PH_3 are substituted by OH groups, since the tendency of the phosphorus atom towards complex formation increases as the redox potential of the intermediate products falls (see Scheme 1). The substitution of H by OH groups activates the phosphorus atom[10] and there is at the same time an increase in the bond angle between the substituents and a change in hybridisation.[38] The majority of phosphorus(III) derivatives have a bond angle of approximately 100°.[38]

Such an angle is as a rule formed by substituents tending to enter into a $p_\pi-d_\pi$ interaction (OH, F, Cl, Br, I, C_6H_5) and a $\sigma-d_\pi$ interaction (Me). Electron-accepting bonding is achieved via the unoccupied d orbital of the phosphorus atom and the non-bonding p_π orbital or the σ-bond of the substituent. As a result, a double bond is formed between the phosphorus atom and the substituent, which alters the hybridisation of phosphorus and intensifies the tendency towards the formation of a complex with SO_3. Substituents of the type of H, CN, and SiH_3, which are incapable of $p_\pi-d_\pi$ and $\sigma-d_\pi$ conjugation, form a bond angle much smaller than 100° and are characterised by weak ligand properties.[38]

The oxygen compounds of selenium and tellurium which are analogues of H_2SO_4 are reduced by phosphine to the elements[82–85,88] (see Table 1):

$$2H_2SeO_3 + PH_3 \rightarrow 2Se + (HO)_3PO + 2H_2O, \quad (45)$$

$$2H_2TeO_3 + PH_3 \rightarrow 2Te + (HO)_3PO + 2H_2O. \quad (46)$$

High rates of reactions (45) and (46) are attained at an acid concentration in excess of 0.1 M.[82–85,88] The rates of these reactions increase after the addition of HCl and especially HBr and HI.[82] Since halide ions stimulate the disproportionation of selenium(II) and tellurium(II) compounds,[36] i.e.

$$3H_2O + 2TeCl_2 \rightleftarrows H_2TeO_3 + Te + 4HCl, \quad (47)$$

$$3H_2O + 2SeCl_2 \rightleftarrows H_2SeO_3 + Se + 4HCl, \quad (48)$$

It follows that reactions (45) and (46) take place via the reduction of selenium(IV) and tellurium(IV) to selenium(II) and tellurium(II) respectively. The polymeric compounds $(TeO_2)_j(H_2O)_l$ and $(SeO_2)_j(H_2O)_l$, predominating in acid solutions,[84] take part in the rate-limiting stages of reactions (45) and (46):

$$(TeO_2)_4 + PH_3 + 8HX \rightarrow 4TeX_2 + (HO)_3PO + 4H_2O, \quad (49)$$

$$(SeO_2)_4 + PH_3 + 8HX \rightarrow 4SeX_2 + (HO)_3PO + 4H_2O. \quad (50)$$

The oxygen compounds of selenium(IV), tellurium(IV), and sulphur (VI), which are capable of forming polymeric compounds, ensure the synchronous many-electron oxidation of PH_3, which is energetically more favourable than the two-electron oxidation (Fig. 1). Therefore, despite the low redox potentials of the oxygen compounds, sulphur(VI) selenium(IV), and tellurium(IV) are fairly rapidly reduced by phosphine.[82–85] In the intermediates formed in reactions (45) and (46) the bond linking the oxygen compounds of selenium(IV) and tellurium(IV) to PH_3 is formed via an O atom. The oxidation-reduction decomposition of the intermediate takes place as a result of the transfer of an oxygen atom from the oxygen compounds of selenium(IV) and tellurium(IV) to the phosphorus atom in PH_3.

VIII. Oxidation by oxygen compounds of 3*d* metals

Sulphuric acid solutions of chromium(VI) and manganese(VII) are widely used in laboratory and industrial practice[2–4] for the removal of PH_3 and AsH_3 from gases.[11,12,89–91] PH_3 and AsH_3 are oxidised by oxygen compounds of chromium(VI) in accordance with the equations[89–91]

$$Na_2Cr_2O_7 + PH_3 + 4H_2SO_4 \rightarrow (HO)_2HPO + Cr_2(SO_4)_3 + Na_2SO_4 + 4H_2O, \quad (51)$$

$$2Na_2CrO_4 + 2AsH_3 + 5H_2SO_4 \rightarrow 2As + Cr_2(SO_4)_3 + 2Na_2SO_4 + 8H_2O. \quad (52)$$

Reaction (51) takes place satisfactorily only in very concentrated sulphuric acid solutions (>12 M) and in the presence of high contents of chromium(VI) ($>10^{-3}$ M). The oxidation of AsH_3 takes place vigorously in relatively dilute H_2SO_4 (>1–2 M) and at a lower chromium(VI) concentration ($<10^{-4}$ M).[89–91] The different behaviour of PH_3 and AsH_3 in sulphuric acid solutions of chromium(VI) is due to the fact that the oxidation of phosphine via a six-electron mechanism and of arsine via a three-electron mechanism to phosphorus(III) and arsenic respectively is energetically favourable (see Table 1 at the end of the review).

Chromium(VI) in solutions participates both in reversible dimerisation reactions and in acid–base reactions:[36,92]

$$CrO_4^{2-} + H^+ \rightleftarrows CrO_3(OH)^-, \quad K = 3.1 \cdot 10^8,$$
$$CrO_3(OH)^- + H^+ \rightleftarrows H_2CrO_4, \quad K = 2 \cdot 10^1,$$
$$2CrO_3(OH)^- \rightleftarrows Cr_2O_7^{2-} + H_2O, \quad K = 4.1 \cdot 10^3.$$

The scheme involving reversible reactions presented above is applicable only to solutions containing HNO_3 and $HClO_4$.[93] A chlorochromate ion is formed in solution in HCl and a sulphate complex is produced in H_2SO_4:[92]

$$CrO_3(OH)^- + HCl \rightleftarrows CrO_3Cl^- + H_2O, \quad K = 17,$$
$$CrO_3(OH)^- + HSO_4^- \rightleftarrows CrO_3(SO_4)^{2-} + H_2O, \quad K = 4.$$

It follows from the above equations that the predominance of a particular form of chromium(VI) in aqueous solutions depends on its concentration and the pH of the medium. The monomeric acid chromate ion exists in dilute solutions. With increase in concentration, the dichromate ion becomes the dominant form. The degree of protonation of these ionic species depends on the pH of the medium. Electron-accepting properties are characteristic of chromium trioxide. When CrO_3 is dissolved in the presence of HCl and H_2SO_4 in hydroxylated organic solvents, chromic acid esters are formed:[69]

$$AcOH + CrO_3 \rightleftarrows AcOCrO_3H,$$
$$2AcOH + CrO_3 \rightleftarrows (AcO)CrO_2 + H_2O.$$

In pyridine, CrO_3 exists as the complex $Py.CrO_3$ with a Cr–N bond.[69]

The interaction of monomeric chromium(VI) complexes with PH_3 is difficult owing to the complementary prohibition. The oxidising capacity of the chromium(VI) monomer corresponds to three electrons, while the reducing capacity of PH_3 corresponds to six or eight electrons.

In contrast to chromium(VI), chromium(V) readily oxidises triphenylphosphine:[93]

$$CrOL_2^+ + Ph_3P \rightarrow CrL_2^+ + Ph_3P{=}O,$$

where HL is 2-ethyl-2-hydroxybutyric acid. The reaction mechanism includes the transfer of an oxygen atom in accordance with the scheme

$$CrOL_2^+ + Ph_3P \rightleftarrows [Ph_3P{-}O{-}CrL_2]^+ \rightarrow Ph_3P{=}O + CrL_2^+.$$

The intermediate complex with a bridging O atom undergoes oxidation-reduction decomposition in the rate-limiting stage.[93] On the other hand, the oxidising capacity of the dimer, corresponding to six electrons, ensures the complementarity of the reaction involving the reduction of the dichromate by phosphine.

Another situation arises in the oxidation of AsH_3 by chromate. In this case, the requirement for the complementarity of the rate-limiting stage is satisfied also in the absence of dichromate. The reducing capacity of AsH_3 and the oxidising capacity of chromate are equal and corresponding to three electrons. As a result, AsH_3 is readily oxidised by chromates to arsenic at relatively low concentrations (1–2 M) and in the presence of a low chromium(VI) content ($< 10^{-4}$ M).[89–91] In the presence of added copper(II) and iron(III) salts, which tend to be involved in one-electron transfer, reactions (51) and (52) proceed readily at a much lower acidity (10^{-1} M). In weakly acid media at a chromium(VI) concentration of 10^{-4} M, monochromate ions, incapable of the complementary oxidation of AsH_3 and PH_3 to the acids, predominate. Copper(II) and iron(III) salts, which participate jointly with monochromate ions in the rate-limiting stage, make the reactions complementary. Chromium(VI), copper(II) ions, or iron(III) ions, used in isolation, oxidise phosphine at the concentrations indicated.[11] Jointly with monochromate, iron(III) or copper(II) ions ensure the occurrence of four-electron transfer in the slow stage:

$$[XCu(CrO_3OH)PH_3] + H_2O \rightarrow CuX + Cr(OH)_3 + (HO)_2HP,$$
$$[XCu(CrO_3OH)PH(OH)_2] + H_2O \rightarrow CuX + Cr(OH)_3 + (HO)_3PO.$$

Copper(II) ions are regenerated via the reaction

$$3CuX + NaCrO_3OH + 7HX \rightarrow 3CuX_2 + CrX_3 + 4H_2O + NaX.$$

Copper(II) and iron(III) ions promote the oxidation of phosphine by oxygen compounds of chromium(VI)[11,12] only at a low acidity of the medium[89–91] where chromate ions predominate in the system. At a high acidity, which promotes the formation of dichromates, iron(III) and copper(II) ions do not affect the rate of oxidation of PH_3 by chromium(VI). The effectiveness of copper(II) and iron(III) salts increases with decrease in acidity and decreases with increase in acidity, passing through a maximum as the X^- concentration rises.

The most significant promoting effect is exerted by added bromide and particularly iodide ions, which ensure the operation of the stepwise reaction mechanism.[11,12,89–91] In the presence of halide ions, phosphine and arsine do not interact directly with chromium(VI). Chromium(VI) oxidises halide ions to the halogens:

$$2Na_2CrO_4 + 6NaBr + 8H_2SO_4 \rightarrow 3Br_2 + Cr_2(SO_4)_3 + 5Na_2SO_4 + 8H_2O, \quad (53)$$

while halogens are in turn reduced back to the halide ion by phosphine or arsine:

$$4Br_2 + PH_3 + 4H_2O \rightarrow (HO)_3PO + 8HBr, \quad (54)$$
$$3Br_2 + AsH_3 + 2H_2O \rightarrow HAsO_2 + 6HBr. \quad (55)$$

Arsine is, as usual, effectively oxidised under milder conditions than phosphine.[89–91] The oxidation of AsH_3 requires chromium(VI), acid, and NaX concentrations lower by an order of magnitude than in the oxidation of PH_3. This is associated with the fact that the atomic halogen, stabilised in the coordination sphere of chromium, functions as the agent transferring electrons from AsH_3 to the chromate, while the transfer of electrons from PH_3 to the dichromate ion is effected by a polyhalide ion. The formation of polyhalide ions requires a higher concentration of halide ions than for the generation

of halogen atoms.[36] The catalytic activity of halide ions increases, as usual, in opposition to their redox potentials.[11,12,89–91] The oxidation of phosphine and arsine by oxygen compounds of manganese(VII) takes place in acid and alkaline media in the following way[82–85,94] (see Table 1):

$$2KMnO_4 + PH_3 + H_2SO_4 \rightarrow 2MnO_2 + (HO)_2HPO + + K_2SO_4 + H_2O, \quad (56)$$

$$2KMnO_4 + AsH_3 + H_2SO_4 \rightarrow 2MnO_2 + HAsO_2 + + K_2SO_4 + 2H_2O. \quad (57)$$

The oxidation of PH_3 and AsH_3 in alkaline and especially in neutral and acid media is rapid (Table 1).[94] Manganese(VII), which forms stable manganese(V) and manganese(VI) ions,[36] ensures both one- and two-electron oxidation of AsH_3 and PH_3. Furthermore, manganese(V) readily disproportionates to manganese(VI) and manganese(IV).[36]

The reactivity of manganese(VII) with respect to PH_3 in a neutral medium decreases in the presence of AsH_3. The coupled oxidation of PH_3 and AsH_3 by manganese(VII), which is fairly rapid, has been used in practice. The synergism is due to the fact that AsH_3 reduces manganese(VII) to manganese(VI), while PH_3 converts manganese(VI) into manganese(IV).

The rate of oxidation of PH_3 and AsH_3 increases significantly after the addition of halide ions.[82,94] The effectiveness of halide ions increases in opposition to the redox potentials.[82–85] In the presence of halide ions, manganese(VII) is reduced to manganese(II):

$$8KMnO_4 + 5PH_3 + 12H_2SO_4 \rightarrow 8MnSO_4 + 5(HO)_3PO + + 4K_2SO_4 + 12H_2O, \quad (58)$$

$$6KMnO_4 + 5AsH_3 + 9H_2SO_4 \rightarrow 6MnSO_4 + 5HAsO_2 + + 3K_2SO_4 + 14H_2O. \quad (59)$$

In the presence of halide ions, the mechanisms of reactions (58) and (59) change. In the absence of X^-, phosphine and arsine react with an O atom in oxygen compounds of manganese. The oxidation-reduction decomposition of the phosphine complex of manganese(VI) leads to the transfer of an O atom from manganese(VII) to PH_3, the decomposition being rapid as a consequence of complementarity. Manganese(VII) is reduced to a transfer of both an even number [reduction to Mn(V)] and an odd number [reduction to Mn(II, IV)] of electrons.

Manganese dioxide vigorously oxidises PH_3 and AsH_3 only above 300 °C. The reaction takes place in the gas phase and is inhibited by the PH_3 oxidation products—manganese(II) phosphates, which preclude the access of PH_3 to MnO_2. In the liquid phase, the reactivity of MnO_2 increases rapidly after the addition of iodide ions.[85] Halide ions ensure the occurrence of reactions (58) and (59) via a new, faster pathway.[85] In this case, PH_3 and AsH_3 do not react directly with manganese(VII), the latter oxidising the halide ions to the molecular halogen:

$$2KMnO_4 + 10KX + 8H_2SO_4 \rightarrow 2MnSO_4 + 5X_2 + 6K_2SO_4 + + 8H_2O. \quad (60)$$

Phosphine and arsine reduce in turn the halogen to the halide.[82–85] Halides are universal effective catalysts of the oxidation of PH_3 and AsH_3 for the majority of known oxidants.[11,12]

Being a strong nucleophile, the halide reacts more readily than PH_3 and AsH_3 with the central atom of the oxygen compound. The complementary oxidant converts X^- into X^+ while a non-complementary one generates from X^- the X^0 radical, which dimerises rapidly to X_2.[11] As a result, both complementary and non-complementary oxidants form the oxidant X_2, which is suitable for the oxidation of PH_3 and AsH_3. Furthermore, the X_2 molecules tend to form the polyhalides X_n.[36] Since the probability of the formation of X_n increases with decrease in the $2X^- \rightarrow X_2$ redox potential and with decrease in the X_2 concentration, a high rate of reaction is attained at fairly appreciable X^- concentrations.[11,12]

Solutions containing $10^{-3}-10^{-2}$ M of iodide ions or $10^{-2}-10^{-1}$ M bromide ions are most often used.[82]

Halogen atoms rather than molecules are the most suitable oxidants for the oxidation of AsH_3. In contrast to PH_3, AsH_3 is therefore oxidised at a lower X^- concentration[94] (Table 1).

It was noted above that the reactivity of the halogens with respect to PH_3 and AsH_3 decreases in parallel with their redox potentials: $Cl_2 > Br_2 > I_2$.[11,12] On the other hand, the catalytic activity of the halogens increases in opposition to the redox potentials of the halide ions: $I^- \gg Br^- > Cl^-$. The point is that the reactivity of X_2 is described by the equation

$$\frac{W}{[X_2][PH_3]} = k_{X_2},$$

while the catalytic activity of halide ions is described by the formula

$$\frac{W}{[PH_3][Ox][X^-]} = kK = k_{X^-},$$

where k is the rate constant and K the equilibrium constant of the reaction

$$Ox + 2X^- \rightleftarrows Red + X_2.$$

Since K increases with decrease in the $2X^- \rightarrow X_2$ redox potential, it follows that k_{X^-} and k_{X_2} form antiparallel series.[11,12]

The behaviour of oxygen compounds of chromium(VI) and manganese(VII), widely used for the removal of PH_3 and AsH_3 from gases,[82–85] was examined above. The oxygen compounds of other 3*d* metals are used for the oxidation of PH_3 in analytical practice.[11] In a strongly acid medium (~10 M), vanadium(V) is slowly reduced by phosphine[95] (see Table 1):

$$8NH_4VO_3 + PH_3 + 12H_2SO_4 \rightarrow (HO)_3PO + 8VOSO_4 + + 4(NH_4)_2SO_4 + 12H_2O. \quad (61)$$

A high acidity is necessary for the formation of polynuclear vanadates, capable of ensuring the complementary many-electron single-stage oxidation of PH_3. In order to accelerate reaction (61), halide ions are usually introduced.[95] Iodide ions exhibit the highest activity.[95] Heteropolyacids, the active principle of which is free VO_2 ions,[96] also oxidise PH_3 slowly. In contrast to PH_3, arsine is oxidised rapidly by heteropolyacids.[97] The rate of oxidation of AsH_3 by a heteropolyacid increases after the introduction of iodide ions.[97] In the HCl–HX system, phosphine and arsine are oxidised by the compounds ClBr and ClI.

The data presented show that, although the oxygen compounds of 3*d* metals do possess high redox potentials, they are reduced slowly by phosphine owing to their inability to ensure the complementary

many-electron single-stage oxidation of PH_3. However, they vigorously oxidise AsH_3, which reduces, in contrast to PH_3, the oxygen compounds of *d* metals via a homolytic mechanism. In the presence of X^- ions, phosphine is rapidly oxidised also by one-electron oxidants.

IX. Oxidation by metal complexes

Iron(III) and copper(II) chlorides are widely used to remove phosphines and arsine from gases,[2-4,12] since iron(II) [98,99] and copper (I) [100,101] chlorides are readily regenerated by dioxygen.[11] For the purification of oxygen-free gases, use is made of periodic action apparatus, on which the PH_3 and AsH_3 oxidation and regeneration stages are separated in time, while continuous operation apparatus is used for the detoxification of oxygen-containing gases.[2-4] Iron(III) chloride oxidises PH_3 in accordance with the scheme

$$8FeCl_3 + PH_3 + 4H_2O \rightarrow 8FeCl_2 + (HO)_3PO + 8HCl. \quad (62)$$

The reaction proceeds only at a high phosphine concentration. At low PH_3 concentrations, reaction (62) is very slow.[102-104] The rate of reaction increases sharply when concentrated (>3 M) $FeCl_3$ solutions are used.[105-107] Such a concentration is attained after the deposition of $FeCl_3$ from aqueous solution onto a carrier.[105-107] The high order of the reaction with respect to $FeCl_3$ indicates the involvement in the process of polynuclear iron(II) complexes, which are generated only at high iron(III) chloride concentrations.

The reactivity of polynuclear iron(III) complexes on carriers increases after the introduction of small amounts of $HgCl_2$ (10^{-4} M).[2,3] At a low $FeCl_3$ concentration ($<10^{-1}$ M), the reactivity is independent of the added $HgCl_2$. Iron(III) sulphates do not exhibit an appreciable reactivity in relation to PH_3 in an acid medium.[102] In weakly acid media, where polynuclear iron(III) complexes arise, phosphine is oxidised rapidly in the presence of silver(I) sulphate. In the absence of silver(I) ions, the reaction does not occur. In acetic acid media, which ensure the formation of the trinuclear complexes $Fe_3(OH)_2(AcO)_6^+$,[27] phosphine is also not oxidised.[103]

Silver(I) and mercury(II) ions stimulate the process by virtue of the formation of the phosphides AgH_2P and $(HgCl)_3P$, which, as already mentioned, have a higher reactivity than the initial phosphine. Only the dinuclear complexes $Fe_2Cl_9^{3-}$ arise in chloride solutions,[36] ensuring the two-electron oxidation of phosphine. In heterogenised systems, more reactive polynuclear iron(III) complexes are formed. They effect the many-electron energetically more favourable single-stage oxidation of PH_3 to $(HO)_3PO$. The reactivities of the deposited and dissolved iron(III) chlorides therefore differ significantly.[105-107] Dissolved iron(III) chlorides have a low reactivity,[104] whilst deposited ones have a high reactivity.[105] Iodide ions accelerate reaction (62) effectively,[102-104] exhibiting the highest activity when dissolved (and not deposited) iron(III) chlorides are used.[102-104,106] In the presence of iodide ions, reaction (62) proceeds via two stages: iron(III) chloride oxidises iodide ions to polyiodides and the latter are then reduced by phosphine, which regenerates iodide ions.[102-104,106]

Thus iodide ions are more suitable for the acceleration of the oxidation of phosphine by non-complementary oxidants, while silver(I) and mercury(II) are best for complementary oxidants. Cerium(IV) behaves similarly to iron(III).[108,109] Despite its very high redox potential (1.5 V), cerium(III) sulphate hardly interacts with PH_3 in the absence of catalysts. In the presence of halide ions, cerium(IV) is rapidly reduced by phosphine via the reaction

$$8Ce(SO_4)_2 + PH_3 + 4H_2O \rightarrow (HO)_3PO + 4Ce_2(SO_4)_3 + 4H_2SO_4. \quad (63)$$

In the presence of halide ions, the reaction is divided into two slow stages: the first of these involves the formation of Cl_2, ClBr, and ClI, which are reduced by phosphine in the second stage.[108,109] When these stages take place separately, they obey the same rules as in a catalytic process.[110] As usual, the catalytic activity of halide ions in reactions (63) increases in opposition to the redox potential: $I^- \gg Br^- > Cl^-$ [108-110] (see Table 1 at the end of the review).

In contrast to iron(III) and cerium(IV) salts, the reactivity of copper(II) chlorides and sulphates increases sharply in the presence of copper(I).[113-115] In the presence of copper(I) ions in concentrated solutions of copper(II) salts (>1 mM), the following reactions proceed at a satisfactory rate:

$$3CuSO_4 + PH_3 + 3H_2O \rightarrow 3Cu + 3H_2SO_4 + (HO)_2HPO, \quad (64)$$

$$8CuCl_2 + PH_3 + 4H_2O \rightarrow 8CuCl + (HO)_3PO + 8HCl, \quad (65)$$

$$3CuCl_2 + AsH_3 \rightarrow As + 3CuCl + 3HCl. \quad (66)$$

Copper(II) ions, which are characterised by high redox potentials of the $Cu^{II} \rightarrow Cu^{I}$ (+0.153 V) and $Cu^{II} \rightarrow Cu^{0}$ (+0.337 V) transitions, oxidise PH_3 and AsH_3 at high rates[111,112] (Table 1). In concentrated solutions[113-115] and when carriers are used,[116,117] polynuclear saturated copper(II) and copper(I) complexes, which exhibit an enhanced reactivity,[111-115] play a dominant role.[118,119] Reactions (64)-(66) are accelerated by the CNS^-,[120] Br^-,[121-123] and I^- [124-126] ions (see Table 1).

Calculations by the CNDO, MVG, and HMO quantum-chemical methods have been performed for the aquophosphine complexes of copper(II) and iron(III) with different contents of X^- ions.[127-133] The $P-H_P$ and $HO-H_O$ bonds are weakened and the amount of their ionic character increases, a positive charge appears on the phosphorus atom, a negative charge appears on H_2O, and strong bonds are formed with the P, H_P, and H_O atoms, especially in the case of oxygen-containing anions. With increase in the negative charge on the complex, the $P-OH_2$ and $Cu-H_P$ bonds are strengthened while the P-Cu bond is loosened. This stimulates the oxidation-reduction decomposition of the complex involving the oxidation of phosphine and the reduction of copper(II). With decrease in the negative charge on the complex, the P-Cu and H_P-OH bonds are strengthened, which induces an acid-base reaction, copper(II) being reduced to copper(I) as a result of the oxidation-reduction decomposition of zerovalent copper. Reaction (65) is effectively accelerated by palladium(II) [134-136] of mercury(II) and copper(I) [134-138] chlorides. The synergistic effects arising under the joint action of copper(I) and palladium(II) or mercury(II) is due to the fact that copper(I) chlorides activate PH_3 differently compared with palladium(II) or mercury(II) chlorides.[137,138] Mercury(II) [138,139] and palladium(II) [140] chlorides activate phosphine by substituting the H atoms by $HgCl^+$ or $PdCl^+$ with formation of the phosphides $(HgCl)_3P$ or $(PdCl)_3P$.[138] Copper(I) chlorides promote the loosening

of the electron cloud of the phosphorus atom by forming a complex with palladium(II) or mercury(II) phosphide.[138] In the mixed complex, the phosphorus atom assumes the sp^3d configuration, which is convenient for oxidation. It is known[32] that the activation energy diminishes as the electronic configurations of the initial reactants and products approach one another. Since according to literature data[61] the phosphorus atom in phosphates has a pronounced d character, the change in hybridisation of the type $sp^3 \rightarrow sp^3d$ favours PH_3 oxidation reactions.

Gold(III) chlorides, which react very rapidly with phosphine even in dilute solutions (see Table 1), are reduced by phosphine in a different way:[141]

$$8AuCl_3 + 3PH_3 + 12H_2O \rightarrow 8Au + 3(HO)_3PO + 24HCl. \quad (67)$$

Like reaction (65), reaction (67) is accelerated by gold(I) chlorides.[11] However, in contrast to copper(II) in reaction (65), gold(III) is reduced also in the absence of gold(I) chlorides.[141] Gold(I) performed a dual function in this reaction. On the one hand, it activates phosphine, like other d^{10} ions, by virtue of the formation of phosphine complexes and, on the other hand, gold(I) ions participate together with gold(III) in the oxidation of PH_3. A mixed heteronuclear gold(III, I) phosphine complex undergoes inner-sphere decomposition with transfer of four electrons from PH_3 to Au(III) and Au(I). Reaction (67) is accelerated particularly effectively by added HBr, HI, and HCl as a result of the formation of ClBr and ClI. Gold(I) is continuously regenerated as a consequence of the oxidation of zerovalent gold by gold(III).

Platinum(IV) chlorides are reduced by phosphine similarly to gold(III):[142]

$$3Na_2PtCl_6 + 2PH_3 + 6H_2O \rightarrow 3Pt + 2(HO)_2HPO + 6NaCl + 12HCl. \quad (68)$$

The reaction is accelerated by platinum(II) chlorides, which perform a dual function: they activate PH_3, forming a phosphine complex, and, together with platinum(IV), they oxidise phosphine via a six-electron mechanism. Platinum(II) is continuously regenerated as a result of the oxidation of zerovalent platinum by platinum(IV). In a HCl–HX solution, reaction (68) is propagated by the ClBr and ClI species. Phosphine reduces platinum(II) chlorides very rapidly[138,140] (Table 1):

$$4PdCl_2 + PH_3 + 4H_2O \rightarrow Pd + (HO)_3PO + 8HCl. \quad (69)$$

The reactions of PH_3 with palladium(II) complexes [$PdCl_2(PhCH)_2$, $Pd(AcO)_2$, $(PPh_3)_2Pd(OAc)_2$] in non-aqueous solvents (chloroform, dioxane) leads to the formation of insoluble palladium compounds.[140] In all the compounds isolated, the oxidation state of palladium has been shown by the X-ray photoelectron spectroscopic method to be close to 2+, Pd–P bonds are present (demonstrated by the EXAFS method), and an acid (HCl, HOAc) is formed in the solutions over the precipitate. This indicates the acid–base nature of the interaction of PH_3 with palladium(II) complexes in a non-aqueous medium, which is accompanied by the heterolysis of the P–H bond and the formation of the PH_2 phosphide species coordinated to palladium (this is indicated by the ^{31}P NMR spectra of the chloride complex):

$$PH_3 + n\,PdX_2 \rightarrow PH_{3-n}(PdX)_n + nHX.$$

The extent of this process is regulated by selecting the basicity of the solvent. After the interaction of palladium acetate complexes with PH_3, an appreciable amount of acetic anhydride is formed in solution over the deposit.[140] This fact (together with ^{31}P MAS NMR data for the deposit) indicates the presence of oxidised forms of phosphine in the coordination sphere of palladium. All the palladium compounds isolated after interaction with PH_3 in non-aqueous media are readily hydrolysed in water with formation of $(HO)_3PO$ and zerovalent palladium. Thus the coordinated phosphine is oxidised via the formation of bonds between the coordinated phosphorus and the O atoms of the ligand. In contrast to oxygen compounds of metals and non-metals, forming outer-sphere complexes with PH_3 via an O atom, the metal complexes oxidise PH_3 via inner-sphere mechanisms.

As already mentioned, phosphine is activated only by metal ions capable of a two-sided exchange interaction. Low-valence forms of the metal usually possess such properties. Therefore the high-valence metal complex reduction reactions are as a rule activated by complexes of metals in low valence states. In a two-sided exchange interaction, the phosphorus atom of phosphine assumes an electronic configuration similar to that of the phosphorus atom in the products. Such activation of the reactant lower significantly the activation energies for the reactions.[143]

X. Oxidation by dioxygen, ozone, and peroxide compounds

The use of O_2, O_3, H_2O_2, and $Na_2S_2O_8$ for the oxidation of PH_3 is an extremely promising procedure, since the reaction products are harmless.[2–4] However, despite the high redox potentials of the oxidants listed above, the reactions

$$2O_2 + PH_3 \rightarrow (HO)_3PO, \quad (70)$$

$$4O_3 + PH_3 \rightarrow (HO)_3PO + 4O_2, \quad (71)$$

$$4H_2O_2 + PH_3 \rightarrow (HO)_3PO + 4H_2O, \quad (72)$$

$$4Na_2S_2O_8 + PH_3 + 4H_2O \rightarrow (HO)_3PO + 4Na_2SO_4 + 4H_2SO_4, \quad (73)$$

are very slow.[11,12,144–146]

The two-electron reduction of dioxygen to the peroxide or the four-electron reduction to water is thermodynamically very favourable, while the one-electron reduction of O_2 to O_2^- or HO_2^- takes place with absorption of heat.[147] On the other hand, the transfer of a pair of electrons to an O_2 molecule is impossible as a consequence of the spin prohibition, since dioxygen has a triplet ground state. The oxidation of organic and inorganic substances by dioxygen therefore proceeds via successive one-electron stages involving radical exchange mechanisms.[147] The rate of these processes is limited by the thermodynamic difficulty of the transition $O_2 \rightarrow O_2^-$. The one-electron transition generates the radicals O_2^- and HO_2^- with a very high redox potential. The non-complementarity and the negative potential of the one-electron transition $O_2 \rightarrow O_2^-$ hinder the oxidation of PH_3 at low concentrations of the latter (10^{-2}–10^{-1} vol.%) and at the normal temperature.[7,9,10] At elevated temperatures and high PH_3 and O_2 concentrations, conditions are created for the transfer of two electrons:[9,10]

$$PH_3 + O_2 \rightarrow PH + H_2O + O. \quad (74)$$

Severe conditions are necessary to overcome the spin prohibition in redox transitions. As mentioned above, the $sp^3 \rightarrow sp^3d$ transition to the triplet state, necessary for the removal of the spin prohibition, is facilitated at elevated temperatures. The O atom deformed by reaction (74) stimulates the explosive oxidation of PH_3.[9]

The oxidation of phosphine at low concentrations by dioxygen is fairly rapid in the presence of $CuCl_2$ and $FeCl_3$.[148–151] Phosphine reduces $CuCl_2$ and $FeCl_3$ to CuCl and $FeCl_2$ respectively. The initial state of the copper and iron salts is regenerated on treatment with O_2.[11] The addition of iodide and bromide ions accelerates the stages involving the reduction of copper(II) and iron(III) by phosphine,[124] but retards the stage in which copper(I) and iron(II) are oxidised by oxygen.[98] Palladium(II) [138] and mercury(II) [152] chlorides have a positive influence on the first stage and do not affect the second.[134,135] Single step mechanisms of the oxidation of PH_3 by dioxygen in the presence of metal complexes have not been described.[11] The I^-/C and PdO/C systems exhibit a high activity (Table 1).

The relative inertness of H_2O_2 in reaction (73) mentioned above is associated with the unusual properties of the frontier orbitals.[153,154] The peroxide bond in H_2O_2 is altogether unpolarised, since the high dipole moment, induced by the presence of the lone electron pairs on the oxygen atom in the peroxide group, is compensated by the uniform charge distribution and does not affect the dipole moment of the O–O bond.[153] The dipole moment of the H_2O_2 molecule is determined by the dipole moments of the H–O bonds and is equal to 2.2 D.[153] A π^*-type antibonding orbital plays the role of the HOMO, while the role of the LUMO is assumed by a σ^*-type antibonding orbital.[153] The type $[\sigma+\sigma]$ interaction of H_2O_2 with PH_3 is symmetry-prohibited, while the oxidative addition of H_2O_2 to PH_3 requires that a high symmetry barrier be overcome owing to the pronounced *s* character of the lone pair. The nucleophilic substitution of the OH^- group in H_2O_2 by phosphine is difficult because of the low polarity of the HO–HO bond and of phosphine. The reaction is accelerated somewhat in highly acid media by virtue of the protonation of the H_2O_2 with formation of the polar $H_3O_2^+$ species.[154] The addition of bromide and iodide ions[144] and also of $FeCl_3$ and $CuCl_2$ [145] accelerates reaction (72). In contrast to the dioxygen, hydrogen peroxide oxidises PH_3 via a single step mechanism in the presence of metal complexes.[145,146]

As a result of complex formation, metal ions increase the polarity of H_2O_2 and facilitate the interaction of PH_3 with an O atom of the peroxide bond. Iron(III) and copper(II) halides are therefore particularly effective at low acidities of the medium where there are no $H_3O_2^+$ ions. Metal and hydrogen ions act similarly, but their effectiveness is significantly different. In order to attain the same effect, a lower concentration of the metal ions than that of hydrogen ions is required.[144,145] The oxidation of AsH_3 by H_2O_2 takes place at lower concentrations of X^-, $CuCl_2$, and $FeCl_3$ than the oxidation of PH_3.[146]

Ozone is one of the most vigorous oxidants[155] and yet reaction (71) is very slow. The low reactivity of O_3 compared with PH_3 [154] is caused by the unusual electronic structure of ozone. The following filling of molecular orbitals corresponds to the unexcited state of the O_3 molecule: $(\sigma)^4(\pi)^2(2p)^4(\pi)^2(\sigma)^2$.[36] The O_3 molecule has an angular shape and a low polarity (0.17 D).[36] Two-sided $[\sigma+\sigma]$ reactions are therefore symmetry-prohibited and one-sided reactions are hindered by the very low basicity of PH_3 ($pK = -14$).

The configurations of the HOMO and LUMO of ozone, like those of H_2O_2, are favourable to the reactions with OH^- and X^-. In an alkaline medium, O_3 reacts with OH^-, generating an OH radical.[155] However, despite the extremely high redox potential, the OH radical oxidises PH_3 only weakly, since it is a one-electron oxidant. The most active catalyst of reaction (71) at pH 11–12 is the iodide ion.[146]

In the presence of SO_2 or P_2O_3, phosphine undergoes coupled oxidation by dioxygen in an alkaline medium:

$$PH_3 + 4SO_2 + 4O_2 + 4NaOH \rightarrow 4Na_2SO_4 + (HO)_3PO + 4H_2O, \quad (75)$$

$$PH_3 + 2P_2O_3 + 4O_2 + 5NaOH + H_2O \rightarrow 5NaH_2PO_4. \quad (76)$$

The addition of alcohol lowers somewhat the rates of reactions (75) and (76) but does not stop them completely. The oxenoid reaction (75) begins with the formation of peroxomonosulphuric acid:

$$HSO_3^- + O_2 \rightarrow HSO_5^-. \quad (77)$$

Subsequently the HSO_5^- anion oxidises PH_3:

$$4H_2SO_5 + PH_3 \rightarrow 4H_2SO_4 + (HO)_3PO. \quad (78)$$

In contrast to H_2O_2 and $H_2S_2O_8$, Caro's acid transmits its oxygen atoms to phosphine. In the rate-limiting stage, the phosphine molecule approaches the peroxide oxygen atom in H_2SO_5 along the O–O bond line; by virtue of the high polarity of the oxidant,[154] its occupied non-bonding *s* orbital overlaps the unoccupied p_{σ^*} orbital of the peroxide bond. The appearance of electrons in the antibonding orbital leads to the weakening and successive dissociation of the O–O bond.[154] This entails the formation of a new bond between the phosphorus atom of phosphine and an oxygen atom of the peroxomonosulphate. The unusual properties of H_2SO_5 are associated with the presence in peroxo-monoacids of a polarised peroxide bond (0.9 D) with a relatively low energy of the LUMO (−9.3 eV). The occurrence of reaction (76) is ensured by the monoperphosphoric acid H_3PO_5, the polarity of the peroxide bond of which is similar to that in H_2SO_5.[153]

Thus phosphine can undergo coupled oxidation by dioxygen in the presence of additives inducing oxenoid oxidation.

XI. Conclusion

The principal features of the kinetics and mechanisms of the majority of the reactions, described in the literature, involving the oxidation of PH_3 and AsH_3 by complexes and oxygen compounds with metals and non-metals and the catalytic and coupled oxidation by dioxygen, ozone, and peroxide compounds were analysed above.

Table 1 presents the rate constants for the majority of the catalytic and non-catalytic low-temperature reactions involving the oxidation of PH_3 and AsH_3 by various oxidants in acid, neutral, and alkaline solutions and in the gas phase. The halogens (Cl_2, Br_2, I_2) and their derivatives (HClO, HBrO, HIO, HIO_3, HIO_4, $HBrO_3$), the oxygen compounds of nitrogen (NO_2), sulphur, selenium, and tellurium (H_2SO_4, H_2SeO_3, H_2TeO_3) as well as transition metals ($KMnO_4$, $H_2Cr_2O_7$, HVO_3), and *d* metal complexes ($AuCl_3$, $AuBr_3$, $AuCl_2I$, $AuCl_2Br$, $CuCl_2$, $CuBr_2$, CuClBr, CuClI, CuBrI, H_2PtCl_6, H_2PtBr_6, H_2PtI_6, Na_2PdCl_4, $FeCl_2I$, $FeBr_2I$, $CeCl_3I$) react faster with PH_3 and AsH_3 than any other oxidants. The most effective catalysts of the reactions in which PH_3 and AsH_3 are oxidised by various oxidants are alkali metal iodides and copper(II) halides.

Table 1. Kinetic parameters of the reactions involving the oxidation of PH_3 and AsH_3 by metal complexes and free and bound oxygen at 298 K and 10^{-2}–10^2 Pa.

Reaction	Catalyst	Rate constant	Refs.
$PH_3+3Cu(OAc)_2+3NaOH \rightarrow 3Cu+(NaO)_2HPO+NaOAc+5HOAc$	$CuOAc-C_3H_5(OH)_3$	$k_3=2.5\cdot10$	[166–169]
	$En-CuOAc-C_2H_4(OH)_2$	$k_3=8.5\cdot10^2$	
	$NH_4OH-CuOAc-C_3H_5(OH)_3$	$k_3=2.1\cdot10^2$	
	$NaOH-CuOAc-C_3H_5(OH)_3$	$k_3=6.2\cdot10^4$	
$PH_3+3CuCl_2+3H_2O \rightarrow 3Cu+(HO)_2HPO+6HCl$	$CuCl-PhCN$	$k_3=4.2\cdot10^2$	[166–169]
	$CuCl-MeCN$	$k_3=6.2\cdot10^2$	
	$CuCl-Py$	$k_3=2.8\cdot10^2$	
	$CuCl-R_2HN$	$k_3=4.5\cdot10^2$	
	$CuCl-R_3N$	$k_3=3.2\cdot10^2$	
	$CuCl-NH_4OH$	$k_3=1.2\cdot10^{-1}$	
$PH_3+1.5Na_2PtCl_6+3H_2O \rightarrow 1.5Pt+(HO)_2HPO+3NaCl+6HCl$	$PtCl_2-ROH$	$k_3=3.2\cdot10^2$	[170]
	$PtBr_2-ROH$	$k_3=8.2\cdot10^2$	
	PtI_2-ROH	$k_3=2.5\cdot10^3$	
$PH_3+2KMnO_4+H_2O \rightarrow 2MnO_2+(OH)_2HPO+2KOH$	–	$k_2=4.5\cdot10^4$	[82–85, 94]
$AsH_3+KMnO_4 \rightarrow As+MnO_2+KOH+H_2O$	–	$k_2=6.5\cdot10^4$	[160]
$PH_3+3NaClO \rightarrow (HO)_2HPO+3NaCl$	$HgCl_2$	$k_3=2.5\cdot10^7$	[11, 156]
$PH_3+4Cl_2+4H_2O \rightarrow (HO)_3PO+8HCl$	–	$k_2=1.3\cdot10^6$	[11, 12, 65, 66]
$PH_3+3Br_2+3H_2O \rightarrow (HO)_2HPO+6HBr$	–	$k_2=1.4\cdot10^5$	[11, 12, 65, 66]
$PH_3+2I_2+2H_2O \rightarrow (HO)H_2PO+4HI$	–	$k_2=9.8\cdot10^4$	[11, 12, 65, 66]
$PH_3+4HClO \rightarrow (HO)_3PO+4HCl$	–	$k_2=5.1\cdot10^4$	[11, 12, 65, 66]
$PH_3+3HBrO \rightarrow (HO)_2HPO+3HBr$	–	$k_2=3.1\cdot10^4$	[11, 12, 65, 66]
$PH_3+2HIO \rightarrow (HO)H_2PO+2HI$	–	$k_2=4.0\cdot10^3$	[11, 12, 65, 66]
$AsH_3+3Cl_2+2H_2O \rightarrow HAsO_2+6HCl$	–	$k_2=9.8\cdot10^6$	[70]
$AsH_3+3Br_2+2H_2O \rightarrow HAsO_2+6HBr$	–	$k_2=1.2\cdot10^6$	[70]
$AsH_3+1.5I_2 \rightarrow As+3HI$	–	$k_2=4.8\cdot10^5$	[70]
$AsH_3+3HClO \rightarrow HAsO_2+H_2O+3HCl$	–	$k_2=5.8\cdot10^5$	[70]
$AsH_3+3HBrO \rightarrow HAsO_2+II_2O+3HBr$	–	$k_2=2.8\cdot10^5$	[70]
$AsH_3+1.5HIO \rightarrow As+1.5H_2O+1.5HI$	–	$k_2=3.4\cdot10^4$	[70]
$PH_3+2NaClO \rightarrow (HO)H_2PO+2NaCl$	$KI-HClO_4$ ($<10^{-6}$ M)	$k_4=5.5\cdot10^{18}$	[11, 12, 65, 66]
$PH_3+3NaClO \rightarrow (HO)_2HPO+3NaCl$	$KBr-HClO_4$ ($<10^{-6}$ M)	$k_4=4.5\cdot10^{15}$	[11, 12, 65, 66]
$AsH_3+1.5NaClO \rightarrow As+1.5NaCl+1.5H_2O$	$KI-HClO_4$ ($<10^{-6}$ M)	$k_4=4.5\cdot10^{14}$	[11, 12, 65, 66]
$AsH_3+3NaClO \rightarrow HAsO_2+H_2O+3NaCl$	$KBr-HClO_4$ ($<10^{-6}$ M)	$k_4=8.3\cdot10^{15}$	[11, 12, 65, 66]
$PH_3+2NaIO \rightarrow (HO)H_2PO+2NaI$	$HClO_4$ ($<10^{-9}$ M)	$k_3=4.0\cdot10^{13}$	[11, 12, 65, 66]
$PH_3+3NaBrO \rightarrow (HO)_2HPO+3NaBr$	$HClO_4$ ($<10^{-8}$ M)	$k_3=2.10\cdot10^{12}$	[11, 12, 65, 66]
$PH_3+3NaClO \rightarrow (HO)_2HPO+3NaCl$	$HClO_4$ ($<10^{-6}$ M)	$k_3=2.5\cdot10^{11}$	[11, 12, 65, 66]
	$KBr-HClO_4$ ($<10^{-6}$ M)	$k_4=7.5\cdot10^{15}$	
$PH_3+NaIO_3 \rightarrow (HO)_2HPO+NaI$	$HClO_4-KBr$	$k_4=7.2\cdot10^7$	[11, 12, 71–81]
	$HClO_4$	$k_3=6.7\cdot10^4$	
$PH_3+NaIO_4 \rightarrow (HO)_3PO+NaI$	$HClO_4$	$k_3=1.2\cdot10^4$	[71–81]
$PH_3+NaBrO_3 \rightarrow (HO)_2HPO+NaBr$	$HClO_4$	$k_3=2.7\cdot10^3$	[71–81]
	$HClO_4-KBr$	$k_4=9.2\cdot10^7$	
	$HClO_4-KBr-K_2MoO_4$	$k_5=3.5\cdot10^{13}$	
$PH_3+NaClO_3 \rightarrow (HO)_2HPO+NaCl$	$HClO_4$	$k_3=1.2\cdot10^2$	[71–81]
	$HClO_4-LiCl$	$k_4=2.1\cdot10^4$	
$PH_3+NaIO_4 \rightarrow (HO)H_2PO+NaI$	$HClO_4-KI$	$k_4=2.2\cdot10^8$	[71–81]
	$HClO_4-KI-K_2MoO_4$ ($<10^{-5}$ M)	$k_5=2.5\cdot10^{17}$	
	$HClO_4-KI-LiWO_4$ ($<10^{-5}$ M)	$k_5=3.6\cdot10^{17}$	
$PH_3+NaIO_3 \rightarrow (HO)H_2PO+NaI$	$HClO_4-KI$	$k_4=4.5\cdot10^9$	[71–81]
	$HClO_4-KI-LiWO_4$ ($<10^{-5}$ M)	$k_5=4.2\cdot10^{17}$	
$PH_3+8HNO_3 \rightarrow (HO)_3PO+8NO_2+4H_2O$	H_2SO_4	$k_3=2.0\cdot10^{-2}$	[11, 12, 82–86]
$PH_3+\frac{8}{3}HNO_3 \rightarrow (HO)_3PO+\frac{8}{3}NO+\frac{4}{3}H_2O$	$H_2SO_4-HNO_2$	$k_4=2.1\cdot10^3$	[11, 12, 82–86]
$PH_3+1.5HNO_3 \rightarrow (HO)_2HPO+0.75N_2O+0.75H_2O$	$H_2SO_4-HNO_2-AgNO_3$	$k_5=6.3\cdot10^8$	[11, 12, 82–86]
	$H_2SO_4-HNO_2-HgCl_2$	$k_5=2.3\cdot10^5$	
	$H_2SO_4-HNO_2-KI$	$k_5=3.2\cdot10^7$	
	$H_2SO_4-HNO_2-LiBr$	$k_5=8.5\cdot10^5$	
	$H_2SO_4-HNO_2-LiCl$	$k_5=6.7\cdot10^3$	
$PH_3+6NO \rightarrow (HO)_2HPO+3N_2O$	H_2SO_4	$k_3=2.2\cdot10$	[11, 12, 82–86]
	H_2SO_4-LiCl	$k_4=2.1\cdot10^2$	
	H_2SO_4-LiBr	$k_4=1.1\cdot10^4$	
	H_2SO_4-KI	$k_4=3.4\cdot10^6$	
$PH_3+6HNO_2 \rightarrow (HO)_2HPO+6NO+3H_2O$	H_2SO_4	$k_3=8.5\cdot10^2$	[11, 12, 82–86]
	H_2SO_4-LiCl	$k_4=6.7\cdot10^3$	
	H_2SO_4-LiBr	$k_4=8.5\cdot10^5$	
	H_2SO_4-KI	$k_4=2.3\cdot10^7$	
$PH_3+3HNO_2 \rightarrow (HO)_2HPO+1.5N_2O+1.5H_2O$	$H_2SO_4-AgNO_3$	$k_4=4.8\cdot10^6$	[11, 12, 82–86]
$AsH_3+HNO_3 \rightarrow As+NO+2H_2O$	$H_2SO_4-HNO_2$	$k_4=6.5\cdot10^5$	[11, 12, 82–86]
	$H_2SO_4-HNO_2-AgNO_3$	$k_5=8.5\cdot10^8$	

Table 1 (continued).

Reaction	Catalyst	Rate constant	Refs.
$PH_3+3H_2SO_4 \rightarrow 3SO_2+(HO)_2HPO+3H_2O$	H_2SO_4	$k_3=6.5\cdot10^2$	[2, 3]
	H_2SO_4–$HgSO_4$	$k_4=6.5\cdot10^5$	
$PH_3+2H_2SeO_3 \rightarrow 2Se+(HO)_3PO+2H_2O$	$HClO_4$	$k_3=2.5\cdot10^5$	[82–85, 88]
	$HClO_4$–LiCl	$k_4=8.2\cdot10^5$	
	$HClO_4$–LiBr	$k_4=3.2\cdot10^6$	
	$HClO_4$–KI	$k_4=1.4\cdot10^8$	
$PH_3+2H_2TeO_3 \rightarrow 2Te+(HO)_3PO+2H_2O$	HCl–LiCl	$k_4=9.1\cdot10^4$	[82–85, 88]
	HCl–LiBr	$k_4=2.2\cdot10^5$	
	HCl–KI	$k_4=1.8\cdot10^7$	
$PH_3+\frac{4}{3}Na_2Cr_2O_7+\frac{16}{3}H_2SO_4 \rightarrow (HO)_3PO+\frac{4}{3}Cr_2(SO_4)_3+\frac{4}{3}Na_2SO_4+\frac{16}{3}H_2O$	H_2SO_4	$k_3=1.3\cdot10^4$	[11, 12]
	H_2SO_4–$CuCl_2$–LiCl	$k_5=2.4\cdot10^6$	
$PH_3+Na_2Cr_2O_7+4H_2SO_4 \rightarrow (HO)_2HPO+Cr_2(SO_4)_3+Na_2SO_4+4H_2O$	H_2SO_4–$CuSO_4$–LiBr	$k_5=5.6\cdot10^7$	[89–91]
	H_2SO_4–$Fe_2(SO_4)_3$–LiBr	$k_5=6.8\cdot10^7$	
	H_2SO_4–LiBr	$k_4=3.3\cdot10^6$	
$PH_3+\frac{4}{6}Na_2Cr_2O_7+\frac{16}{6}H_2SO_4 \rightarrow (HO)H_2PO+\frac{4}{6}Cr_2(SO_4)_3+\frac{4}{6}Na_2SO_4+\frac{16}{6}H_2O$	H_2SO_4–KI	$k_4=4.6\cdot10^8$	[89–91]
$AsH_3+Na_2Cr_2O_7+4H_2SO_4 \rightarrow HAsO_2+Cr_2(SO_4)_3+Na_2SO_4+5H_2O$	H_2SO_4–LiCl	$k_4=4.5\cdot10^6$	[89–91]
	H_2SO_4–$CuCl_2$–LiCl	$k_5=3.5\cdot10^7$	
$AsH_3+Na_2Cr_2O_7+5H_2SO_4 \rightarrow As+Cr(HSO_4)_3+2NaHSO_4+4H_2O$	H_2SO_4 – $CuSO_4$ – LiBr	$k_5=4.5\cdot10^8$	[89–91]
	H_2SO_4–$Fe_2(SO_4)_3$–LiBr	$k_5=8.9\cdot10^8$	
	H_2SO_4–LiBr	$k_4=9.1\cdot10^6$	
	H_2SO_4–KI	$k_4=8.2\cdot10^8$	
	H_2SO_4	$k_3=6.5\cdot10^4$	
$PH_3+\frac{8}{3}KMnO_4+\frac{4}{3}H_2SO_4 \rightarrow \frac{8}{3}MnO_2+(HO)_3PO+\frac{4}{3}K_2SO_4+\frac{4}{3}H_2O$	H_2SO_4	$k_3=1.2\cdot10^{12}$	[82–85]
$AsH_3+2KMnO_4+H_2SO_4 \rightarrow 2MnO_2+HAsO_2+K_2SO_4+2H_2O$	H_2SO_4	$k_3=5.4\cdot10^{12}$	[94]
$PH_3+\frac{6}{5}KMnO_4+\frac{9}{5}H_2SO_4 \rightarrow \frac{6}{5}MnSO_4+(HO)_2HPO+\frac{3}{5}K_2SO_4+\frac{9}{5}H_2O$	H_2SO_4–LiBr	$k_4=3.2\cdot10^{13}$	[94]
$PH_3+\frac{4}{5}KMnO_4+\frac{6}{5}H_2SO_4 \rightarrow \frac{4}{5}MnSO_4+(HO)H_2PO+\frac{2}{5}K_2SO_4+\frac{6}{5}H_2O$	H_2SO_4–KI	$k_4=2.1\cdot10^{14}$	[94]
$AsH_3+\frac{3}{5}KMnO_4+\frac{4.5}{5}H_2SO_4 \rightarrow \frac{1.5}{5}K_2SO_4+\frac{3}{5}MnSO_4+\frac{5}{12}H_2O+As$	H_2SO_4–LiBr	$k_4=8.4\cdot10^{13}$	[94]
	H_2SO_4–KI	$k_4=7.9\cdot10^{14}$	
$PH_3+8NH_4VO_3+12H_2SO_4 \rightarrow (HO)_3PO+8VOSO_4+4(NH_4)_2SO_4+12H_2O$	H_2SO_4	$k_3=5.0\cdot10^5$	[95]
	H_2SO_4–LiBr	$k_4=8.2\cdot10^6$	
	H_2SO_4–KI	$k_4=3.0\cdot10^9$	
$PH_3+8FeCl_3+4H_2O \rightarrow 8FeCl_2+(HO)_3PO+8HCl$	HCl	$k_3=1.2\cdot10$	[102–104]
$PH_3+3Fe_2(SO_4)_3+3H_2O \rightarrow 6FeSO_4+(HO)_2HPO+3H_2SO_4$	Ag_2SO_4	$k_3=3.2\cdot10^7$	[105–107]
$PH_3+2Fe_2(SO_4)_3+2H_2O \rightarrow 4FeSO_4+(HO)H_2PO+2H_2SO_4$	H_2SO_4–KI	$k_4=1.2\cdot10^8$	[105–107]
$PH_3+6FeX_3+3H_2O \rightarrow 6FeX_2+(HO)_2HPO+6HX$	HCl–KI	$k_4=2.3\cdot10^5$	[105–107]
	HBr–KI	$k_4=4.2\cdot10^6$	
$AsH_3+3FeCl_3 \rightarrow As+3FeCl_2+3HCl$	HCl	$k_3=2.6\cdot10^3$	[105–107]
	HCl–KI	$k_4=4.6\cdot10^5$	
$PH_3+8Ce(SO_4)_2+4H_2O \rightarrow (HO)_3PO+4Ce_2(SO_4)_3+4H_2SO_4$	HCl–LiCl	$k_4=2.4\cdot10^3$	[108, 109]
	HCl–LiBr	$k_4=4.2\cdot10^5$	
	HCl–KI	$k_4=3.4\cdot10^7$	
$PH_3+3CuSO_4+3H_2O \rightarrow 3Cu+3H_2SO_4+(HO)_2HPO$	Cu_2SO_4	$k_3=1.2\cdot10^{-1}$	[113–115]
$PH_3+8CuCl_2+4H_2O \rightarrow 8CuCl+8HCl+(HO)_3PO$	HCl–CuCl–LiCl	$k_5=2.5\cdot10^2$	[134–138]
	HCl–CuCl–$PdCl_2$	$k_5=3.4\cdot10^9$	
	HCl–CuCl–$HgCl_2$	$k_5=8.6\cdot10^9$	
$PH_3+6CuCl_2+3H_2O \rightarrow 6CuCl+6HCl+(HO)_2HPO$	HCl–CuCl–LiBr	$k_5=3.3\cdot10^5$	[157–159]
$PH_3+4CuCl_2+2H_2O \rightarrow 4CuCl+4HCl+(HO)H_2PO$	HCl – CuCl – KI	$k_5=5.8\cdot10^9$	[120–126]
$AsH_3+3CuCl_2 \rightarrow As+3CuCl+3HCl$	HCl–CuCl–LiCl	$k_5=3.2\cdot10^4$	[111, 112,
	HCl–CuCl–LiBr	$k_5=5.4\cdot10^8$	120–126, 161]
	HCl–CuCl–KI	$k_5=6.2\cdot10^{12}$	
$PH_3+\frac{8}{3}AuCl_3+4H_2O \rightarrow \frac{8}{3}Au+8HCl+(HO)_3PO$	HCl–AuCl–LiCl	$k_5=8.2\cdot10^9$	[141]
	HCl – AuCl – LiBr	$k_5=7.8\cdot10^{11}$	
	HCl–AuCl–KI	$k_5=6.8\cdot10^{12}$	
$PH_3+1.5Na_2PtCl_6+3H_2O \rightarrow 1.5Pt+(HO)_2HPO+3NaCl+6HCl$	HCl–$PtCl_2$–KI	$k_5=5.6\cdot10^{11}$	[142]
	HCl–$PtCl_2$–LiBr	$k_5=6.4\cdot10^9$	
	HCl–$PtCl_2$–LiCl	$k_5=4.2\cdot10^7$	
$PH_3+4PdCl_2+4H_2O \rightarrow Pd+(HO)_3PO+8HCl$	HCl–$PdCl_2$–LiCl	$k_5=4.5\cdot10^8$	[138–140]
$PH_3+4H_2O_2 \rightarrow (HO)_3PO+4H_2O$	HCl–HBr	$k_4=2.6\cdot10^4$	[144–146]
	HCl–HI	$k_4=1.5\cdot10^6$	
	HCl–$CuBr_2$	$k_4=8.4\cdot10^5$	
	HCl–$FeBr_3$	$k_4=5.2\cdot10^5$	
$AsH_3+3H_2O_2 \rightarrow HAsO_2+4H_2O$	HCl–LiCl	$k_4=3.2\cdot10^5$	[146]
	HCl–LiBr	$k_4=4.8\cdot10^6$	
	HCl–$FeBr_3$	$k_4=1.5\cdot10^8$	
	HCl–$FeCl_3$	$k_4=2.2\cdot10^6$	

Table 1 (continued).

Reaction	Catalyst	Rate constant	Refs.
$AsH_3+1.5H_2O_2 \rightarrow As+3H_2O$	HCl–KI	$k_4=7.8\cdot10^8$	[146]
$AsH_3+3Na_2S_2O_8+3H_2O \rightarrow HAsO_2+3H_2SO_4+3Na_2SO_4$	H_2SO_4–KI	$k_4=3.2\cdot10^8$	[146]
$PH_3+4Na_2S_2O_8+4H_2O \rightarrow (HO)_3PO+4Na_2SO_4+4H_2SO_4$	$HClO_4$–KI	$k_4=1.2\cdot10^8$	[146]
$PH_3+1.5O_2 \rightarrow (HO)_2HPO$	$HClO_4$–LiBr	$k_4=6.2\cdot10^6$	[162–165]
	KI–C	$k_1=2.3$	
	PdO–C	$k_1=1.8$	
	$CuCl_2$–$PdCl_2$–C	$k_1=1.2\cdot10$	
	$CuCl_2$–$HgCl_2$–C	$k_1=2.6\cdot10$	
$AsH_3+1.5O_2 \rightarrow HAsO_2+H_2O$	KI–C	$k_1=4.5$	[163]
$Ph_3+8CuCl_2+4ROH \rightarrow (RO)_3PO+RCl+8CuCl+7HCl$	CuCl–LiCl	$k_3=2.4\cdot10^3$	[166–172]
$PH_3+6CuCl_2+3R'OH \rightarrow (R'O)_2HPO+6CuCl+R'Cl+5HCl$	CuCl–LiCl	$k_3=1.2\cdot10^3$	[173]
$PH_3+3Na_2PtCl_6+3ROH \rightarrow 3Na_2PtCl_4+(RO)_3P+6HCl$	$PtCl_2$	$k_3=4.3\cdot10^2$	[170]
	$PtBr_2$	$k_3=1.2\cdot10^3$	
	PtI_2	$k_3=4.6\cdot10^3$	
$PH_3+6CuCl_2+3R_2HN \rightarrow 6CuCl+(R_2N)_3P+6HCl$	CuCl	$k_3=9.2\cdot10^3$	[174]
$PH_3+3CH_3CN+6Cu(OAc)_2 \rightarrow 6CuOAc+6HOAc+(CNCH_2)_3P$	CuOAc	$k_3=4.8\cdot10^2$	[166–171]
$PH_3+3(EtCH_2CH_2)_3N+18Cu(OAc)_2 \rightarrow 18CuOAc+18HOAc+[(Et-CH=CH)_2(PrCH)N]_3P$	CuOAc	$k_3=5.6\cdot10^2$	[166–171]
$PH_3+3C_5H_5N+6Cu(OAc)_2 \rightarrow 6CuOAc+6HOAc+(o\text{-}C_5H_4N)_3P$	CuOAc	$k_3=6.2\cdot10^2$	[166–171]
$PH_3+3C_6H_5CN+6Cu(OAc)_2 \rightarrow 6CuOAc+6HOAc+(o\text{-}C_6H_4CN)_3P$	CuOAc	$k_3=8.2\cdot10^2$	[166–171]
$PH_3+3C_6H_6+6Cu(OAc)_2 \rightarrow 6CuOAc+(C_6H_5)_3P$	CuOAc	$k_3=1.5\cdot10^3$	[166–171]
	Py		
$PH_3+3Cu(OAc)_2+3CH_3(CH_2)_nOH \rightarrow [HO(CH_2)_{n+1}]_3P+3Cu+6AcOH$	CuOAc	$k_3=6.8\cdot10^2$	[173]
$PH_3+3Na_2PtCl_4+3RCH_2OH \rightarrow (HOCHR)_3P+3Pt+6NaCl+6HCl$	—	$k_2=2.8\cdot10$	[170]

The catalytic activity of catalysts deposited on carbon (C) in reactions involving the oxidation of PH_3 and AsH_3 by oxygen is characterised by first-order rate constants (k_1, min^{-1}). The reactivity of substances oxidising PH_3 and AsH_3 without catalysts is characterised by second-order rate constants:

$$k_2 = W/[Ox][Red], \text{ litre mol}^{-1} \text{ min}^{-1},$$

where W is the reaction rate (mol litre^{-1} min^{-1}) and [Ox] and [Red] are the molar concentrations of the oxidant and reductant in the liquid phase.

The catalytic activity of hydrogen ions and metal complexes is characterised by third-order rate constants:

$$k_3 = W/[Ox][Red][H^+], \text{ litre}^2 \text{ mol}^{-2} \text{ min}^{-1},$$

$$k_3 = W/[Ox][Red][M^{n+}], \text{ litre}^2 \text{ mol}^{-2} \text{ min}^{-1},$$

where $[H^+]$ and $[M^{n+}]$ are the molar concentrations of hydrogen and metal ions.

The catalytic activity of two-component mixed systems containing H^+ and X^- ($X^- = Cl^-, Br^-, I^-$) ions is characterised by fourth-order rate constants:

$$k_4 = W/[Ox][Red][H^+][X^-], \text{ litre}^3 \text{ mol}^{-3} \text{ min}^{-1},$$

where $[X^-]$ is the molar concentration of X^- ions.

The catalytic activity of three-component mixed systems incorporating the H^+, X^-, and M^{n+} ions is characterised by fifth-order rate constants:

$$k_5 = W/[Ox][Red][H^+][X^-][M^{n+}], \text{ litre}^4 \text{ mol}^{-4} \text{ min}^{-1}.$$

The rate constants were measured with a relative error of $\pm 10\%$. The catalysts based on *d* metal ions in the highest oxidation states [W(VII), Mo(VII)] propagate the process, like hydrogen ions, via an associative mechanism. They activate oxidants via coordination, which increases their redox potential and polarity.

The ions of *d* metals in intermediate oxidation states [Cu(II), Pd(II), Ag(I)] and alkali metal halides effect the reaction via a separate stage (oxidation-reduction) mechanism. Arsine and phosphine reduce the halogens and metal ions to halide ions and the metals, which oxidants regenerate the initial states of the metal ions and the halogens.

The complexes of *d* metals in the highest oxidation states [Hg(II), Cu(I)] activate phosphine and arsine via coordination. By virtue of the close positions of the *d* and *s* orbitals and the tendency towards a two-sided exchange interaction, they stimulate the $sp^3 \rightarrow sp^3d$ hybridisation of the phosphorus atom in PH_3. The oxygen compounds of high valence metal and non-metal ions oxidise phosphine via an outer-sphere mechanism, oxygen ions acting as a bridge, while metal complexes in an intermediate valence state oxidise phosphine via an inner-sphere mechanism.

In contrast to metal ions, halide ions are poorly coordinated to non-polar oxidants. Alkali metal halides therefore exhibit a high catalytic activity only in the presence of protic acids or metal ions which intensify the electrophilicity of oxidants.

In order to reduce the acidity of the medium, mixed systems containing a protic and an aprotic acid simultaneously are frequently employed. Thus negatively charged oxidants, present in the form of anions, oxidise PH_3 and AsH_3 acted upon jointly by hydrogen, metal, and halide ions. With the aid of H^+ and M^{n+} ions, it is possible to ensure in a three-component system in a weakly acid medium an effective positive charge in the oxidant, which is necessary for the manifestation of the catalytic properties of halide ions.

In neutral and alkaline solutions, the complexes of *d* metals in an intermediate valence state, which are soluble in such media, exhibit a high reactivity in relation to PH_3. The solubility of metal ions at high pH is increased sharply by ammonia, amines, polyhydric alcohols and hydroxyacids. An increased rate of oxidation of PH_3 by metal complexes is attained in an alkaline solution by virtue of the joint action of hydroxide and metal ions, generating the phosphite ion, which is a stronger reductant than PH_3. In alkaline systems, the reduced metal complexes are regenerated by oxygen. Metal complexes are therefore highly active catalysts of the oxidation of PH_3 by oxygen in an alkaline medium.

The phosphide ion is generated not only in an alkaline solution but also in a neutral medium under the influence of metal complexes containing "hard" ligands (AcO^-, SO_4^{2-}, Py, NR_3). Such ligands induce the inner-sphere acid–base decomposition of phosphine complexes of metals with formation of metal phosphides. The acid–base mechanism predominates as a result of the strengthening of the bonds between the metal and the phosphorus atom of PH_3. Phosphine is converted into the phosphite ion and acquires nucleophilic reactivity. In the presence of "soft" ligands (Cl^-, Br^-), phosphine becomes an electrophile by virtue of the manifestation of an effective positive charge on the phosphorus atom and reacts vigorously with the nucleophiles in the coordination sphere. By varying the nature of the ligands, it is therefore possible to induce either nucleophilic or electrophilic reactivity in the coordinated phosphine.

In the presence of Cl^-, Br^-, and I^- ions in aqueous solutions, phosphine reacts with coordinated H_2O molecules to form the products of its oxidative hydroxylation [$(OH)_3PO$, $(OH)_2HPO$, $(OH)H_2PO$]. In non-aqueous solutions with metal salts, the previously unknown reactions involving the O-, N-, and C-phosphorylation of organic compounds proceed selectively and rapidly. In alcoholic solutions of copper(II), platinum(IV), and iron(III) halides, phosphine interacts with the inner-sphere ROH molecules (R = Me, Et, Pr, iso-Pr, Bu, iso-Bu, Pe, iso-Pe, Oct) with formation of the products of the oxidative alkoxylation of phosphine—trialkyl phosphates [$(RO)_3PO$] and dialkyl phosphites [$(RO)_2HPO$]. In solutions of $CuCl_2$ or $Cu(OAc)_2$ in primary or secondary amines (NRH_2, NR_2H), the products of the oxidative amination of phosphine are formed—phosphorus triamides [$P(NR_2)_3$ and $P(NRH)_3$]. In alcoholic solutions of PtX_2 and $Cu(OAc)_2$, the products of the oxidative hydroxyalkylation of phosphine are obtained—the tris(α-hydroxyalkyl)phosphines $P(HOCRH)_3$ and $P[HO(CH_2)_n]_3$. In solutions of $Cu(OAc)_2$ in acetonitrile (MeCN) and benzonitrile (PhCN), the products of the oxidative cyanomethylation [tricyanomethylphosphine $P(CNCH_2)_3$] and cyanoarylation [tris(*o*-cyanoaryl)phosphine $P(o\text{-}CNC_6H_4)_3$] are formed. The product of the oxidative C-phosphorylation of pyridine by phosphine is synthesised in pyridine solutions of $CuCl_2$ or $Cu(OAc)_2$—tris(*p*-pyridyl)phosphine $P(o\text{-}C_5H_4N)_3$.

In mixed non-aqueous solutions of copper(II) salts, a mixture of products is obtained, in contrast to single component solutions. Thus the products of the oxidative C-phosphorylation of benzene (PPh_3) and pyridine [$P(o\text{-}C_5H_4N)_3$] are formed in solution in C_6H_6–C_5H_5N in the presence of $CuCl_2$ or $Cu(OAc)_2$.

The processes involving the oxidative O-, N-, and C-phosphorylation of organic compounds by phosphine and $CuCl_2$ and $Cu(OAc)_2$ solutions are accelerated by copper(I) ions like other reactions of PH_3. The yield of the products of the oxidative O-, N-, and C-phosphorylation by phosphine falls sharply after the addition of H_2O (> 5%), since there is an increase in the yield of inorganic phosphates.

In processes involving the O-, N-, and C-phosphorylation by phosphine, copper(II) ions are reduced to copper(I) ions or zerovalent copper. These products are readily regenerated by oxygen. A solution containing $CuCl_2$ or $Cu(OAc)_2$ after regeneration can be used again for the absorption of PH_3. The copper salts are separated by vacuum distillation from the products of the oxidative phosphorylation by phosphine and can be reused.

The new oxidative O-, N-, and C-phosphorylation reactions are much simpler than those known previously. Either metallated organic products and phosphorus halides or alkali metal phosphides and halo-derivatives of organic compounds participate in these reactions.[175,176]

By virtue of the high rates of the new oxidative O-, N-, and C-phosphorylation reactions, gases with a low PH_3 content (< 1.0%), for example, the effluent gases from phosphorus and hypophosphite factories, can be used as the raw materials in these processes.[4]

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Translated from *Uspekhi Khimii* 60 1229–1254 (1991) U.D.C. 546.24.07

The structure and the electron-donating and electron-accepting properties of tellurium tetrahalides and halogen-containing σ-telluranes

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ABSTRACT. The review gives a systematic account and surveys the available data on the structures of tellurium tetrahalides, σ-telluranes, and the complexes based on them.

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I. Introduction

The great interest shown in the last two decades in the chemistry of organotellurium compounds is due to the possibility of using them in various branches of science and engineering[1,2] and in preparative organic chemistry.[3–5] Derivatives of tetracoordinate tellurium (σ-telluranes) of the type $RTeX_3$ and R_2TeX_2, where X is an electronegative substituent, occupy a key position in the chemistry of organotellurium compounds. It is possible to convert them comparatively readily into various types of derivatives of dicoordinate, tricoordinate, pentacoordinate, and hexacoordinate tellurium.[1,2] σ-Telluranes are distinguished by an increased stability compared with the selenium and especially sulphur compounds with analogous structures. The presence of lone electron pairs and unoccupied *d*-orbitals in the tellurium atom in these compounds as well as in tellurium tetrahalides is responsible for their electron-donating properties (in interactions with Lewis acids) and electron-accepting properties (in interactions with Lewis bases). This review gives a systematic account and surveys the available data on the structures of tellurium tetrahalides and σ-telluranes in the crystalline state and in solutions and of the complexes based on them.

II. The structures of tellurium tetrahalides and σ-telluranes in the crystal state and in solutions

1. The structure of tellurium tetrahalides in the crystal state and in solutions

In conformity with the theory of valence electron pair repulsion,[6] tellurium tetrahalides should have a trigonal bipyramidal (TBP) structure with a lone electron pair (LP) as a phantom ligand occupying one of the equatorial positions. Such a structure of the above compounds has been confirmed by studies on $TeCl_4$ in the gas phase by electron diffraction.[7] The tellurium tetrachloride molecule has the TBP structure with an average Te–Cl length of 2.33 Å. According to the authors,[7] the $Cl_{eq}-Te-Cl_{eq}$ bond angle is probably less than 120° but more than 90°, while the $Cl_{ax}-Te-Cl_{ax}$ bond angle is about 170°.

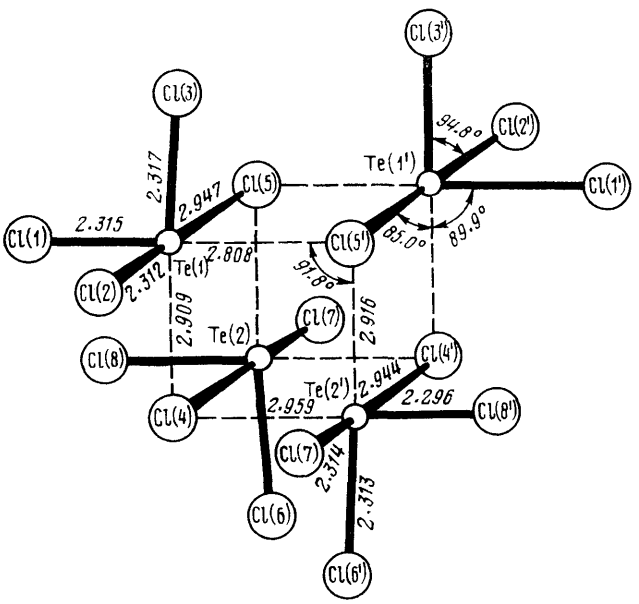


Figure 1. The structure of the tetramer Te_4Cl_{16}.[9]

However, as a consequence of secondary interactions involving tellurium atoms, the structure of tellurium tetrahalides in the crystal state is not quite so evident. Structures of all tellurium

tetrahalides have now been investigated by X-ray diffraction: the tetrachloride,[8–10] the tetrabromide,[8,11] the tetraiodide,[12–14] and the tetrafluoride.[15,16]

The crystal structure of tellurium tetrachloride is made up of isolated Te_4Cl_{16} tetramers[9,10] (Fig. 1). Each tellurium atom is joined to three terminal chlorine atoms by bonds whose average length is 2.311 Å, which is close to the Te–Cl bond length found in gaseous $TeCl_4$ (2.33 Å). The terminal chlorine atoms and the tellurium atom form a trigonal pyramid with average bond angles of 94.8°. The tellurium atom is also joined to three bridging chlorine atoms by bonds 2.929 Å long, which complete the environment around the tellurium atom to form a highly distorted octahedron. The average $Cl_{bridge}–Te–Cl_{bridge}$ bond angle is 85°.

Comparison of the data for tellurium tetrachloride with X-ray diffraction data for compounds with bonds of saturated types—ionic in $[TeCl_3]^+[AlCl_4]^-$,[17] where the tellurium atom has a distorted octahedral configuration ($Te–Cl_{term}$ = 2.276 Å, Te...Cl = 3.062 Å), and covalent in the $[TeCl_6]^{2-}$ ion[18] (Te–Cl = 2.54 Å) led the authors[10] to the conclusion that bonding intermediates between the two extreme types of bonds described above takes place in $TeCl_4$ and that there is only partial charge transfer from the bridging chlorine atoms to the tellurium atoms.

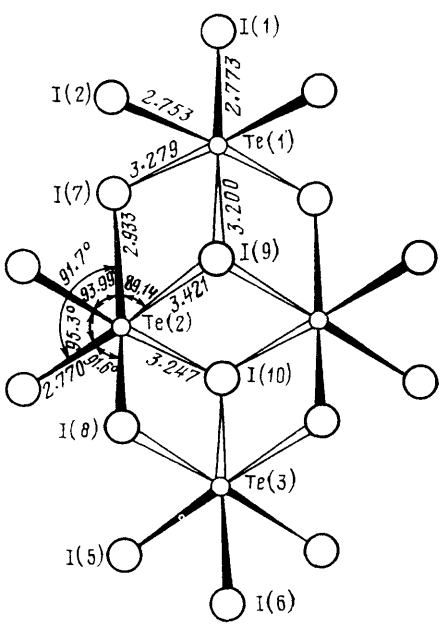


Figure 2. The structure of the tetramer $Te_{14}I_{16}$.[13]

Tellurium tetrabromide has a similar structure.[11] In the tetramers Te_4Br_{16}, the bond lengths are $Te–Br_{term}$ = 2.496 Å and $Te–Br_{bridge}$ = 3.054 Å.

Although the TeI_4 structure[13,14] (Fig. 2) is made up of $(TeI_4)_4$ tetramers, like those of $TeCl_4$ and $TeBr_4$, it is not isomorphous in relation to them. This structure consists of four edge-linked TeI_6 octahedra. As a result of this and in contrast to $TeCl_4$ and $TeBr_4$, three types of iodine atoms were detected in tellurium tetraiodide: those linked to a single tellurium atom (terminal bonds whose length is 2.769 Å), those linked to two tellurium atoms (bridged bonds whose length is 3.108 Å), and those linked to three tellurium atoms (pyramidal bonds whose length is 3.232 Å). The comparatively short intermolecular I...I bonds (3.870, 3.892, and 3.932 Å) join together separate tetramers.[14]

Tellurium tetrafluoride has a different structure.[15,16] The tellurium atom in this compound has three terminal fluorine atoms (average bond length 1.866 Å) and two bridging fluorine atoms with an average bond length of 2.181 Å. The fluorine atoms are located at the vertices of a distorted square pyramid and the individual TeF_5^- fragments are joined via the bridging fluorine atoms, forming infinite chains (Fig. 3). When account is taken of the lone pairs, the coordination around tellurium can be regarded as octahedral.

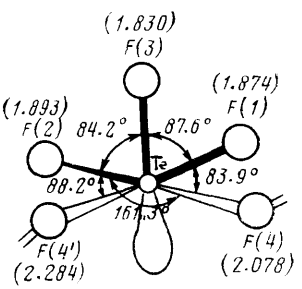


Figure 3. The structure of TeF_4.[15,16]

The availability of crystallographic data permitted the correct interpretation of spectroscopic data, in particular the ^{35}Cl NQR spectrum of $TeCl_4$,[19–21] the ^{81}Br NQR spectrum of $TeBr_4$,[21] and the ^{127}I NQR spectrum of TeI_4.[22,23] The NQR spectrum of $TeCl_4$ consists of six lines, which can be assigned to covalently linked chlorine atoms forming part of the composition of two non-equivalent $TeCl_3$ groups in the tetrameric structure (bridging chlorine atoms which are largely ionic are not manifested in the spectrum).[20,21] The ^{81}Br NQR spectrum of $TeBr_4$ is similar.[21] In the ^{127}I NQR spectrum, 10 non-equivalent iodine atoms can be detected in conformity with crystallographic data. Of these, six were identified as terminal atoms, two were identified as bridging atoms, and two were identified as pyramidal iodine atoms, which follows from their quadrupole splitting constants and the asymmetry parameters.[23]

X-Ray diffraction data for tellurium tetrahalides, and in the first place tellurium tetrachloride,[8–10] made it possible to explain the earlier extremely contradictory conclusions, obtained mainly with the aid of IR spectroscopy, concerning the structures of these compounds in the crystal state and in solutions. On the basis of the electrical conductivity of $TeCl_4$ in the melt, determined by dissociation in accordance with the scheme $TeCl_4 \rightleftarrows TeCl_3^+ + Cl^-$,[24] and also comparison of the IR and Raman bands of TeX_4 in the solid state[25–28] with the spectra of complexes of tellurium tetrahalides containing $TeCl_3^+$ ions,[17,26,28–30] it was concluded that the compound has an ionic structure ($TeCl_3^+Cl^-$)., This finding is confirmed by the results of conductimetric measurements for $TeCl_4$ solutions in a number of solvents.[29,31] Many other workers[32–34] concluded, on the basis of the same data, that tellurium tetrahalide has a covalent structure both in the solid state and in solutions.

Table 1. The average bond lengths (Å) and bond angles (degrees) in the molecules of the σ-telluranes $RTeX_3$.

Compound	Te–X_{term}	Te–X_{bridge}	Te–C	C–Te–X_{term}	C–Te–X_{bridge}	Type of associated species	Te...X	Refs.
$C_2F_5TeF_3$	1.872	2.193	2.20	88.8	77.6	polymer	–	[41]
$ClCH_2CH_2TeCl_3$	2.386	2.717	2.164	92.7	82.5	"	–	[42]
$C_6H_5TeCl_3$	2.377	2.755	2.122	91.68	85.46	"	–	[43]
$4\text{-}C_2H_5OC_6H_4TeCl_3$	2.396	2.749	2.12	91.0	88.2	"	–	[44]
$4\text{-}C_6H_5OC_6H_4TeCl_3$	2.374	2.768	2.111	91.3	87.2	dimer	3.702	[45]
$CH_2(TeCl_3)_2$	2.351	2.760	2.120	90.8	75.6	monomer	–	[46]
$C_6H_5TeBr_3$	2.526	2.829	2.140	92.2	85.4	polymer	–	[50]
$4\text{-}C_2H_5OC_6H_4Br_3$	2.531	2.932	2.10	93.6	88.4	dimer	4.143	[44]
$2\text{-}C_6H_5C_6H_4TeBr_3$	2.490 2.661 [a]	–	2.136	–	–	monomer	3.713	[51]
$1,2\text{-}(Br_3Te)_2\text{-cyclo-}C_6H_{10}$	2.541	2.88	2.224	92.4	83.2	"	–	[52]
$4\text{-}CH_3OC_6H_4TeI_3$	2.788	3.153	2.15	94.6	89.7	dimer	3.827	[44]
$2\text{-}C_6H_5C_6H_4TeI_3\text{-}\alpha$	2.769 2.966 [a]	–	–	–	–	monomer	[b]	[54]
$2\text{-}C_6H_5C_6H_4TeI_3\text{-}\beta$	2.748; 2.928	–	2.153	–	–	"	[c]	[55]

[a] The first figure denotes the Te–X_{eq} bond length and the second denotes the average Te–X_{ax} bond length. [b] The Te...I = 3.703 Å and I...I = 3.337 Å secondary bonds. [c] The I...I = 3.239, 3.772 Å secondary bonds.

The weak bonding of the structural units in the TeX_4 tetramers in the solid phase is responsible, according to Buss and Krebs,[10] for the ready decomposition, both homolytic and heterolytic, depending on the temperature, the nature of the solvent, and concentration. This explains many of the properties of the melt and solutions of $TeCl_4$, in particular the electrical conductivities and the solubilities in polar and non-polar solvents. In the latter (benzene, toluene), $TeCl_4$ is monomeric,[34,35] exhibiting limited association with increase in concentration, although according to the results of Greenwood et al.,[36] $TeCl_4$ and $TeBr_4$ are trimeric in the solvents indicated. Data concerning the structure of $TeCl_4$ in solutions in polar solvents are again contradictory. Some investigators[30,34,37] believe that $TeCl_4$ is not ionised in acetonitrile and propionitrile, while others[31,36] concluded that ionisation takes place in these and other polar solvents (acetone) with formation of $TeCl_3^+$ and Cl^- or of $L_2TeX_3^+$ and X^-, where L is a solvent molecule. At the same time, there is no doubt about the presence of complexes of the latter type in highly electron-donating solvents [dimethyl sulphoxide (DMSO), dimethylformamide (DMF), and pyridine].

2. The structure of σ-telluranes

Derivatives of tetracoordinate tellurium, which can be formally regarded as the products of the substitution of one ($RTeX_3$) or two (R_2TeX_2) halogen atoms in molecules of tellurium tetrahalides, have the common name σ-telluranes. The non-equivalence of the substituents at the tellurium atom in these compounds poses the problem of their preferential disposition (axial or equatorial). According to the polarity rule,[38] which has been extended to σ-telluranes,[39,40] the axial positions in the trigonal bipyramids in σ-telluranes are always occupied by the most electronegative substituents—the halogen atoms. This structure of organic derivatives of tetracoordinate tellurium has been confirmed by X-ray diffraction data.

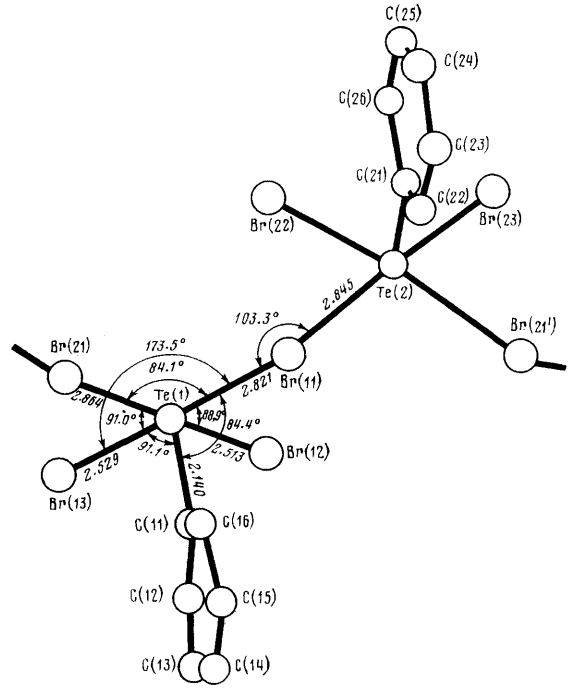


Figure 4. Geometry of the phenyltellurium tribromide molecule.[50]

(a) The structure of the σ-telluranes $RTeX_3$

The structures of a considerable number of organyl tellurium trihalides have now been investigated by X-ray diffraction: the trifluorides,[41] trichlorides,[42–49] tribromides,[44,50–53] and triiodides.[44,54,55] The principal data on the geometries of these compounds are presented in Table 1.

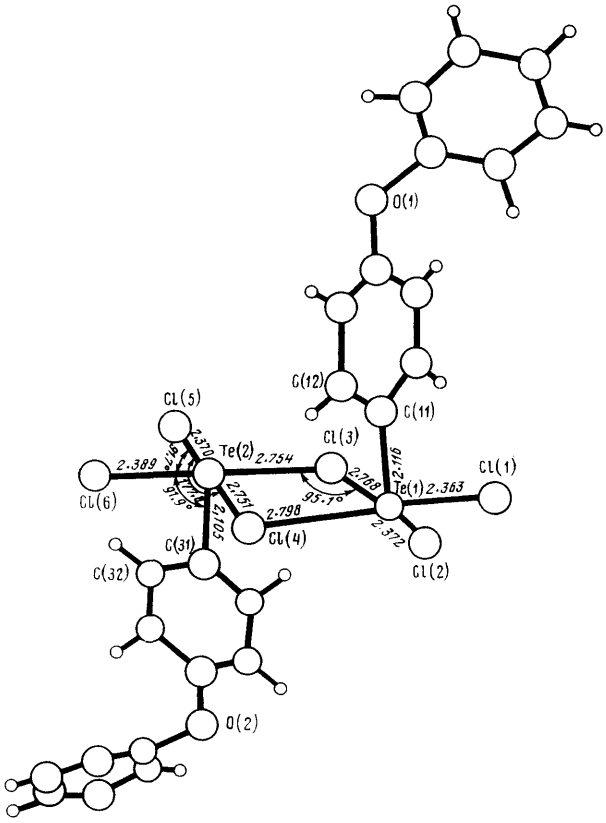


Figure 5. Geometry of the 4-phenoxyphenyltellurium trichloride molecule.[45]

As for tellurium tetrahalides, the real structure of the majority of the σ-telluranes $RTeX_3$ in the crystal state barely corresponds to the theoretically predicted trigonal bipyramidal structure. When account is taken of secondary interactions, the principal structural unit in these compounds $CTeX_4$, containing a pentacoordinate tellurium atom, has the square pyramidal configuration of the bonds around the tellurium atom with the organic group in the apical position. The tellurium atom is located virtually in the plane of the base of the square pyramid formed by the four halogen atoms, deviating slightly from it. Two halogen atoms form shorter (terminal) bonds, while the other two form longer (bridge) bonds which link the tellurium atoms of individual pyramids into polymeric or dimeric structures. The individual dimers are joined to one another by weak secondary Te...X bonds whose lengths greatly exceed those of the $Te-X_{bridge}$ bonds. The structures of typical representatives of polymeric and dimeric organyl tellurium trihalides (phenyltellurium tribromide[50] and 4-phenoxyphenyltellurium trichloride[45]) are presented in Figs. 4 and 5.

The σ-telluranes with two trihalotelluro-groups located at the same [bis(trichlorotelluro)methane[46]] (Fig. 6) or neighbouring [1,2-bis(tribromotelluro)cyclohexane][52] carbon atoms have the monomeric structure. Each tellurium atom in these compounds has a square pyramidal geometry with the exception that both Te–X bridge bonds are intramolecular. The structure of bis(trichlorotelluro)methane is presented in Fig. 6. It is noteworthy that the intermolecular Te...Te contacts in the above compounds are much shorter than in the σ-telluranes with a single TeX_3 group and amount to 3.417 Å in bis(trichloro)methane, for example.

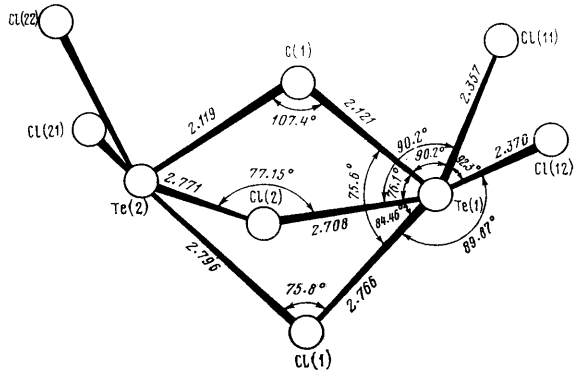


Figure 6. Geometry of the bis(trichlorotelluro)methane molecule.[46]

2-Biphenylyltellurium trihalide, containing the bulky 2-biphenylyl group, also has a monomeric structure with a trigonal-bipyramidal disposition of the ligands around the tellurium atom.[51,54,55] The geometry of the 2-biphenylyltellurium tribromide molecule[51] is illustrated in Fig. 7. The axial positions in the trigonal-bipyramidal structures of these compounds are occupied by halogen atoms, the angles between which are 178.5° for the tribromide, 176.5° for the α-modification of 2-biphenylyltellurium triiodide, and 176.0° for the β-modification. In other words, electronegative axial ligands are repelled to a greater extent from the lone pair than from the organic groups. It is of interest to note that, in conformity with the polarity rule,[38] the axial Te–X bonds are much longer than the equatorial bonds (Table 1). Short intermolecular Te...C contacts are observed in the molecules of 2-biphenylyltellurium trihalides, their length being 2.945 Å for the tribromide and 3.32 and 3.18 Å for the α- and β-triiodides respectively (the sum of the van der Waals radii of tellurium and carbon is 3.90 Å [56]). These contacts are responsible for the ease of the conversion of 2-biphenylyltellurium trihalides into 5,5-dihalodibenzotellurophenes on heating.[57] Intermolecular Te...X contacts have been detected in 2-biphenylyltellurium trihalides: 3.713 Å for the tribromide and 3.703 Å for the β-triiodide. Although they are smaller than the sums of the van der Waals radii of the corresponding elements (4.15 Å for Te and Br and 4.35 Å for

Te and I), they greatly exceed the lengths of the Te–X_{bridge} bonds (Te–Br = 2.829–2.932 Å, Te–I = 3.153 Å). The structures of the α- and β-modifications of 2-biphenylyltellurium triiodide are similar, differing only in the intermolecular contacts involving heavy atoms. Whereas β-modification contains, together with the Te...I secondary contacts, also I...I contacts whose length is 3.337 Å,[55] I...I contacts, whose lengths are 3.239 Å and 3.772 Å, were found in the α-modification.[54] The difference between the natures of these intermolecular interactions affects the colour of the compounds: the crystals of the β-modification are red and those of the α-modification are black.

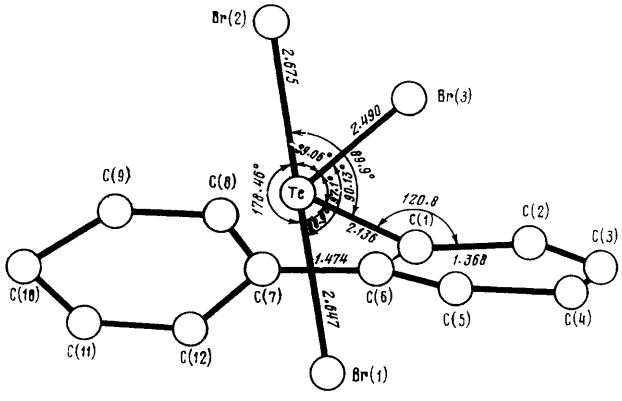


Figure 7. Geometry of the 2-biphenylyltellurium tribromide molecule.[51]

The degree of association and, what is most important, the molecular geometry of organyltellurium trihalides change significantly when they contain electron-donating atoms (oxygen, nitrogen) capable of intramolecular coordination to the tellurium atom. 8-Ethoxy-4-cyclooctenyltellurium trichloride[47] (Fig. 8) has a square pyramidal structure, like other organyltellurium trichlorides whose apex is occupied by a carbon atom. However, whereas in other σ-telluranes $RTeCl_3$ there are four chlorine atoms in the base of the pyramid, two of which are bridging, in the given compound there are three chlorine atoms, the lengths of the bonds of which with tellurium have the usual values (2.355–2.505 Å) and an O atom in the base of the pyramid. The Te...O distance (2.419 Å) is much smaller than the sum of the van der Waals radii of tellurium and oxygen (3.60 Å). Very weak secondary Te...Cl bonds, linking the molecules into dimers, were also found in the crystals. Their length (3.558 Å) is appreciably greater than those of the Te–Cl_{bridge} bonds (2.717–2.768 Å) observed in other organyltellurium trichlorides. 7-Ethoxycycloheptyltellurium tribromide probably has a similar structure.[53]

Another representative of the σ-telluranes $RTeX_3$, in which strong intramolecular Te ← N coordinate bonds were found is 2-(phenylazophenyl-C,N′)tellurium trichloride[48] (Fig. 9). Its bonds around the tellurium atom have an octahedral configuration. The apical Cl atoms (the Te–Cl bond lengths are 2.483 and 2.491 Å) form an angle of 171.7° with one another; the equatorial positions are occupied by the third Cl atom (the Te–Cl bond length is 2.406 Å), the bidentate organic ligand (the Te–C bond length is 2.114 Å), and the lone pair. The intramolecular Te ← N coordinate bond is of special interest. Its length (2.417 Å) is much smaller than the sum of the van der Waals radii (3.70 Å) and approaches the lengths of the usual Te–N covalent bonds. The molecule is monomeric and no Te...Cl contacts shorter than the sum of the van der Waals radii were detected in it.

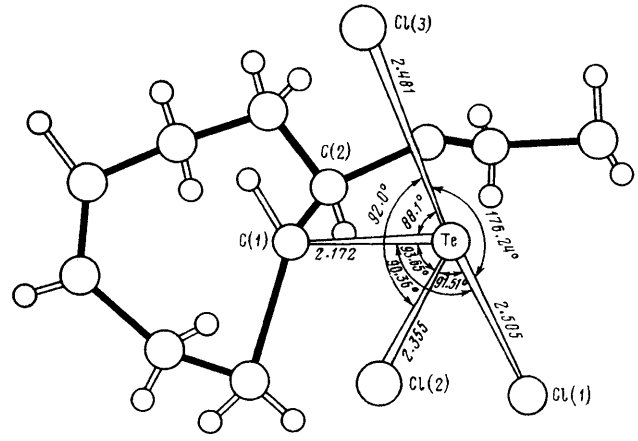


Figure 8. Geometry of the 8-ethoxy-4-cyclooctenyltellurium trichloride molecule.[47]

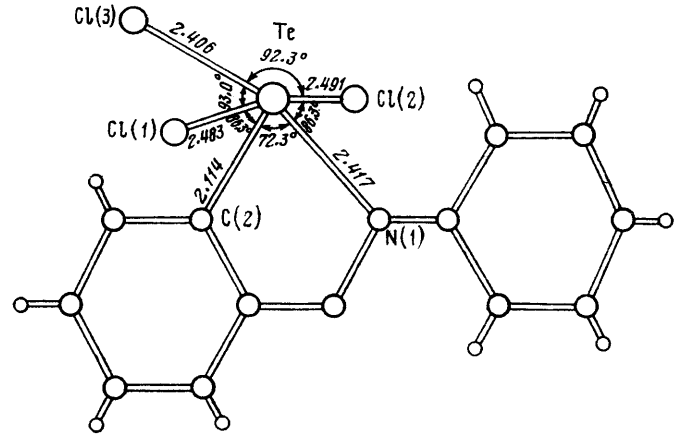


Figure 9. Geometry of the (2-phenylazophenyl-*C,N′*)tellurium trichloride molecule.[48]

The polydenticity of the organic ligand in 2,6-diacetylpyridinetellurium trichloride[49] leads to a structure of a new type which had not been encountered previously in the series of organyltellurium halides (Fig. 10). The coordination polyhedron of

the tellurium atom can be described as a distorted pentagonal bipyramid with two axial Te–Cl bonds (2.492 and 2.500 Å); the equatorial positions are occupied by a Cl atom ($Te-Cl_{eq}$ = 2.431 Å), the lone pair, and the three atoms of the tridentate organic group: the carbon atom (Te–C = 2.129 Å), the nitrogen atom (Te...N = 2.402 Å), and the oxygen atom (Te...O = 2.878 Å).

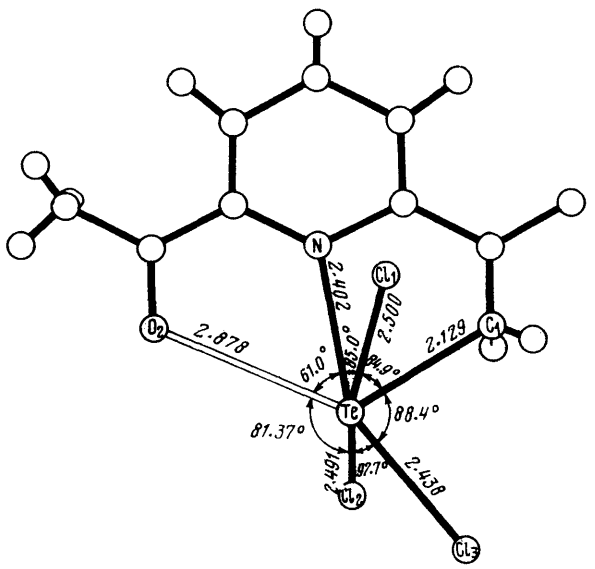


Figure 10. Geometry of the 2,6-diacetylpyridinetellurium trichloride molecule.[49]

Although the lengths of the neighbouring two bonds do exceed the sums of the covalent radii of the corresponding elements (2.07 Å for Te and N and 2.03 Å for Te and O), nevertheless they are much smaller than the sum of the van der Waals radii of these elements (3.70 Å for Te and N and 3.60 Å for Te and O [56]). The presence of the Te–N and Te–O coordinate bonds has been confirmed also by IR spectroscopic data: the shift of the vibrations of the pyridine ring from 997 cm^{-1} in 2,6-diacetylpyridine to 1012 cm^{-1} in the trichloride; the two carbonyl absorption bands at 1676 and 1712 cm^{-1}, observed in the spectrum of free 2,6-diacetylpyridine, are replaced in tellurium trichloride by a single vibration at 1707 cm^{-1}.[49] It is also of interest that the presence of coordinate bonds in the given trichloride increases significantly its resistance to hydrolysis.

The IR and Mössbauer spectra of organyltellurium trihalides, mainly the aryl derivatives, examined in Refs. 58–63 and 64–67 respectively, in general agree with X-ray diffraction data. By virtue of the wide variety of the Te–Hal bonds found in the σ-telluranes $RTeX_3$, they are of interest for NQR spectroscopy. However, the NQR spectroscopic data for these compounds are so far lacking in the literature.

The question of the aggregation of organyltellurium trihalides in solutions is important for the chemistry of the complexes based on them. Conductimetric data for solutions in acetonitrile, acetone, and nitrobenzene show that organyltellurium trichlorides do not dissociate into ions.[68–71] Organyltellurium tribromides and triiodides dissociate in the same solvents into ions ($RTeX_2^+$ and X^-) according to Khandelwal and co-workers,[70,71] although it has been claimed[61] that CH_3TeBr_3 is a non-electrolyte in nitrobenzene. On the other hand, aryltellurium trihalides containing amino(or dimethylamino)-groups in the ring, behave as 1:1 electrolytes in the solvents listed above regardless of the nature of the halogen.[63,72] This is probably due to the greater polarity of the Te–Hal bonds in the latter compounds owing to the presence in them of strong electron donors — the amino(or dimethylamino)-groups.

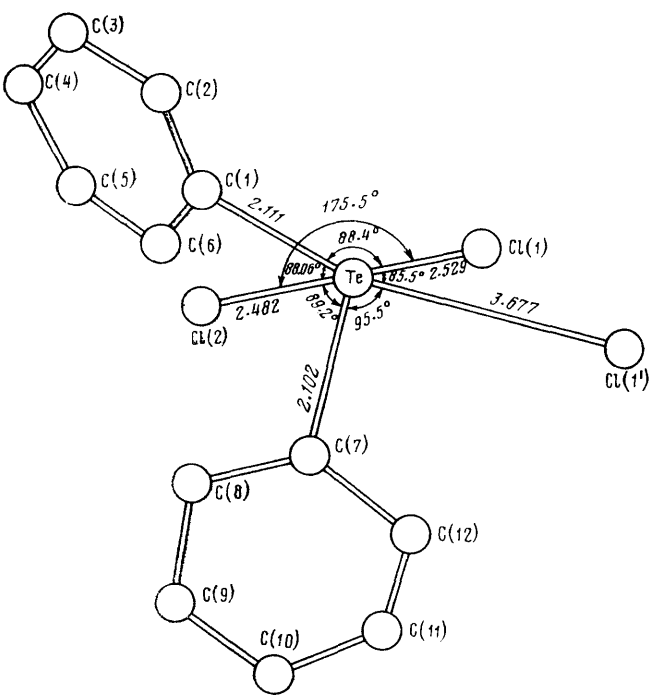


Figure 11. Geometry of the diphenyltellurium dichloride molecule.[43]

The results of cryoscopic studies on organyltellurium trihalides in general agree with conductimetric data. Aryltellurium trichlorides are monomeric in solutions [with the exception of amino(dimethylamino)-derivatives], exhibiting a weak association with increase in concentration,[39,68–70] while the tribromides and triiodides are partly dissociated.[63,70–72] On the other hand, in the case of the methyltellurium trihalides there is a monomer–dimer equilibrium in solution in benzene,[60,61] methyltellurium tribromide being more associated than its chlorine analogue.

(b) The structure of the σ-telluranes R_2TeX_2

Among diorganyltellurium dihalides, diorganyltellurium dichlorides have been most thoroughly investigated by X-ray diffraction.[43,73–81] Other tellurium dihalides (difluorides,[82] dibromides,[83] and diiodides[84,85]) are represented by single examples.

Table 2. The average bond lengths (Å) and bond angles (degrees) in the molecules of the σ-telluranes R_2TeX_3.

Compound	Te—X	Te—C	X—Te—X	C—Te—C	Te...X[a]	Te...X/Te—X[b]	Type of associated species	Refs.
$(C_6H_5)_2TeF_2$	2.006	2.115	173.1	96.1	3.208	1.60	A[c]	[82]
$(CH_3)_2TeCl_2$	2.511	2.09	172.3	98.2	3.46–3.52	1.39	A	[73, 74]
$(CH_3CHClCH_2)_2TeCl_2$	2.501	2.149	169.1	98.2	footnote[d]	–	A	[75]
$(C_6H_5)_2TeCl_2$	2.506	2.107	175.54	99.01	3.677	1.47	A	[43]
$C_6H_5TeCl_2C_6H_4Br$-4	2.513	2.114	176.3	95.05	3.413–3.723	1.41	B	[76]
$(4\text{-}BrC_6H_4)_2TeCl_2$	2.500	2.131	178.24	96.1	4.67–5.54	1.86	A[e]	[77]
$(4\text{-}CH_3OC_6H_4)_2TeCl_2$	2.519	2.112	178.35	96.45	3.446–3.675	1.41	B	[78]
$(4\text{-HO-3-}CH_3C_6H_3)_2TeCl_2$	2.518	2.104	174.8	99.2	3.884	1.54	A[f]	[79]
$(2\text{-Cl-cyclo-}C_6H_{10})_2TeCl_2$	2.493	2.19	177.6	103.0	footnote[d]	–	–	[80]
$(2\text{-Cl-cyclo-}C_6H_{10})TeCl_2-C_6H_4CH_3$-4	2.485	2.16	176.4	101.0	footnote[d]	–	–	[81]
$(C_6H_5)_2TeBr_2$	2.682	2.16	182.2	95.35	3.93	1.47	A	[83]
$(CH_3)_2TeI_2$	2.924	2.127	177.9	95.0	3.659–4.030	1.33	A	[84]
$(4\text{-}ClC_6H_4)_2TeI_2$	2.935	2.115	173.5	101.1	4.13–4.46	1.46	A	[85]

[a] The extreme limits of the bond lengths are quoted in a number of instances for the secondary bonds. [b] The arithmetical mean lengths of individual types of bonds have been adopted. [c] A, infinite chains; B, tetramers. [d] Data are lacking. [e] The chains are formed as a result of the Te...Br secondary interactions (3.71, 3.80 Å). [f] The chains are formed via O—H...Cl intermolecular hydrogen bonds (2.45 Å).

This review does not deal in detail with cyclic σ-telluranes, information about which can be found in other publications.[2,86,87] The most important structural characteristics of diorganyl tellurium dihalides are presented in Table 2.

The σ-telluranes R_2TeX_2 are characterised by the trigonal-bipyramidal disposition of the ligands around the tellurium atom, the halogen atoms always occupying axial positions. The X—Te—X angles are less than 180°, which shows that the halogen atoms are more strongly repelled from the lone pair of tellurium than from the equatorial organic groups. Diphenyltellurium dibromide, for which the Br—Te—Be angle exceeds 180°, is an exception.[83] The steric interactions between the bromine atoms and the phenyl rings[83] cannot be the cause of the increase in the angle, since in di(4-chlorophenyl)tellurium diiodide,[85] containing the more bulky iodine atoms, the I—Te—I bond angle is less than 180°. The structure of diphenyltellurium dichloride[43] is presented in Fig. 11.

In the majority of the σ-telluranes R_2TeX_2 investigated secondary Te...X interactions have been observed, the weakest being those in the difluorides. The lengths of these bonds are smaller than the sums of the van der Waals radii with the corresponding elements but greatly exceed the lengths of the Te—X bridge bonds in the σ-telluranes $RTeX_3$. The halogen atoms involved in the secondary bonds supplement the coordination around tellurium to the octahedral configuration. These interactions bind the individual molecules into infinite chains or tetramers. The bond length ratio Te...X/Te—X makes it possible to estimate roughly the degree of intermolecular association of the corresponding diorganyltellurium dihalides. Difluorides are least associated; dialkyltellurium dihalides are more associated than the diaryl derivatives.

In certain σ-telluranes R_2TeX_2, the Te...X secondary interactions are insignificant and the secondary bonds involving other atoms are shorter. In di(4-bromophenyl)tellurium dichloride,[7] the shortest linkages arise due to the Te...Cl interactions (4.67 and 5.54 Å), but they exceed significantly the sum of the van der Waals radii of Te and Cl (4.0 Å [56]). The individual molecules of this compound are linked by weak secondary Te...Br interactions (3.71 and 3.80 Å), the corresponding bond lengths being smaller than the sum of the van der Waals radii of Te and Br (4.15 Å [56]). The Te...Cl secondary interactions (3.884 Å) do not play an important role also in di(4-hydroxy-3-methylphenyl)tellurium dichloride.[79] The O—H...Cl intermolecular hydrogen bonds (2.45 Å) are energetically more favourable.

The secondary interactions with participation of heavy atoms (tellurium and iodine) in the molecules of diorganyltellurium dihalides are of special interest. The colour of these compounds, which varies from orange to dark-violet, is determined by the nature of the intermolecular bonds (Te...I or I...I). The compounds less coloured in the crystalline state have only the intermolecular Te...I bonds, while the dark-violet compounds contain in the main the I...I intermolecular bonds. Indeed, in the dark-violet di(4-chlorophenyl)-tellurium diiodide[85] and 1,1-diiodo-1-thia-4-telluracyclohexane[88] the intermolecular bonds are of the I...I type, whose lengths are 3.85 and 4.14 Å for the first compound and 3.66 and 3.90 Å for the second. On the other hand, in the yellow-orange 1,1-diiodo-3,4-benzo-1-telluracyclopentane[89,90] (Te...I = 3.653, 3.878 Å), the pale-red 1,1-diiodo-1-oxa-4-telluracyclohexane[91] (Te...I = 3.692, 3.814 Å), 10,10-diiodophenoxatellurin[92] (Te...I = 3.74, 3.79 Å),

and the red 5,5-diiododibenzotellurophene[93] (Te...I = 3.696, 3.617 Å), the secondary Te...I bonds are observed.

The IR spectra of the σ-telluranes R_2TeX_2 [58,94–97] agree with the trigonal-bipyramidal structure of the molecules of these compounds.[94,96,97] The Mössbauer spectra of diorganyltellurium dihalides, indicating that, regardless of the nature of the halogens these compounds have the same structure in the crystalline state, have been examined in a number of studies.[64–67,98]

The available information about the NQR spectra of compounds of the type R_2TeX_2 is extremely limited.[99,100] Two resonance lines have been observed in the ^{35}Cl NQR spectrum of dimethyltellurium dichloride,[99] while only one such line has been found in the NQR spectra of the diphenyl derivatives $(C_6H_5)_2TeX_2$ (X = Cl, Br, I).[100] While the first result agrees with X-ray diffraction data[73,74] (non-equivalence of the Te–Cl bonds), the data for diphenyltellurium dihalides do not. According to the results of Kondo et al.,[99] the Te–Cl bond in $(CH_3)_2TeCl_2$ is more ionic than in $TeCl_4$.

In contrast to organyltellurium tribromides and triiodides, which dissociate in solution into $RTeX^+$ and X^-, the σ-telluranes R_2TeX_2 are not electrolytes according to conductimetric data.[61,69–71] This is also indicated by the results of the determination of the molecular weights. An exception is 1,1-diiodo-3,4-benzo-1-telluracyclo-pentane,[89] the conductivity of which in dimethylformamide is typical for a 1:1 electrolyte and the observed molecular weight of this compound is appreciably lower than the theoretical value, indicating its existence in the ionic form.

III. Electron-donating properties of tellurium tetrahalides and σ-telluranes

Tellurium tetrachloride and its organic derivatives exhibit electron-donating properties in their reactions with Lewis acids. One of two alternative structures is usually attributed to the complexes formed: the donor–acceptor structure (I) or the ionic structure (II):

$$TeCl_4 + MX_n \rightarrow Cl_4Te \cdot MX_n, \quad \text{(I)}$$

$$TeCl_4 + MX_n \rightarrow [TeCl_3]^+ [MX_nCl]^-. \quad \text{(II)}$$

The conclusions concerning the existence of structures (I) or (II) are based mainly on vibrational spectroscopic data.[17,29,30,101,102–104] Bands in the range 343–345 cm^{-1}, characteristic of the $AlCl_4^-$ anion, have been observed in the Raman spectra of the complex of $TeCl_4$ with $AlCl_3$ in the melt and in the solid phase. This supports the structure (II).[101] The structure is also indicated by X-ray diffraction data for the complex.[17] The structure of the complex is made up of layers formed by highly distorted octahedra in which three terminal chlorine atoms are much closer to the tellurium atom than the other three, which are in their turn part of the composition of the $AlCl_4^-$ tetrahedra (Fig. 12).

Analysis of the vibrational spectra led to the conclusion that the crystalline complexes $TeCl_3^+ . AlCl_4^-$, $TeCl_3^+ . SbCl_6^-$, $TeCl_3^+ . AsF_6^-$, and $PCl_6^- . TeCl_7^+$ [actually $TeCl_4 . PCl_5$ in Ref. 30 (Ed. of Translation)] and their solutions in solvents of different polarity (benzene and acetonitrile) are ionic.[30] However, more detailed study of the Raman spectra of the complex $TeCl_4 . SbCl_5$ in the solid state[102] showed that its structure resembles that of the molecular complex $SeCl_4 . SbCl_5$ and is of the donor–acceptor type. In the highly polar nitromethane, it dissociates into the ions $TeCl_4^+$ and $SbCl_6^-$. It is of interest to note that the solid, freshly prepared, complex $TeCl_4 . SbCl_5$ is ionic and metastable. Its prolonged exposure to room temperature entails the disappearance of the bands characteristic of the $SbCl_6^-$ ion.[102]

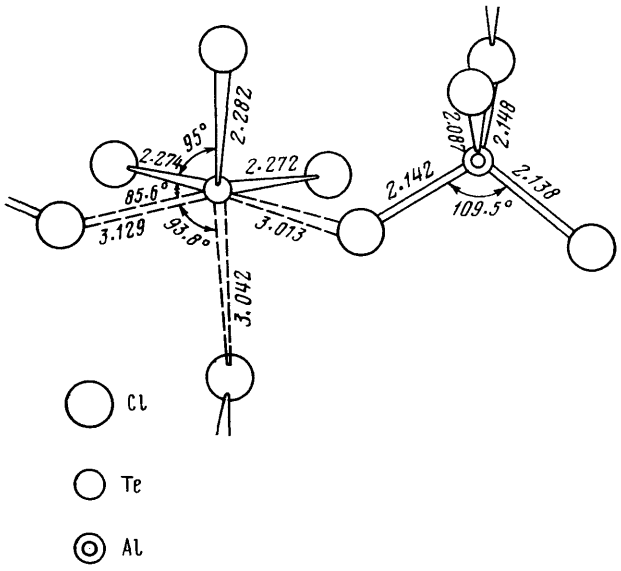


Figure 12. The crystal structure of the complex $TeCl_4 . AlCl_3$.[17]

The complexes of $TeCl_4$ with BCl_3 in polar solvents exhibit an electrical conductivity typical for 1:1 electrolytes,[104] which indicates the presence of the ions $TeCl_3^+$ and BCl_4^-. This has been confirmed by IR spectroscopic data.[105] It is of interest to note that $TeCl_4$ and BBr_3 afford $TeBr_4$ quantitatively on interaction, but the latter does not react with BBr_3.[106]

The interaction of TeF_4 with SbF_5 [107] leads to the formation of trifluorotelluro(IV)-μ-fluorobis[pentafluoroantimonate(V)], which also has the ionic structure $TeF_3^+ . Sb_2F_{11}^-$ with appreciable interaction between the ions via the fluorine atoms. On the other hand, the interaction of $TeCl_4$ with Group III metal halides ($AlBr_3$, $GaBr_5$, $GaCl_3$) [108] results in the formation of stable, highly polar, 1:1 electron-donating complexes.

Conclusions concerning the structure of the complexes of σ-telluranes with Lewis acids are also as a rule based on the analysis of the vibrational spectra and these systems are regarded as ionic.[109,110] The possibility of the formation of the cations $RTeCl_2^+$ has been demonstrated by a series of complexes of

organyltellurium trichlorides with $SbCl_5$, which are insoluble in non-polar solvents.[109] The ionic structure of these complexes, whose composition is $RTeCl_3.SbCl_5$, follows from the similarity of their IR spectra to those of the ionic complexes $RSeCl_3.AlCl_3$ [109] and from the observation of bands characteristic of the $SbCl_6^-$ ion.[110]

The interaction of $RTeCl_3$ with $AlCl_3$ is of special interest. The formation of compounds of the type $[RTeCl_2]^+[AlCl_4]^-$ has been postulated in a series of studies. Indeed $C_6H_5TeCl_3$ does not interact with benzene to form $(C_6H_5)_2TeCl_2$,[111] while 2-trichlorotellurodiphenylmethane does not cyclise to 10,10-dichlorotelluroxanthene in the absence of $AlCl_3$.[112] On the other hand, the addition of $AlCl_3$ makes it possible to achieve the above reactions by virtue of the enhancment of the electrophilic nature of the trichlorotelluro-groups in the above aryltellurium trichlorides probably as a result of the formation of the complexes $[RTeCl_2]^+[AlCl_4]^-$.

Thus in the majority of the studies quoted, carried out using vibrational spectroscopy, it was concluded that the complexes of $TeCl_4$ and σ-telluranes with Lewis acids are ionic. It is believed[30,101,102,104,109,110] that the complexes are formed as a result of the transfer of a Cl^- ion from the tellurium-containing donor to the acceptor. However, this mechanism cannot be regarded as the only one possible. Much depends on the strength of the Lewis acid and the nature of the medium in which the complexes are present. Thus, according to IR and UV spectroscopic and mass-spectrometric data, the complexes of R_2TeI_2 with I_2 have a distorted octahedral structure in the crystalline state and are donor–acceptor compounds.[113,114] This conclusion also follows from a study[115] in which the crystal and molecular structures of dimethyltellurium tetraiodide were investigated. It has the structure of a molecular adduct in which the individual $(CH_3)_2TeI_2$ and I_2 molecules are linked mainly by the $-I\ldots I-I$ intermolecular bonds. The interaction of dialkyltellurium diiodides with mixed halides also results in the formation of the molecular complexes $R_2TeI_2.IX$ (X = Cl, Br).[116]

The above data refer to the structure of the complexes of $TeCl_4$ and σ-telluranes with Lewis acids in the crystalline state or in solution in highly polar solvents. However, on passing to non-polar solvents, these systems acquire a qualitatively different structure. The dipole moments of the complexes of $TeCl_4$ with Group IIIA metal halides, having the composition $TeCl_4.MX_3$ (MX = $AlBr_3$, $GaCl_3$, $GaBr_3$), are in the range 6–10 D.[35] Such polarity precludes the attribution of the structure of ion pairs to these complexes. On the other hand, the bridged structures, whose formation cannot be ruled out *a priori*, should have significantly smaller dipole moments. On the basis of these data and the absence of electrical conductivity in benzene, it has been concluded that these are donor–acceptor complexes.[35] The bond in them is formed via the lone pair of the tellurium atom and the unoccupied orbitals of the central atom of the Lewis acid and, judging from calorimetric data and dielectric constant measurements, it is fairly strong and polar. Comparison of the IR spectra of solutions of these complexes in benzene with those of typical donor–acceptor systems $R_2S.MX_3$ [117] reveals a virtually complete identity of the spectra in the region corresponding to the absorption by the acceptor. Other studies[118,119] have led to a similar conclusion about the nature of the bond in the complexes of the σ-telluranes $RTeX_3$ and R_2TeX_2 with $SbCl_5$ in benzene.[118,119] A characteristic feature of the latter systems is also the formation of the complexes $D.3SbCl_5$ (D = donor molecule).[118] An exception is the $(C_6H_5)_2TeI_2$ + $SbCl_5$ system in which halogen exchange probably takes place.[119] The results obtained by combined thermal analysis indicate the molecular nature of the complexes formed.[119] The dipole moments of the 1:1 complexes are in the range 6–8 D, while those of the 1:3 complexes are in the range 10–13 D, which indicates the ionic structure of the latter.[118] The electrical conductivity of the complexes having the simplest composition, observed in nitrobenzene,[118] does not rule out the possibility that they are donor–acceptor in nature. Judging from the heats of formation of the complexes, the electron-donating capacity of the tellurium atom in the σ-telluranes is determined primarily by the number of aromatic groups and their nature.[119,120]

IV. Electron-accepting properties of tellurium tetrahalides and σ-telluranes

1. Electron-accepting properties of tellurium tetrahalides

The relatively low-lying unoccupied *d* orbitals of the tellurium atom are responsible for the electron-accepting properties of its tetracoordinate derivatives, the subject of numerous investigations. A considerable proportion of them involve the study of the electron-accepting properties of tellurium tetrahalides, which are moderately strong Lewis acids in relation to various N-, P-, O-, S-, and Se-containing organic donors. The complexes have been, as a rule, isolated in the solid state and investigated by various physicochemical methods.

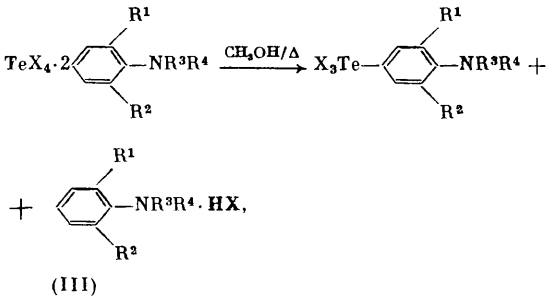
(a) Complexes with N-donors

In the literature devoted to the study of the electron-accepting properties of tellurium tetrahalides, most attention has been devoted to their interaction with N-containing bases. The reactions of TeF_4 with aliphatic amines (trimethylamine and tetramethylethylenediamine) result in the formation of crystalline 2:1† and 1:2 adducts.[121] Bands characteristic of the TeF_5^- anion have been detected in the IR spectra of these systems,[122] which made it possible to attribute to them the ionic structures $[TeF_3.L_2]^+[TeF_5]^-$ and $[TeF_3.L]^+[TeF_5]^-$ respectively. An octahedral structure has been proposed for the cation $[TeF_3.L_2]^+$, in which the tellurium atom is surrounded by three fluorine atoms, two electron-donating ligand atoms in the *cis*-positions, and the lone pair at one of the vertices. The nature of the relative positions of the monodentate ligands in the complexes has not been elucidated.[121]

On interaction with TeX_4 (X = Cl, Br, I), aromatic amines[72,123–126] form 2:1 complexes which are sparingly soluble in the usual organic solvents. However, after prolonged heating of these complexes in dry methanol, electrophilic substitution of one of the aromatic rings takes place in the *p*-position (relative to the amino-groups) with formation of tellurium trihalides (III) or, if the *p*-position is

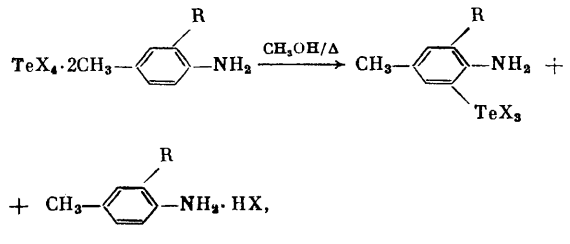
† In the designation of the composition of the complexes, here and henceforth the first figure denotes the number of electron-donating molecules and the second denotes the number of electron-accepting molecules.

occupied, substitution in the *o*-position takes place with formation of compounds (IV):[72,123]



(III)

$R^1 = R^2 = R^3 = R^4 = H$; $R^1 = R^2 = R^3 = H$; $R^4 = CH_3$; $R^1 = R^2 = H$; $R^3 = R^4 = CH_3$; $R^1 = R^3 = R^4 = H$, $R^2 = CH_3$; $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$,



(IV)

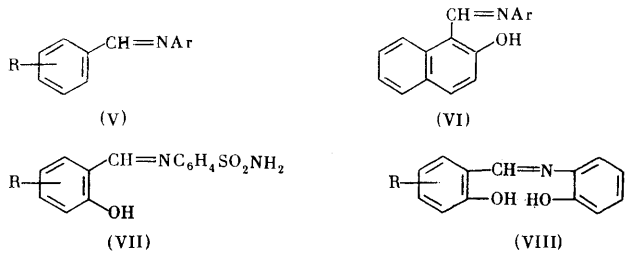
R = H, CH_3.

The interaction of $TeCl_4$ with heterocycles containing an sp^2-hybridised nitrogen atom results in the formation of mainly 2:1 complexes.[29,127–130] The reaction with the bidentate 2,2′-bipyridyl results in the formation of a 1:1 adduct[128] and the formation of complexes of both compositions has been noted only for pyridine.[29,31] According to conductimetric and vibrational spectroscopic data, these complexes are ionic.[29] The anion is Cl^-, while the cation, $[TeCl_3.L_2]^+$, is a pseudo-octahedron with a lone pair at one of the vertices. X-Ray diffraction demonstrated the *trans*-octahedral structure of the 2:1 adduct of $TeCl_4$ with pyridine.[131] In this case, the lone pair of the tellurium atom is not stereoactive.

In contrast to $TeCl_4$, the reaction of TeF_4 with pyridine affords only a 1:1 adduct.[132] Its treatment with aqueous HF results in the formation of more complex fluorides: $C_6H_5NH.TeF_5$ and $(C_6H_5NH)_2.TeF_6$.

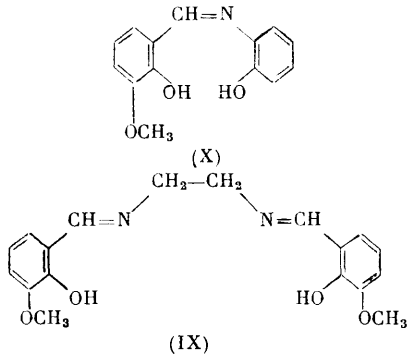
Thiopicolinamides[130] react with $TeCl_4$ to form 2:1 complexes. It follows from the analysis of IR and ^1H NMR spectroscopic data that the tellurium atom is coordinated to the pyridine nitrogen atom and the nitrogen atom of the thioamide group. Judging from the molar conductances in solutions in DMF, these complexes can be regarded as 1:2 electrolytes.

Tellurium tetrachloride exhibits electron-accepting properties also in relation to hydrazones[133] and Schiff bases (V)–(VIII),[134–136] with which it forms mainly 2:1 complexes. The complexes with type (VII) azomethines possess antibacterial properties.[135]



(V) (VI) (VII) (VIII)

However, the reaction of $TeCl_4$ with the azomethines (IX) and (X) affords 1:1 complexes. The reason for the conflict between the results of the above studies[136,138] is obscure, since the electron-donating compounds (VIII) and (IX) employed in these investigations have very similar structures.



(X)

(IX)

The shift of the stretching vibration bands of the C=N bond in the IR spectra of the adducts compared with the initial Schiff bases has led to the conclusion[134,135,137] that N → Te coordinate bonds are formed via the lone pairs of the azomethine nitrogen atoms.

(b) Complexes with O-donors

Tellurium tetrachloride exhibits electron-accepting properties in relation to the oxygen atom in the C=O, N → O, P → O, and S → O groups. The interaction of $TeCl_4$ with acetamide and its derivatives[138] and 2-hydroxybenzylideneacetophenones[139] results in the formation of 2:1 complexes, in which, judging from IR spectroscopic data, the tellurium atom is coordinated to the carbonyl oxygen atom. The electrical conductivities of solutions of the complexes of $TeCl_4$ with acetamide and its derivatives are characteristic of 1:1 electrolytes and made it possible to attribute the structure $[TeCl_3L_2]^+Cl^-$ to the complexes.[138]

Pyridine[31] and 2,6-lutidine[140] *N*-oxides form 2:1 complexes on interaction with $TeCl_4$ (pyridine *N*-oxide also gives rise to a 1:1 complex). Conductimetric measurements and analysis of the IR spectra indicated that the complexes of pyridine *N*-oxide, containing Cl^- as the anion, have an ionic structure.[31] The splitting of the stretching vibration bands of the N → O group in the IR spectrum of the complex of 2,6-lutidine, similar to that observed for the *cis*-octahedral complexes $MCl_4.2L$ (M = Hf, Ta, Th; L = R_nYO,

Y = N, P, S, etc., n = 2, 3), made it possible to postulate a *cis*-disposition of the ligands also in the 2,6-lutidine complex.[140]

Dialkyl sulphoxides react with $TeCl_4$ to form 2:1 and 1:1 complexes. This is particularly characteristic of dimethyl sulphoxide.[20] The complex with the simplest composition is a molecular compound both in solution and in the crystalline state. This follows from the dipole moment determined in benzene and the ^{35}Cl NQR spectrum in the solid phase. On the other hand, conductimetric data for the 2:1 complexes indicate the ionic structure $[TeCl_3.2(CH_3)_2SO]^+Cl^-$. It has been postulated[20] that the structures of complexes of both types are made up of octahedra, one of the vertices of which in the 1:1 complex is occupied by the lone pair of the tellurium atom. Dicyclohexyl sulphoxide reacts with $TeCl_4$ to form the complex having the simplest composition.[120] The complexes of $TeCl_4$ with diethyl and dibutyl ethers, investigated by the dielectric constant titration method, have a similar composition.[35]

According to the dielectric constant titration data, under isomolar series concentration conditions in solutions in benzene, $TeCl_4$ reacts with $(C_6H_5)_3PO$ to form complexes having only two compositions: 1:1 and 2:1.[141] Judging from the dipole moments, they are donor–acceptor complexes. One of the vertices of the octahedron in the 1:1 complex is probably occupied by the lone pair of tellurium, while the octahedral 2:1 complex has the *cis*-structure.

(c) Complexes with S-donors

According to the dipole moment and calorimetric titration data, $TeCl_4$ reacts with the dialkyl sulphides $(C_3H_7)_2S$ and $(C_7H_{15})_2S$ to form 1:1 complexes.[20,35] The dipole moments of the complexes (5–9 D) and the low electrical conductivities in benzene demonstrate their donor–acceptor nature. Complexes with the simplest composition are formed also on interaction of $TeCl_4$ with the sulphides $RS(CH_2)_nSR$ (R = alkyl, n = 2–10) [142] despite the presence of two sulphur atoms in the latter.

Much attention has been devoted to the study of complexes in which an sp^2-hybridised sulphur atom functions as the donor centre. Both $TeCl_4$ and $TeBr_4$ form 2:1 complexes with tetramethylthiourea (TMTU).[143–145] It has been established by X-ray diffraction[143–145] that these complexes have an octahedral structure in which the sulphur atom is in the equatorial plane in the *trans*-position. The structure of the complex $TeBr_4.2TMTU$ is illustrated in Fig. 13. The slight distortions of the coordination unit are treated as a consequence of packing effects[144] or of the influence of the lone pair of the tellurium atom.[145]

Comparison of the long-wavelength IR spectra of the complexes of TMTU in the solid state and in solution[128] in the light of X-ray diffraction data[143–146] indicated that the *trans*-octahedral structure is retained also in solutions. The determination of the molecular weights in solution in tetramethylene sulphone and of the electrical conductivity in solutions in nitrobenzene and tetramethylene sulphone led to the conclusion that these complexes are monomeric and weakly ionised.[128]

N,N'-Substituted thioureas also form 2:1 complexes with $TeCl_4$ which are non-conducting in DMF and DMSO.[147] The shift of the bands in the range 600–700 cm^{-1}, referring to the vibrations of the C=S groups, led to the conclusion that the adducts have an octahedral structure with the apical S-coordination of the organic bases.

It is of interest to note that TMTU reduces tellurium(IV) derivatives in acid solutions, which leads to the formation of the complexes $Te^{(III)}:Te(L)Cl_2$.[143]

Various thiones can also function as S-containing donors. The 2:1 complex of $TeCl_4$ with benzimidazolethione has the *cis*-configuration with coordination to the sulphur atoms according to X-ray diffraction data.[149] On the other hand, the analogous complex with benzothiazolethione, isolated from solution in dioxane, has the *trans*-octahedral structure.[150]

Adducts of the type $TeX_4.L_2$ have also been obtained by the reaction of TeX_4 (X = Cl, Br, I) with thiazolidine-2-thione. IR spectroscopic data in the solid state have lead to the hypothesis that the complexes have an octahedral structure[151] in which the tellurium atom is coordinated to the nitrogen atom of one of the ligand molecules and the sulphur atom of the other.

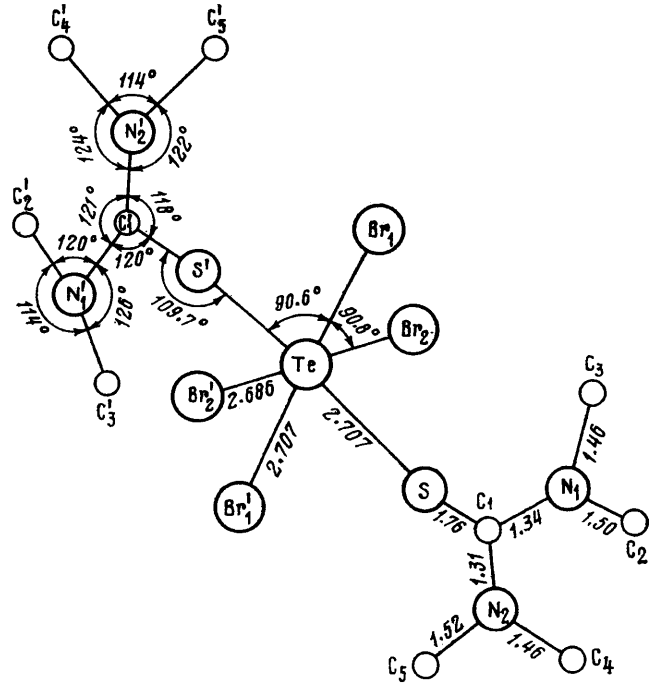


Figure 13. The structure of the adduct $TeCl_4.2TMTU$.[143,144]

Measurements of the electrical conductivities of the above systems showed that these are 1:1 electrolytes and the low electrical conductivities in solution in DMF have been explained by the tight bond between the cation and the anion.

Tetramethyl(ethyl)dithiooxamides constitute another type of sulphur-containing donors forming 1:1 complexes with $TeCl_4$ and $ArTeCl_3$.[152,153] The long-wavelength IR and the Raman spectra indicate an octahedral structure of the complexes containing bidentate ligands coordinated to the sulphur atoms of the thiocarbonyl groups.

The complex formation reaction of tetramethylthiuran disulphide is unusual. The interaction of this donor with TeX_4 (X = Cl, Br, I) results in the elimination of one sulphur atom and the formation of 1:1 complexes between tetramethylthiuram sulphide and TeX_4.[154] It follows from the IR spectra that tellurium is coordinated to the thione sulphur atoms.

Complexes of $TeCl_4$ with the thiosemicarbazones and semicarbazones of benzaldehyde, salicylaldehyde, acetophenone, and 2-hydroxyacetophenone, having the 1:1 structure, have also been described.[155] The IR and NMR spectra confirm the coordination of the tellurium atom via the azomethine nitrogen atom, the sulphur atom of the C=S/O group, and the phenolic oxygen atom (if it is present in the benzene ring).

The interaction of $TeCl_4$ with $(C_6H_5)_3PS$ leads to the complex with the simplest composition whose structure is analogous to that of the complex of $TeCl_4$ with $(C_6H_5)_3PO$ described above.[141]

2. Electron-accepting properties of the σ-telluranes $RTeX_3$

In contrast to tellurium tetrahalides, a characteristic feature of which is the formation of 2:1 adducts, organyltellurium trichlorides form mainly 1:1 complexes.

Aryltellurium trichlorides react with pyridine (Py), 4-picoline, and 4-picoline *N*-oxide to form 1:1 complexes.[68] The first two complexes which behave in solution in nitromethane as 1:1 electrolytes, have the structure $[ArTeCl_2.L]^+Cl^-$. The complex of 4-picoline *N*-oxide is a weak electrolyte and its formula is $ArTeCl_3.L$.

According to IR spectroscopic and conductimetric data, an octahedral structure has been attributed to the 1:1 complexes of $ArTeCl_3$ with the bidentate ligands bipyridyl and phenanthroline and to the 2:1 complexes of 4-phenoxyphenyltellurium trichloride with the monodentate pyridine, pyridine *N*-oxide and tri(*n*-octyl)-phosphine oxide.[156] The complexes of aryltellurium trichlorides with a series of N-, P-, and O-containing bases (trimethylamine, pyridine, benzimidazole, triphenylphosphine, triphenylphosphine oxide, and dimethyl sulphoxide), isolated in a pure state, have been described.[157–159] The complexes have the 1:1 composition and are apparently dissociated in acetonitrile judging from the electrical conductivities of the solutions. The composition and enthalpy of formation of the complex of $C_6H_5TeCl_3$ with $(C_6H_{13})_2SO$ have been investigated by calorimetric titration in benzene.[120]

Organyltellurium trichlorides exhibit electron-accepting properties also in relation to S-containing bases. In the study[154] quoted above, it was shown that the aryltellurium trihalides $4\text{-}C_2H_5OC_6H_4TeX_3$ (X = Cl, Br, I) as well as tellurium tetrahalides interact with tetramethylthiuram disulphide. This entails the elimination of one sulphur atom and the formation of 1:2 tetramethylthiuram sulphide complexes. However, no conclusions were reached about the structure of these complexes.

The 1:1 complexes of $RTeCl_3$ and $RTeBr_3$ with TMTU [62,160] have a square pyramidal structure with organic substituents in the apical positions and the three halogen atoms and the S-coordinated ligand molecule in the base of the pyramid according to IR and ^1H NMR spectroscopic data. As in the case of tellurium tetrahalides, the interaction of aryltellurium trichlorides with thiourea is accompanied by the reduction of tellurium (IV) and the formation of tellurium(II) complexes.[161]

The interaction of a number of aryltellurium trichlorides with electron donors of the type $(C_6H_5)_3P=X$ (X = LEP, O, S, Se) and also with $C_6H_5PO(CH_3)_2$ has been investigated[141] by the dipole moment method under isomolar series concentration conditions in solutions in benzene. The formation of 1:1 complexes in reactions with aryltellurium trichlorides and of 1:1 and 2:2 complexes in reactions with $TeCl_4$ was observed. The dipole moments corresponding to the interaction of the components indicate the donor–acceptor nature of the bond between them. Analysis of the dipole moments shows that the coordination unit of the complex consists of a pseudo-octahedron in which the donor is in the *cis*-position relative to the lone pair of tellurium and in the *trans*-position relative to the chlorine atom. Judging from the dipole moment (13.21 D) of the octahedral complex $TeCl_4.(C_6H_5)_3PO$, the donor molecules in it are in the *cis*-position relative to one another. The decrease in the dipole moments on passing from the $TeCl_4$ complexes to the $C_6H_5TeCl_3$ complexes for the same donors shows that the electron-accepting capacity of tellurium in its tetracoordinate derivatives is determined by the number of phenyl groups linked directly to the tellurium atom. It is of interest to note[162] that, on interaction of $ArTeCl_3$ with the thiosemicarbazones (TSC) of benzaldehyde, salicylaldehyde, acetophenone, and 2-hydroxyacetophenone, ionic tricoordinate tellurium(II) complexes $[ArTe.(TSC)_2]^+Cl^-$, in which the tellurium atom is coordinated via the sulphur atom, are formed.

3. Electron-accepting properties of the σ-telluranes R_2TeX_2

The amount of data on the electron-accepting capacity of diorganyltellurium dihalides is extremely limited. The 1:1 complexes of $(C_6H_5)_2TeCl_2$ [157] and $(C_6H_5)_2Te(NO_3)_2$ [163] with certain N-, P-, O-, and S-containing Lewis bases (trimethyl- and triethyl-amines, pyridine, triphenylphosphine, pyridine *N*-oxide, tetramethylthiourea, triphenylphosphine oxide, and others) have been isolated. The 2:1 adducts of dicyclohexyltellurium dihalides,[164] α,α-bispropiophenone-tellurium dihalides,[165] and diphenacyltellurium dihalides[166] with N-containing donors such as diethylamine, pyridine, piperidine, morpholine, and pyrrolidine have been investigated. Spectroscopic studies (IR and ^1H NMR) have shown that, whereas the initial tetracoordinate tellurium compounds exhibit keto-enol tautomerism, the adducts exist mainly in the keto-form. The 1:1 complex of $(C_6H_5)_2TeCl_2$ with $(C_6H_{13})_2SO$ has been investigated by calorimetric titration in benzene.[120] Comparison of the enthalpy of formation of this complex with the analogous quantities for the complexes of $TeCl_4$ and $C_6H_5TeCl_3$ with the same donor indicates that the electron-accepting capacity of tellurium-containing compounds decreases with the increase in the number of phenyl groups in the acceptor molecule.

Data published[167] on a series of complexes of "dibenzotelluorophene dichloride" with various donors are erroneous. The compound to which the authors attributed the structure of dibenzotelluorophene dichloride is not in fact the latter.

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The literature data presented in this review show that, despite the considerable number of studies devoted to complexes of tellurium tetrahalides and σ-telluranes, this field of coordination compounds requires further studies. Whereas the electron-accepting properties of tellurium compounds have been more or less investigated, their electron-donating capacity, especially that of σ-telluranes, has been studied to a very slight extent. Nevertheless, complexes of this type can play an important role in the chemistry of derivatives of tetracoordinate tellurium. The virtual lack of energy characteristics of the complex formation reactions of derivatives of tetracoordinate tellurium makes it essential to carry out planned and systematic studies in this field. Hitherto investigations have been limited to a narrow range of σ-telluranes. In view of this, the study of the complex formation reactions of σ-telluranes, in which the electronic and steric nature of the substituents at the tellurium atom as well as the nature of the organic donors and acceptors involved in the complex formation are varied widely, is of definite interest. Investigations of this kind make it possible to establish the rules

governing the variation of the electron-donating and electron-accepting properties of σ-telluranes as a function of the nature and number of the halogen atoms and the organic groups at the tellurium atom. The results of studies on the complex formation reactions of the σ-telluranes $RTeX_3$ and R_2TeX_2, in which the tellurium atom is involved in intramolecular interaction with an atom or groups of atoms forming part of the composition of the same molecules, may be of definite interest for the problem of competitive reactivity. The X-ray diffraction and NQR methods should be applied to an increasing extent in the study of complexes based on derivatives of tetracoordinate tellurium. Finally, it is entirely likely that certain tellurium complexes can find practical applications about which nothing is known with the exception of data on the antibacterial properties of complexes of tellurium tetrachloride with Schiff bases containing sulphamide groups.

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Translated from *Uspekhi Khimii* **60** 1255–1282 (1991) U.D.C. 542.91:547.379

Synthetic application of the Pummerer reaction

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ABSTRACT. **The latest information on the use of the Pummerer reaction for conversions of primary and secondary sulphoxides in fine organic chemistry is classified and correlated.**

The bibliography includes 171 references.

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I. Introduction

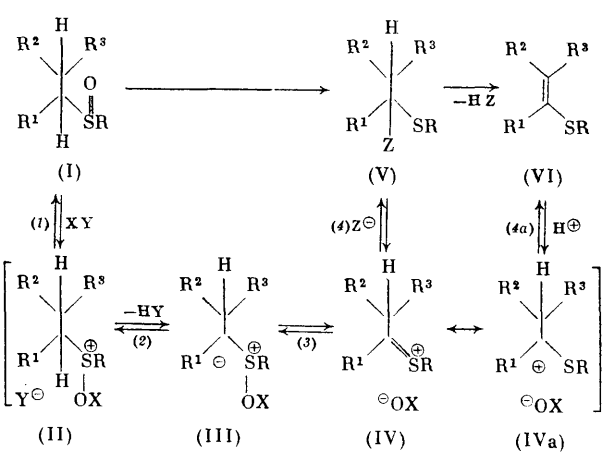
The conversion of sulphoxides by electrophilic reagents to α-substituted sulphides, which was discovered by R Pummerer in 1909,[1] was named after him by Horner[2] half a century later in honour of the original discoverer of this reaction. A number of reviews[3–11] are devoted to a study of its mechanism and certain synthetic aspects. At the same time, the use of the Pummerer reaction (PR) and related conversions in fine organic synthesis, which has undergone a particularly intense development in recent years, has hardly been reviewed at all, if the short selection of material by Welzel[12] and the highly specialised review of Fedorov et al.[13] devoted to the use of the PR in the synthesis of heterocyclic compounds are excluded. This circumstance has prompted us to analyse the available information on this topic, mainly covering the literature of the last ten years.

II. Current theory of the mechanism of the Pummerer reaction

The most comprehensive information about the probable mechanism of the PR is contained in reviews by Oae.[10,11] The overall scheme now reduces to four successive reversible stages *(1)*–*(4/4a)* (Scheme 1), and the rate-determining stage can change depending on the nature of the initial reaction components. Examples are known in which either of these stages becomes rate-determining.[11] The first of them consists of the formation of an oxysulphonium salt (II) (an "activated" sulphoxide)[14] or, in other words, a pre-Pummerer intermediate (PPI), from a primary or secondary sulphoxide (I). The second involves the generation of an oxysulphonium ylid (III) by removal of an α-proton by the counterion. Heterolysis of the S–O bond in the ylid at the third stage leads to the formation of the Pummerer intermediate (PI) proper (IV)/(IVa), which is stabilised finally by an external nucleophile to give an α-substituted sulphide (V) or forms a vinyl sulphide (VI) through elimination of the β-proton. In the case of acyloxysulphonium ions (II), the acyl residue within the corresponding PPI can act as this nucleophile.[11,15]

The reagents XY used to "activate" the initial sulphoxide are usually simple and mixed anhydrides and chorides of carboxylic acids, other halides of (in)organic acids, and the acids themselves, including Lewis acids, catalytic quantities of which added to these "activators" sometimes accelerate the PR, and also certain other reagents.[11,14] Acyloxy and chloride ions are most common among the external nuclephiles $Z^{\ominus}$, although uncharged molecules and functional groups of the substrate that become involved in the PR can fulfil this role. When these compounds are acid-labile, in order to neutralise the acids formed at stages *(2)* and *(4/4a)*, extensive use is made of bases; these are as a rule nitrogenous, including dicyclohexylcarbodiimide, which in particular achieves high enantio-selectivity in a reaction involving chiral sulphoxides.[15,16]

Scheme 1



The existence of the cationoid S-containing species (II)–(IV) as actual intermediates of the PR has so far not been established unequivocally.[10,11] However, the ability of sulphoxides, and in particular DMSO,[6,17] to give thermally labile complexes with different electrophilic reagents, such as adducts with HCl[17] or with trifluoroacetic anhydride (TFAA),[18] the latter decomposing to a PR product even at −30 °C, is well known. Indirect confirmation of the involvement of the PPI (II) in the PR is provided by the large

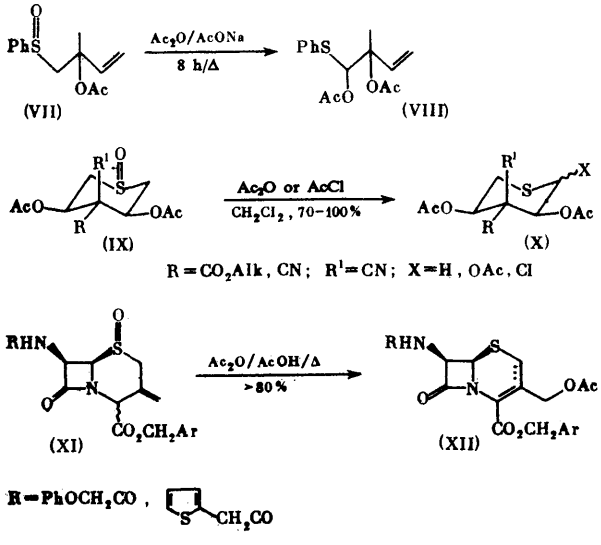
amount of data on the reaction between "activated" sulphoxides and *O*- and *N*-nucleophiles.[11,14]

With regard to the PI (IV/IVa), as representatives of a class of methylenesulphonium salts[11] their instability generally appears to be quite natural. The simplest example of this type of cationoid species, $H_2C{=}\overset{\oplus}{S}Me/SbCl_6$, was obtained from methylthiochloromethane comparatively recently.[19] In relation to the PR, there is only indirect evidence, as in the case of the PPI (II), for the existence of such an intermediate.[10,11] Additional information will be given below (Section VII).

III. Synthesis of α-substituted sulphides, carbonyl compounds, and alcohols

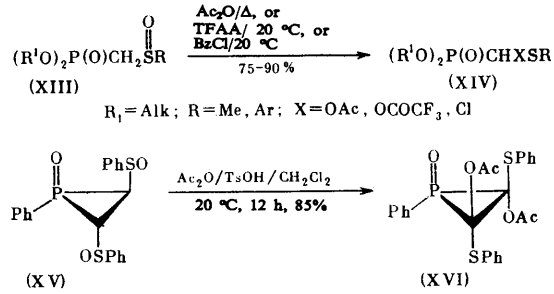
At the present time the Pummerer reaction serves as an extremely valuable synthetic method of achieving a simple conversion from readily available primary and secondary sulphoxides to *gem*-functionalised sulphides. Further hydrolytic, redox, and other conversions of the latter to various carbonyl compounds and their derivatives is simply a question of procedure, the efficiency of which depends in many respects on the nature of the functional groups that are present in the molecule of the initial substrate. Just as important for the overall process as a whole is the nature of the electrophilic and nucleophilic reagents that are used, which has been recorded in most of the reviews mentioned above. The same questions are discussed below with account taken of the latter results concerning the possibility of achieving a selective conversion of the sulphinyl group in the presence of other functional substituents. For example, the isoprene derivative (VII) can be readily converted to the acetoxysulphide (VIII),[20] while sulphoxides (IX) are converted to α-substituted tetrahydrothiopyrans (X)[21] (Scheme 2). In the case of allyl sulphoxides it is possible in this way to introduce an acetoxy group into the γ-position relative to the sulphur atom. In particular, the PR of the cephalosporin derivatives (XI) readily gives γ-acetoxy sulphides (XII),[22] which are apparently formed by allylic isomerisation of the initial *gem*-product.

Scheme 2



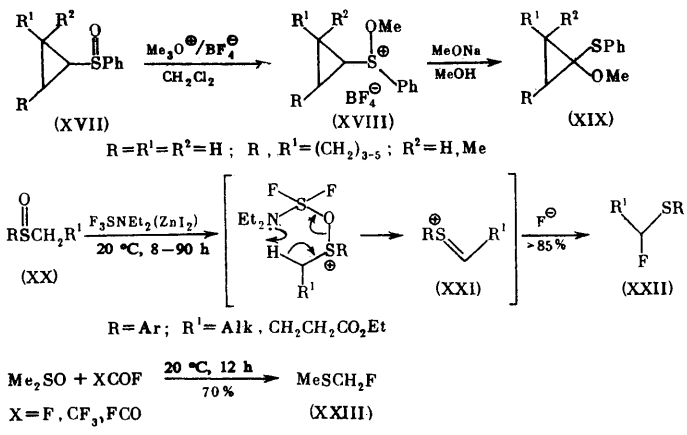
The presence of an electron-withdrawing group at the α-position relative to sulphinyl assists the participation of the latter in the PR, and in addition increases the degree of asymmetric induction for optically active substrates.[11,15] Thus α-phosphoryl sulphoxides (XIII) under different conditions and in high yield are converted to the corresponding acyloxy- or chloro-sulphides (XIV).[23] For example, chiral (XIII) (R^1 = Me, R = *p*-Tol) gives the acetoxy-sulphide (XIV) (X = OAc) with an enantiomeric purity (EP) of about 25%[23] (Scheme 3). Similarly, the phosphirane disulphide (XV) yields *trans*-diacetate (XVI).[24]

Scheme 3



Using the Pummerer reaction it is possible to carry out the synthesis of structures that were only recently considered exotic. For example, cyclopropanone derivatives such as methoxysulphides (XIX) are prepared from (XVII) and a Meerwein salt with a total yield of 40–60% via the stable oxysulphonium salts (XVIII)[25] (Scheme 4). Other such fairly important compounds include the α-fluorides (XXII), which were recently synthesised in almost quantitative yield by "activation" of the sulphur atom in (XX), catalysed in a number of cases by ZnI_2, and apparently occurring via a PI of the type (XXI).[26,27] As a result of the PR of DMSO with certain acyl fluorides, methylthiomethyl fluoride (XXIII) was isolated in high yield.[28]

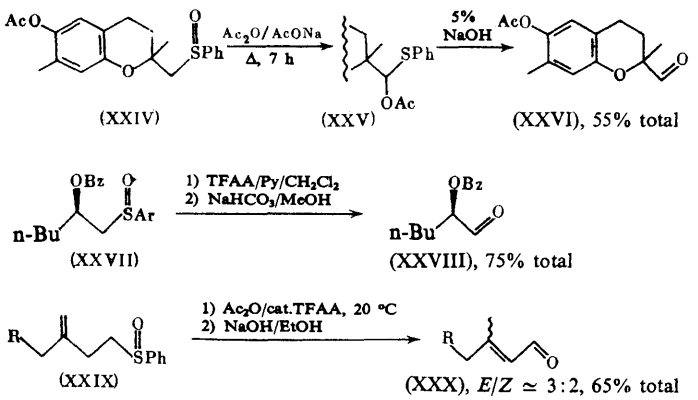
Scheme 4



It stands to reason that α-substituted sulphides (V), in particular their acyloxy derivatives, can be readily converted to the corresponding aldehydes and ketones; and in this sense primary and secondary sulphoxides are latent precursors of such compounds by

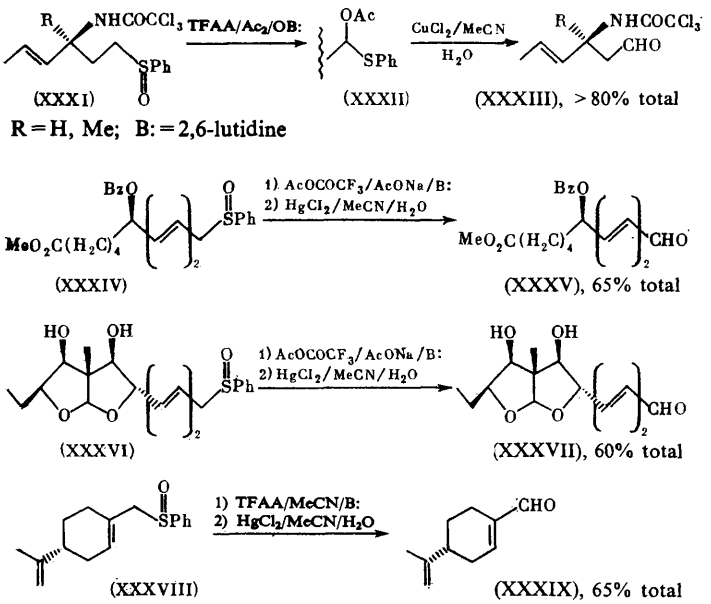
the Pummerer reaction. For example (Scheme 5), in one of the variants for the synthesis of α-tocopherol from the sulphoxide (XXIV) via the acetoxysulphide (XXV), aldehyde (XXVI) is derived.[29] In another case the unstable intermediate *gem*-acetoxysulphide formed by the PR from the chiral sulphoxide (XXVII) is readily converted in high yield in a weakly alkaline medium to the aldehyde (XXVIII) without appreciable racemisation of the α-centre.[30] On the other hand, the β,γ-unsaturated aldehydes initially formed from the isoprenoid homallylic sulphoxides (XXIX) undergo smooth isomerisation to the conjugated aldehydes (XXX).[31]

Scheme 5

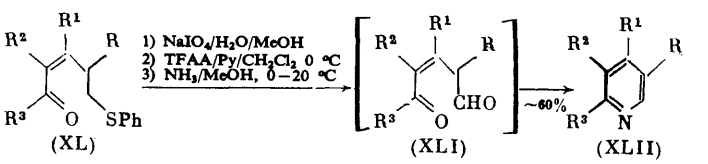


It should be noted that the conditions recorded above for the hydrolytic cleavage of *gem*-acyloxysulphides are not optimal in every case, especially when base- or acid-labile functional groups are present in their molecules. In such cases it is recommended to use Cu(II) and Hg(II) salts, which provide mild conditions for conducting the reaction, as catalysts (c.f. the study of Sugihara et al.).[32] In particular, in the synthesis of certain antitumour antibiotics, the labile β-trichloroacetamidoaldehydes (XXXIII) can be readily obtained from sulphoxides (XXXI) via the hydrolytic cleavage of acetoxysulphides (XXXII) catalysed by $CuCl_2$.[33] The use of $HgCl_2$ for the same purpose is illustrated by the conversion of the functionalised sulphoxides (XXXIV), (XXXVI), and (XXXVIII) without isolation of the intermediate trifluoroacetoxysulphides to the corresponding diene aldehydes (XXXV)[34] and (XXXVII),[35] which have served as building blocks in the total syntheses of 5-desoxy-leukotriene *D* and (±)-asteltoxin (an inhibitor of oxidative phosphorylation) respectively, as well as perillaldehyde (XXXIX)[36] (Scheme 6).

Scheme 6



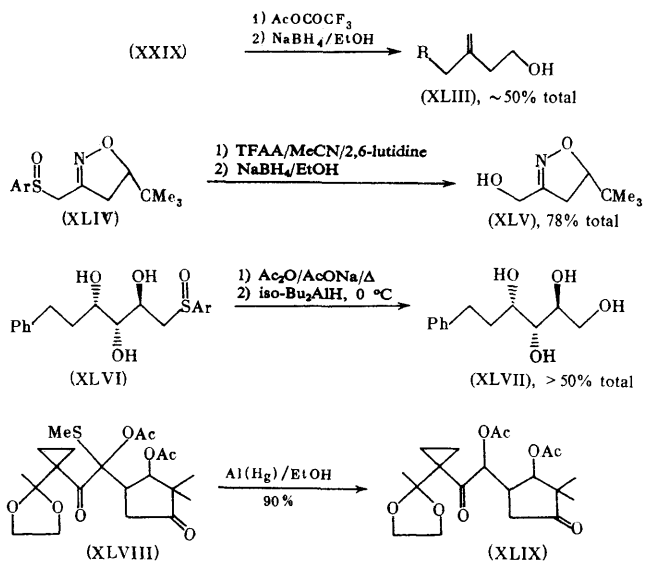
The use of a sulphoxide as a masked carbonyl compound, particularly if the latter is very unstable, is demonstrated by the preparation of pyridines (XLII) from sulphides (XL) once again without isolation of both the intermediate sulphinyls and the glutaconic aldehyde derivatives (XLI).[37] This method is successfully used at a key stage in the synthesis of the neurotoxin molecules—acromelic acids A[38] and B.[39]



R, R^1 = H, Me, $(CH_2)_2OMe$; R^2 = H; R^3 = Me; R^2, R^3 = $(CH_2)_4$

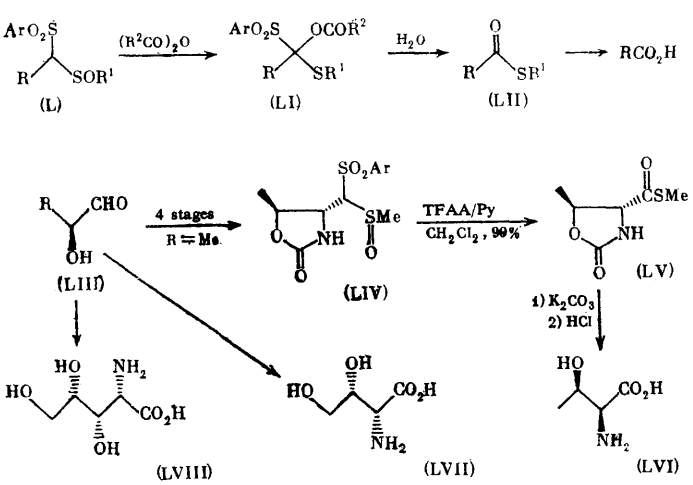
Sufficiently stable products of the PR of a number of acyloxysulphides can provide a direct source of primary and secondary alcohols, and the number of examples of such reactions, which are carried out as a rule in two variants, has steadily increased in recent times. Thus in Scheme 7, hydride reduction of the products of the PR involving (XXIX), and without their isolation, readily yields the corresponding linear γ-terpenols (XLIII),[40,41] which clearly could not be obtained with the inclusion of an intermediate hydrolytic stage (c.f. Scheme 5). Similarly the isoxazolidine sulphoxide (XLIV) is converted to the masked α-ketol (XLV) without saturation of the C=N bond,[42] while (XLVI) is converted to the arabitol derivative (XLVII).[43] Another variant of the reductive conversion from PR products to alcohols and their esters is illustrated by the desulphurisation with an aluminium amalgam of the relatively stable acetoxysulphide (XLVIII) prepared from the corresponding ketosulphoxide to give the α-keto acetate (XLIX)—a key compound in one of the schemes for the total synthesis of illudane sesquiterpenes.[44]

Scheme 7

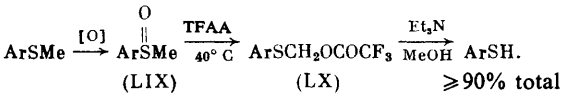


The Pummerer reaction can be readily used for the conversion to carboxylic acids from sulphoxides of the type (L), which contain an effective leaving group such as arylsulphonyl, making it possible to generate the thiol ester (LII) from intermediate (LI) (Scheme 8). In omitting a review of the methods for making the initial structures (L), based primarily on S-containing C_1-synthons,[45] we shall merely note here the recently developed stereocontrolled method of obtaining *syn*-β-hydroxy-α-amino acids from chiral α-hydroxyaldehydes (LIII).[46] Thus, the α-sulphinylsulphone (LIV) in the end gives thioester (LV) in high yield, which is then converted in a conventional manner to *D*-threonine (LVI). *L*-γ-Hydroxythreonine (LVII) and the polyhydroxyamino acid (LVIII) are obtained in a similar manner.

Scheme 8



The possibility of simple demethylation of (hetero)aromatic methylthioesters is an example of the use of the PR in the chemistry of protected groups that is worth considering.[47,48] Thus, the readily available sulphoxides (LIX) are converted in boiling TFAA to the corresponding arylthioesters (LX), which are then cleaved to the required thiophenols in virtually quantitative overall yield.

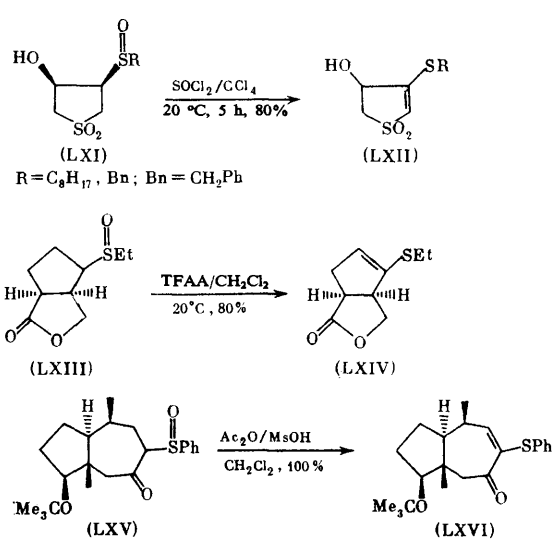


Thus, a primary or secondary sulphinyl group is a fairly versatile source for obtaining α-substitututed sulphides, carbonyl compounds, and their corresponding alcohols via the Pummerer reaction. It should be emphasised that the first of these compounds, primarily *gem*-acyloxysulphides and/or *gem*-chlorosulphides, under certain conditions act as counterparts of cationoid species of the type (IV)/(IVa), which open up new and currently quite extensively used opportunities for forming a C–C bond (see Section VII).

IV. Synthesis and certain properties of vinyl sulphides

Because of the cationoid nature of the PI (IV)/(IVa), one of the methods used to stabilise it involves the elimination of a β-proton to give vinyl sulphides (VI), which can also be formed through α-elimination of the *gem*-derivatives (V), especially if an electron-withdrawing substituent occurs at the β-position relative to the sulphur atom (see several studies).[1–11] Amongst recent examples, the preparation of vinyl sulphides of the type (VI) using $SOCl_2$ and certain other standard reagents such as $Sn(OTf)_2$ (Tf = F_3CSO_2) [54] as "activators" has been reported in a series of studies by Warren et al.[49–53] Similarly, treatment of *cis*-hydroxysulphinyl derivatives of sulpholane (LXI) with $SOCl_2$ gives vinyl sulphides (LXII) in high yield,[55] and the bicyclic sulphoxides (LXIII)[56] and (LXV)[57] on treatment with acid anhydrides readily afford olefins (LXIV) and (LXVI) respectively (Scheme 9).

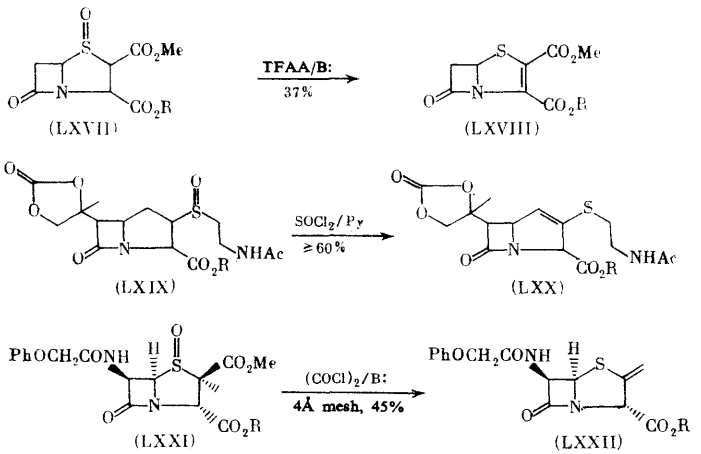
Scheme 9



The Pummerer reaction is very widely used at the present time in the synthesis of penicillin analogues, in particular those containing a vinyl sulphide residue (Scheme 10). Thus, for example, sulphoxides

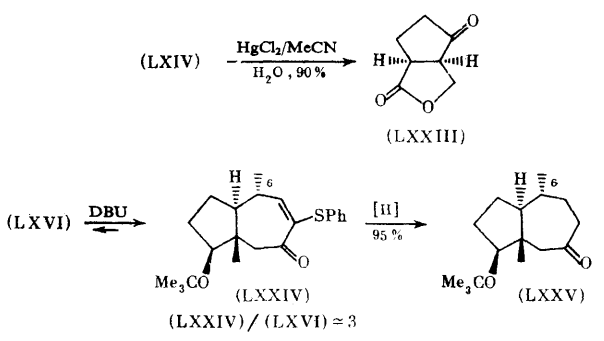
(LXVII) are converted to individual diesters (LXVIII),[58] carbapenams (LXIX) gives sulphides (LXX),[59] and compounds (LXXI), containing a carboxyl group in the vicinity of sulphinyl, are converted to olefins (LXXII).[60]

Scheme 10



B: = 2,6-collidine; R = *p*-$CH_2C_6H_4NO_2$

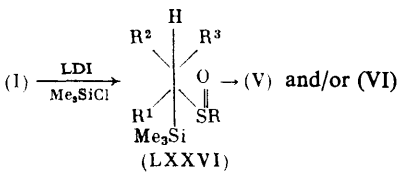
One of the obvious aspects of the synthetic use of vinyl sulphides is their conversion to carbonyl compounds; for example, (LXIV) gives the precursor (LXXIII) of sarkomycin in a recently published scheme of its total synthesis.[56] Exhaustive reduction of the vinyl sulphide function is rarely encountered. In the case of the ketovinyl sulphide (LXXIV) this method has been successfully used for yielding the precursor (LXXV) of the sesquiterpene pseudoguaiane after isomerisation of the C(6) site of the initial epimer (LXVI) using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[57]



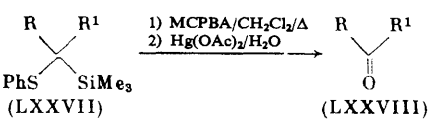
Thus, primary and secondary sulphoxides may be regarded as a direct source of obtaining substituted vinyl thioethers.

V. Silyl variant of the Pummerer reaction

It is well known[61] that thermally labile α-silyl sulphoxides (LXXVI), one of the methods for the synthesis of which is the *C*-silylation of initial compounds (I) deprotonated by lithium diisopropylamide (LDI), readily isomerise to α-silyloxysulphides (V) (Z = $OSiMe_3$). Further study of this silyl variant of the PR (SPR), which accompanies the formation of vinyl sulphides (VI), has identified the considerable possibility of using this reaction by interaction of (I) with silyl halides, in particular trimethylsilyl halides or their equivalents, as "activators" of the process, which evidently involves intermediates (II)–(IV)/(IVa) (X = $SiMe_3$, $SiMe_2Bu$-t, etc.).[62–64] It should be noted that in this case as well as the formation of products purely from the SPR—(V) (Z = $OSiMe_3$) and (VI)—a competing reduction of sulphoxides (I) to the corresponding sulphides occurs at the same time, and this is especially typical for (cyclo)aliphatic compounds.[65]

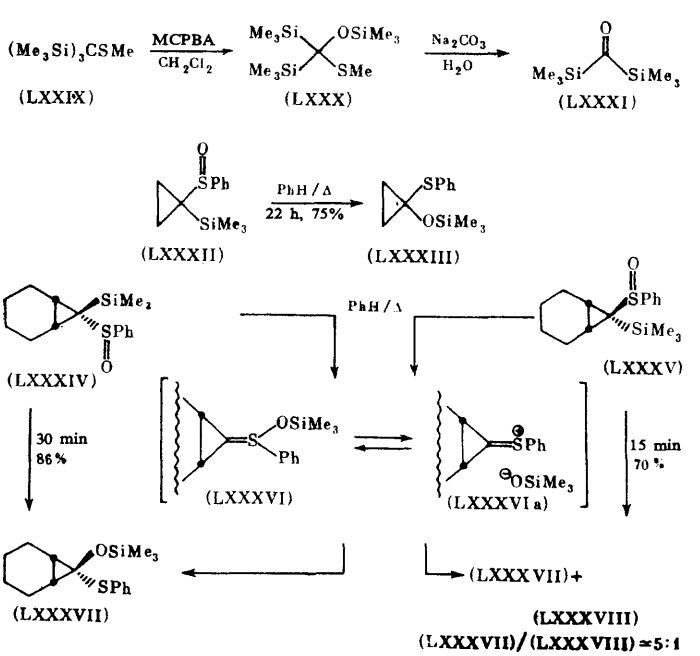


gem-Silyloxysulphides of the type (V) that are accessible using the SPR are, as a rule, very unstable compounds which are readily converted under hydrolytic conditions to the carbonyl products corresponding to the initial (LXXVI). This circumstance has predetermined a method of obtaining them *in situ* from silylsulphide C_1-synthons[45] as an alternative to the *C*-silylation of sulphoxides (I). For example, refluxing in THF or CCl_4 of the products of the oxidation of silylsulphides (LXXVII) by *m*-chloroperbenzoic acid (MCPBA) and subsequent hydrolytic treatment of SPR products catalysed by Hg(II) gives ketones (LXXVIII) in 50–80% yield.[66]



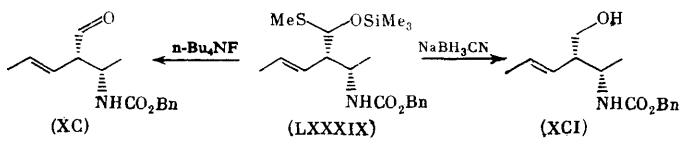
R, R^1 = Alk, All, Bn. Ph; All = $CH_2CH{=}CH_2$.

Scheme 11



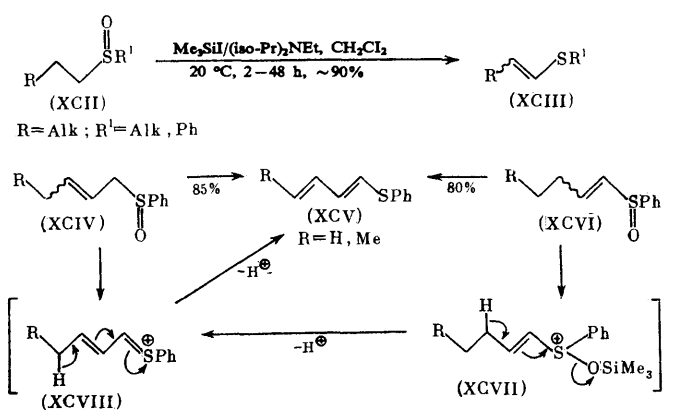
In specific cases the unstable α-silyloxysulphides can be isolated and used as individual compounds. Thus, as in Scheme (11), the tris(trimethylsilyl) sulphide (LXXIX) is smoothly converted to the heteroatomic methane derivative (LXXX), which is then converted to the simplest bis(trimethylsilyl) ketone (LXXXI).[67] Correspondingly, the *gem*-phenylsulphinyltrimethylsilylcyclopropanes (LXXXII), (LXXXIV), and (LXXXV) rearrange in boiling benzene to the cyclopropane derivatives (LXXXIII), (LXXXVII), and (LXXXVIII),[68] which are related to (XIX). The stereochemical result of the reaction in the case of (LXXXIV) and (LXXXV) indicates the preference for *exo*-attack by the counterion on the cation in (LXXXVIa), formed from intermediate (LXXXVI).

Like acyl derivatives (V) (Z = OCOR), the related silyloxy derivatives can be readily converted to the corresponding carbonyl compounds or their hydride reduction products; this is illustrated by the preparation of the aldehyde (XC) and alcohol (XCI) from *gem*-silyloxysulphide (LXXXIX).[69]



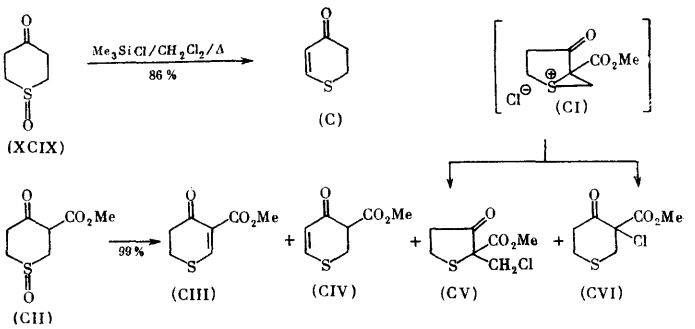
In the same way as the traditional variant, the SPR opens up a simple means of access to a whole range of functionalised vinyl sulphides. Thus, treatment of sulphoxides (XCII) with Me_3SiI in the presence of a Hünig base gives vinyl thioethers (XCIII) in high yield[70] (Scheme 12). In the case of allyl sulphoxides (XCIV) and vinyl sulphoxides (XCVI), whatever their stereochemistry, diene sulphides (XCV) are stereospecifically formed under the same conditions, probably via intermediates (XCVII) and (XCVIII).[70]

Scheme 12



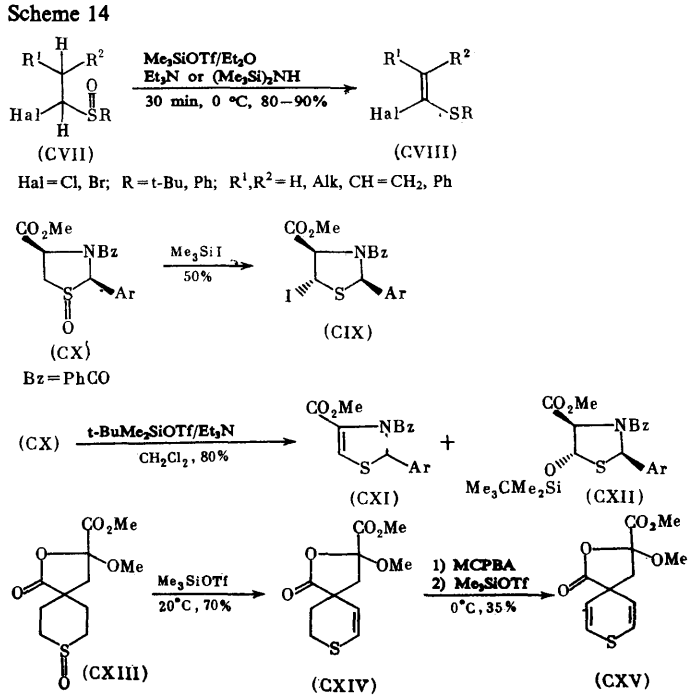
The presence of other functional groups in the vicinity of sulphinyl in molecules involved in the SPR of sulphoxides can cause other processes to take place. For example, in Scheme 13,[71] ketone (XCIX) on treatment with Me_3SiCl is readily converted to ketosulphide (C), whereas ketoester (CII) under the same conditions gives a mixture of sulphides in the ratio (CIII):(CIV):(CV):(CVI) ≃ 75:10:10:5, of which derivatives (CV) and (CVI) are evidently formed from the episulphonium intermediate (CI). It is interesting to note that when Ac_2O or TFAA are used as "activators", the same sulphoxide (CII) mainly (90%) gives a mixture of the (trifluoro)-acetates corresponding to chlorides (CV) and (CVI) in the ratio of ≃ 5:1.[71]

Scheme 13

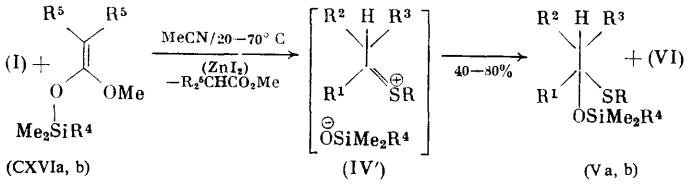


Considerable opportunities for the synthesis of different functionalised vinyl sulphides are opened up by the use of trimethylsilyl trifluorosulphonate (trimethylsilyl triflate, Me_3SiOTf) and other silyl triflates, which on "activation" of the initial sulphoxide liberate a virtually non-nucleophilic counterion. In particular, in Scheme 14, application of this method starting from α-halosulphoxides (CVII) leads to the smooth preparation of a series of acid-labile vinyl sulphides (CVIII), which is difficult to achieve when Me_3SiCl or Me_3SiI are involved.[72,73] Similarly, when the latter is used, the thiazolidine sulphoxide (CX) is mainly converted to the iodide (CIX), whereas with the use of t-$BuMe_2SiOTf$, a mixture of sulphides in the ratio (CXI):(CXII) ≃ 2:1 is obtained from (CX).[74] Finally, by carrying out the SPR with Me_3SiOTf twice, it is possible to synthesise the unstable vinyl sulphide (CXV) in satisfactory overall yield from (CXIII) via the monovinyl sulphide (CXIV).[75]

Scheme 14



Using this silyl variant of the PR, there is a current trend towards research into "activators" that achieve both the mildest conditions for generating the key PPI (II) and the possibility of effective control over the course of subsequent reactions involving the counterion $Y^{\ominus}$. In this respect the use of silyl triflates in combination with different bases appears in many cases to be the best way of suppressing unwanted side reactions. As a development of this approach, the use of the ketenacetals (CXVIa, b) as "activators" of



(CXVIa, b) (IV′) (Va, b)

R^4 = Me (a), t-Bu (b); R^5 = H, Me

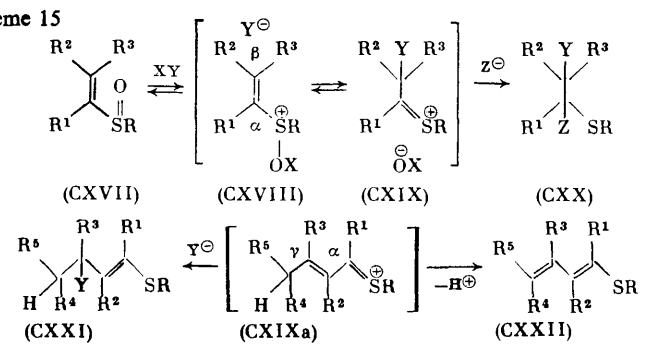
the SPR was recently proposed.[76–78] In this variant when components (I) and (CXVI) are allowed to stand in MeCN in the presence of 1.2–2.4 mole equivalents of ZnI_2, this generally gives a mixture of silyl ethers (Va, b) and vinyl sulphides (VI), whose ratio depends on the nature of the initial substrate (I). The reaction evidently occurs via a stage involving the PI (IV′), which when the trimethylsilyl ketenacetal (CXVIa) is used can react with the carbanion of methyl acetate or methyl isobutyrate formed as a result of decomposition of the latter (see Section VII). This does not occur in the case of acetal (CXVIb), which contains a sterically bulky substituent.

Thus, the SPR provides a simple means of converting sulphoxides to α-silyloxysulphides or related vinyl thioethers that have considerable synthetic potential.

VI. Vinyl sulphoxides in the Pummerer reaction

Up to the present time the Pummerer reaction involving linear and cyclic vinyl sulphoxides (CXVII) (Scheme 15), achieving simple ways for their effective functionalisation, has been studied quite extensively.[79] The main feature of these compounds is that because of the electron-acceptor properties of the PPI (CXVIII), there is the possibility of attack by an external (or internal) nucleophile on its β-centre. A similar stabilisation of the cationoid PI (CXIX) leads in the end to α,β-disubstituted sulphides (CXX). When a hydrogen atom occurs at the γ-position of the initial molecule of (CXVII), the PI, as a result of an allylic shift, can take the form of (CXIXa), which gives the vinylogue derivatives (CXXI) or the diene sulphides (CXXII) (c.f. Scheme 12). Heterolysis of the C–Y bond in the PI (CXIX) will formally give reduction products of the initial vinyl sulphoxides (CXVII).

Scheme 15

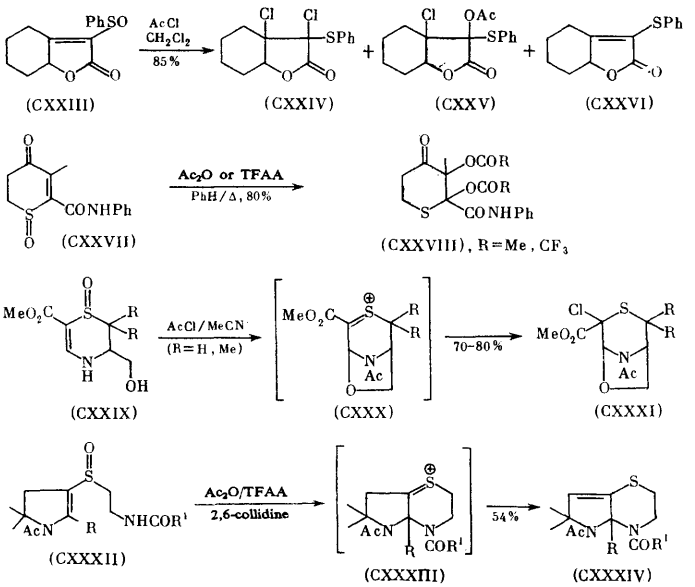


(CXVII) (CXVIII) (CXIX) (CXX)

(CXXI) (CXIXa) (CXXII)

All of these PR routes for (CXVII) have been widely introduced at the present time. In particular, in Scheme 16, treatment of the sulphinyllactone (CXXIII) with AcCl gives a mixture of sulphides in the ratio (CXXIV):(CXXV):(CXXVI) ≃ 5:1:1,[79] whereas the diacycloxysulphides (CXXVIII) are obtained from (CXXVII) by treatment with Ac_2O or TFAA.[80,81] Conversion of the sulphoxides (CXXIX)[82] and (CXXXII)[83] to the corresponding bicyclic derivatives (CXXXI) and (CXXXIV) can serve as an example of the intramolecular stabilisation of a PPI of the type (CXVIII) via the intermediate ions (CXXX) and (CXXXIII).

Scheme 16



(CXXIII) (CXXIV) (CXXV) (CXXVI)

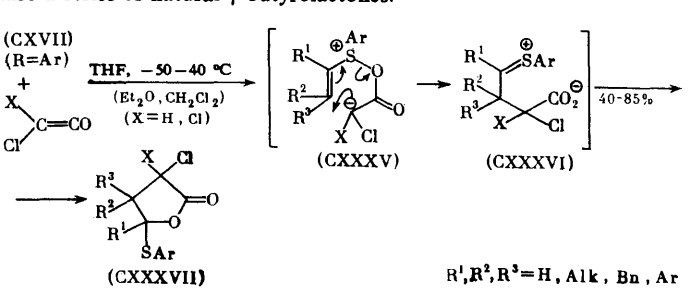
(CXXVII) (CXXVIII), R = Me, CF_3

(CXXIX) (CXXX) (CXXXI)

(CXXXII) (CXXXIII) (CXXXIV)

R = CO_2Me; R^1 = p-$CH_2C_6H_4NO_2$

"Activation" of aryl vinyl sulphoxides (CXVII) with chloroketenes which are readily generated from suitable acid chlorides has become the basis of a method that is widely used at the present time to obtain substituted γ-butyrolactones (CXXXVII), including natural products.[84–90] The reaction evidently occurs via the [3,3]rearrangement of the compact zwitterionic PPI (CXXXV) followed by intramolecular cyclisation of the PI (CXXXVI). The relatively high rate of the latter compared to rotation of the C–CS bond accounts for the high enantioselectivity of this process, which makes it possible when using a monosubstituted chloroketene to go from optically active (CXVII) to lactones with three induced chiral centres.[85] The method has been successfully applied to the synthesis of (–)-methyl jasmonate,[86] certain physostigmine alkaloids,[89] and also a series of natural γ-butyrolactones.[87,88,90]



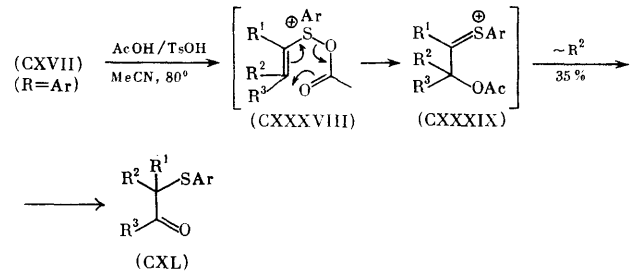
(CXXXV) (CXXXVI)

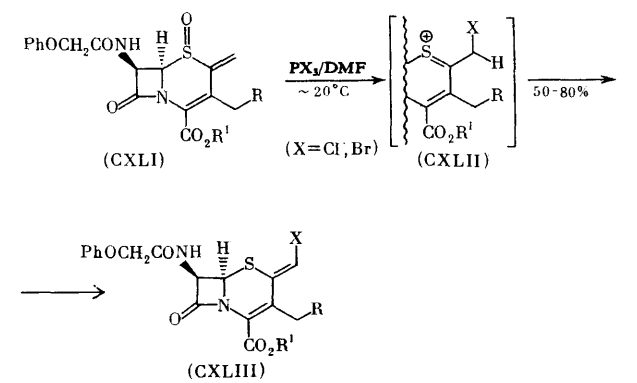
(CXXXVII)

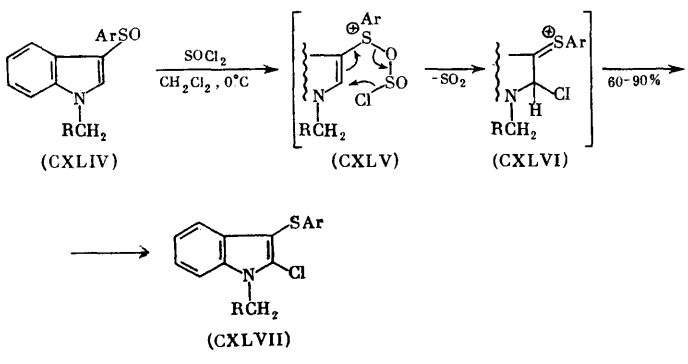
R^1,R^2,R^3 = H, Alk, Bn, Ar

With regard to the possible PR mechanism, one of the ways of stabilising the cationoid PI (CXIX) not included in Scheme 15 may involve a 1,2-shift of the R^2 and R^3 β-substituents. Examples of reactions of this type are for the time being fairly limited, but amongst them special mention should be made of the recently reported skeletal rearrangement of (CXVII) series aryl vinyl sulphoxides to ketosulphides (CXL), induced by TsOH in boiling MeCN and occurring preferentially via the formation of (CXXXVIII) and (CXXXIX)[91] (Scheme 17). The preparation of the halosulphoxides (CXLIII), which are evidently formed via PI (CXLII), under conditions of the Vilsmeier reaction from cephalosporin sulphoxides (CXLI) can be regarded as a specific case.[92] Similarly, the β-indole derivatives of the type (CXLIV), which are formally classed as vinyl sulphoxides, are readily converted by $SOCl_2$, probably via intermediates (CXLV) and (CXLVI), to the α-chloro-β-sulphides (CXLVII).[93,94]

Scheme 17

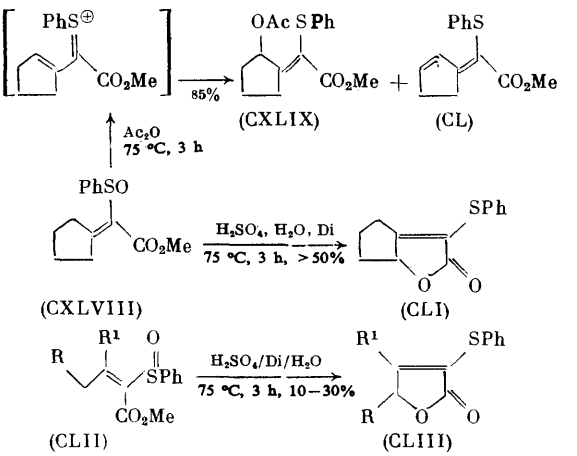






In addition to the routes given above in Scheme 15, the vinyl variant of the PR is illustrated by the conversion of the sulphoxide (CXLVIII) to a mixture of vinyl sulphides in the ratio (CXLIX):(CL) ≃ 3:2 or to the lactone (CLI)[79] (Scheme 18). Similarly, vinyl sulphoxides (CLII) on heating with dilute H_2SO_4 give the dihydrofuranones (CLIII).[79]

Scheme 18



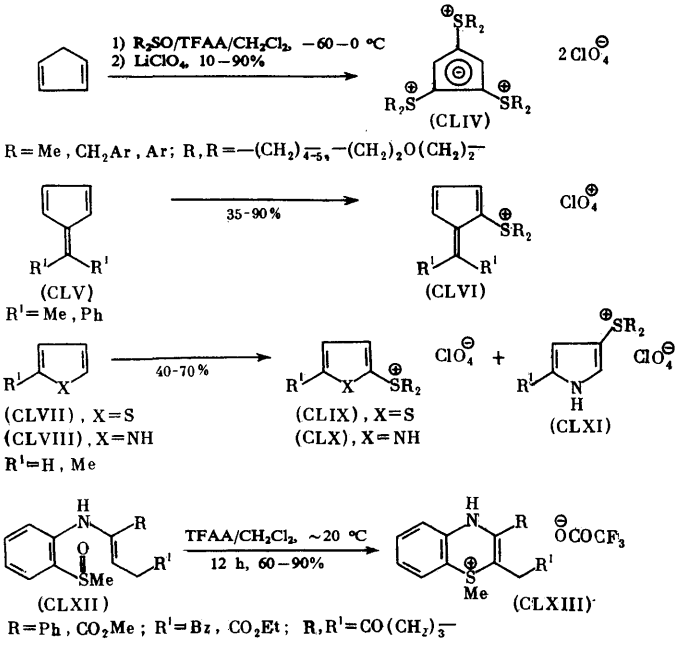
Thus, there is a direct Pummerer route from vinyl sulphoxides to sulphides that are functionalised at the α, β-, and γ-positions.

VII. Electrophilic properties of the intermediates of the Pummerer reaction

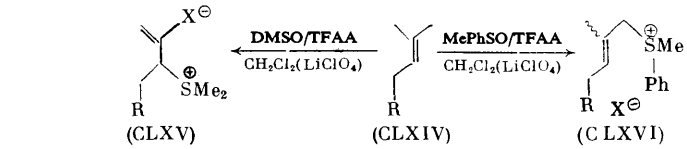
As mentioned above (Section II), the existence of the probable PR intermediates (II) and (IV)/(IVa), which are classified as weakly electrophilic species, has been indirectly supported by the results of the reaction between sulphoxides and different nucleophiles (external and internal). At the same time recent data provide additional information about the nature of the individual stages of this reaction, extending the possibilities for controlling it, and hence new horizons are opened up in the rapidly developing synthetic organic chemistry of sulphur-containing compounds.

In this respect the recently developed method for the synthesis of stable perchlorates of sulphonium salts from cyclopentadiene and (benzo)fulvenes[95-98] (Scheme 19) is of considerable interest. Thus, low-temperature treatment of sulphoxides "activated" by TFAA with cyclopentadiene or fulvenes (CLV) gives the tris-(CLIV) or mono-sulphonium salts (CLVI) in up to 90% yield, which are evidently formed respectively by attack on PPI of the type (II) by these *C*-nucleophiles. Derivatives of thiophene,[99] pyrrole, and indole[100-102] may fulfil a similar role. In particular, thiophenes (CLVII) are readily converted in this way to perchlorates (CLIX), while pyrroles (CLVIII) are converted to a mixture of the regioisomeric salts (CLX) and (CLXI) that is equilibrated on treatment with a proton acid. An example of the intramolecular interaction of a probable PPI with a reactive C=C bond is the smooth conversion of enaminosulphoxides (CLXII) to trifluoroacetates (CLXIII) by treatment with TFAA.[103]

Scheme 19



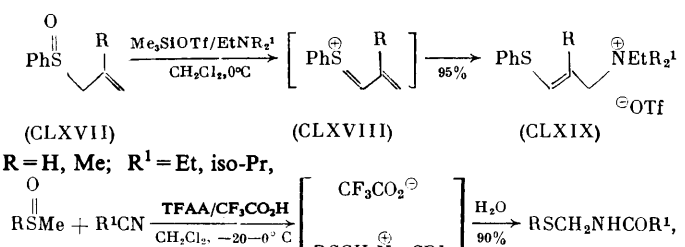
Taking into account the above, the recently established possibility of obtaining the fairly stable dimethyl sulphonium salts (CLXV) in this way from unactivated trisubstituted olefins (CLXIV)[104,105] proved unexpected. It was established in this case that this reaction, formally an ene reaction and accelerated by added quantities of $LiClO_4$, is regiospecific in a series of linear isoprenoid oligoolefins and is accompanied by allylic isomerisation with formation of the terminal sulphonium salt (CLXVI) in the case of thioanisole *S*-oxide.



The results of the synthetic application of the electrophilic properties of PR intermediates at the present time have proved much more fruitful in relation to the PI (IV) than to the evidently much more stable PPI (II). In this case inter- and intra-molecular stabilisation of the probable cationoid species (IV) by nucleophiles is now represented equally well and is illustrated below by the derivation of various α-functionalised sulphides from suitable linear and cyclic sulphoxides.

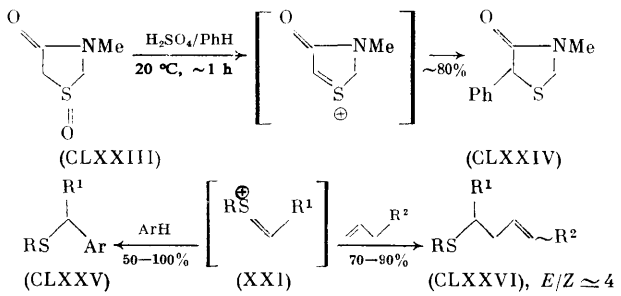
A unique example of this type of intermolecular interaction is the Me_3SiOTf-induced formation of ammonium salts (CLXIX) from allyl sulphoxides (CLXVII) in the presence of tertiary amines, including a Hünig base, which proved to be the only external nucleophiles capable of stabilising the PI (CLXVIII),[106,107] and there is also the Ritter reaction of sulphoxides (CLXX) to amides (CLXXII), which evidently occurs via the formation of nitrile salts (CLXXI)[108] (Scheme 20).

Scheme 20



Recorded cases of the involvement of a PI of the type (IV) in a reaction with external *C*-nucleophiles are much more widespread. Thus, in Scheme 21, the thiazolidine β-ketosulphoxide (CLXXIII) is readily phenylated on treatment with conc. H_2SO_4 in benzene to the ketosulphide (CLXXIV),[109] which is a special case of the (hetero)-arylation of PIs (XXI) that are generated by different methods from linear sulphoxides (XX) and mainly have a β-electron-withdrawing susbtituent, and resulting in products (CLXXV).[110–115] The presence of such a substituent is in no way obligatory for the formation of β-vinyl sulphides (CLXXVI) from PI (XXI) and functionalised terminal alkenes, which occurs quite readily by an ene type of reaction; (CLXXVI) have been successfully used at the key stages of the synthesis of a number of natural products.[116–122]

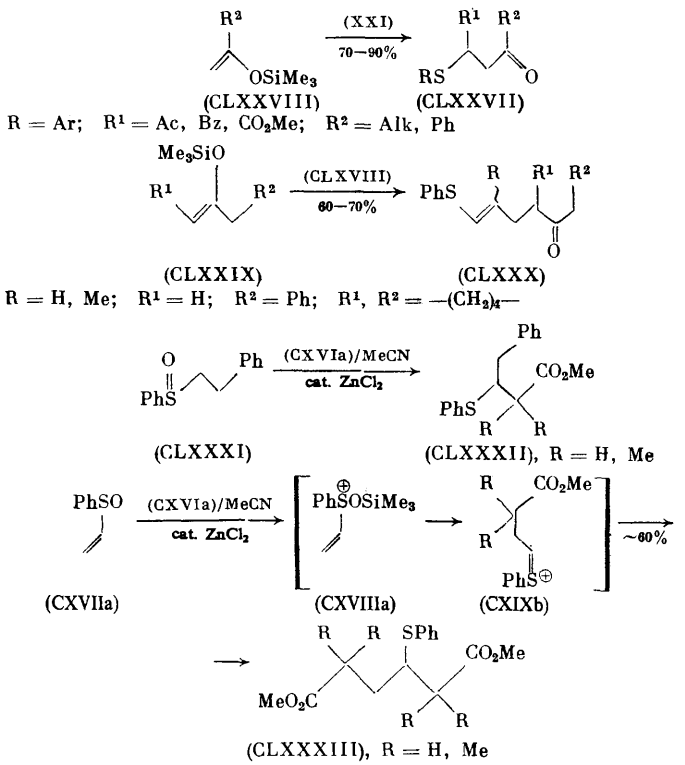
Scheme 21



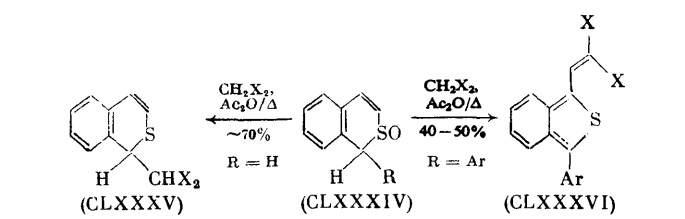
Of the *C*-nucleophiles that are suitable for intermolecular combination with a PI of the type (VI), particular importance is starting to be attached to silyloxyolefins such as (CLXXVIII) and (CLXXIX) (Scheme 22), which are widely used in current synthetic practice to form a C−C bond by a directed aldol condensation.[63,123] In accordance with this approach, the low-temperature generation of PI (XXI) or (CLXVIII), usually carried out with the involvement of "activator" reagents such as $Sn(OTf)_2$ or Me_3SiOTf in the presence of a Hünig base, bis(trimethylsilyl)(trifluoro)acetamide, or Me_3SiI finally gives the corresponding products of α-*S*-ketoalkylation (CLXXVII)[124,125] or γ-*S*-ketoalkylation (CLXXX).[107,126] Similarly, on treatment with an excess of ketenacetal (CXVIa)—an "activator" and *C*-nucleophile at the same time—the sulphoxide (CLXXXI) is readily converted to sulphide (CLXXXII),[77] evidently as a result of attack on a PI of the type (XXI) by the carbanions of methyl acetate or methyl isobutyrate (c.f. Section V). Under such conditions (CXVIa) and vinyl sulphoxide (CXVIIa) give adduct (CLXXXIII),

whose formation can only be logically accounted for by the successive reaction of the above carbanions with PPI (CXVIIIa) and PI (CXIXb).[78]

Scheme 22



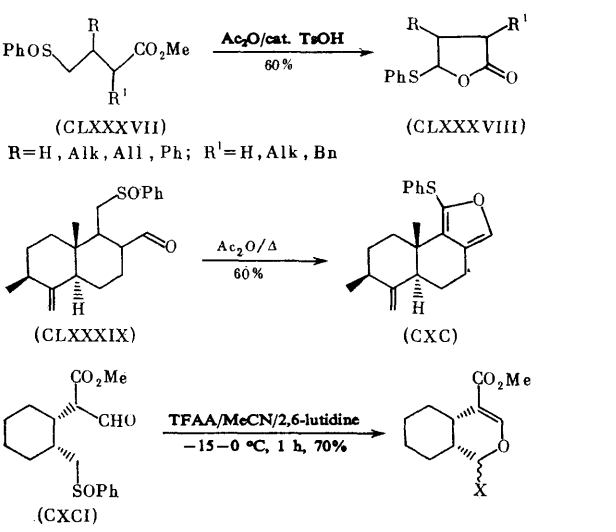
A familiar method for generating *S*-ylids from sulphoxides and C–H acids[11] in the case of derivatives of benzothiapyrans (CLXXXIV) leads to products of their α-*C*-alkylation (CLXXXV) or ring contraction products—benzothiophenes (CLXXXVI).[127]



X = Ac, CO_2Et, Bz; Ar = Ph, *o*-BrC_6H_4, *o*-MeC_6H_4, 2, 3, 5, 6-Me_4C_6H

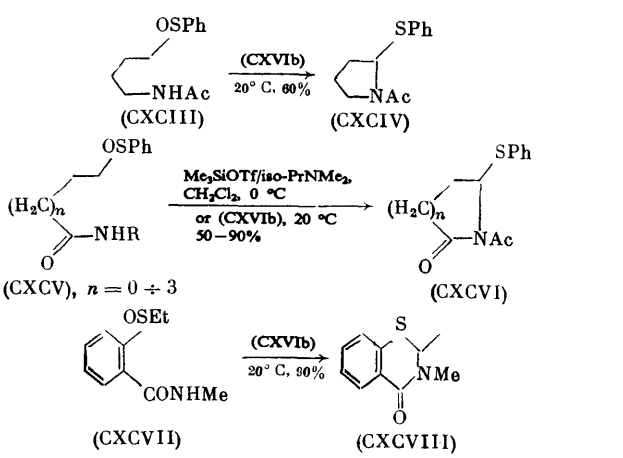
The methods of stabilising PIs of the type (IV) generated *in situ* using internal *O*-, *N*-, or *C*-nucleophiles as predicted from the probable mechanism of the PR open up considerable possibilities for the regiocontrolled synthesis of different heterocyclic and carbocyclic structures from suitable precursors. The conversions of γ-sulphinylcarboxylate esters (CLXXXVII) to lactones (CLXXXVIII),[128] aldehyde (CLXXXIX) to furan (CXC),[129] and sulphoxide (CXCI) to a mixture of (CXCIIa) and (CXCIIb) in the ratio ≃ 1:4, which is subsequently used in the synthesis of the iridoid aglycone of sweroside,[130] can be given as examples (Scheme 23).

Scheme 23



Of *N*-nucleophilic functional groups that are capable of undergoing an intramolecular reaction with a PI, the only known example up to the present time is the amide group.[131–135] For example, in Scheme 24, the amidosulphoxide (CXCIII) in the presence of ketenacetal (CXVIb) readily gives the pyrrolidine derivative (CXCIV),[134] whereas sulphinylamides (CXCV) are readily converted under mild conditions to the heterocyclic sulphides (CXCVI). Treatment of the optically active sulphoxide (CXCV) (*n* = 0, R = H) with Me_3SiOTf gives the corresponding chiral lactam (CXCVI) with an enantiomeric purity of 70%.[132] By using ketenacetals (CXVIb) in the case of (CXCVII) it is possible to synthesise the benzothiazine (CXCVIII),[134] which is unobtainable when traditional "activators" such as Ac_2O are used.[133]

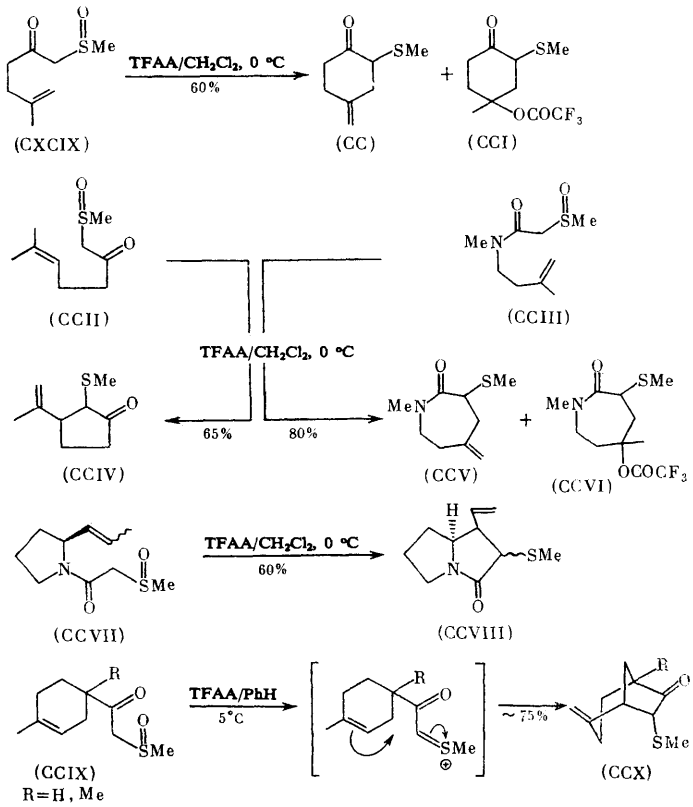
Scheme 24



An unactivated C=C bond within the molecules of unsaturated sulphoxides also can and does serve as a nucleophilic residue that participates in the stabilisation of the corresponding PI, and in all of the known examples this variant of the PR requires β-ketosulphinyl substrates.[136–141] Thus, in Scheme 25, the keto derivative (CXCIX) can be readily converted to the mixture of cyclohexane

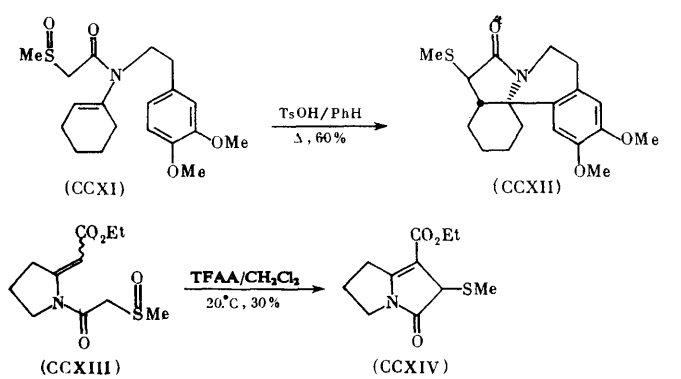
α-ketosulphides (CC) and (CCI).[138] The five-membered product (CCIV) (*cis*:*trans* ≃ 2:1)[138] and seven-membered (CCV) and (CCVI)[139] are obtained from sulphoxides (CCII) and (CCIII) by the same method. The bicyclic compounds (CCVIII)[140] and (CCX)[141] are prepared in high yield by electrophilic cyclisation of the precursors (CCVII) and (CCIX) respectively.

Scheme 25



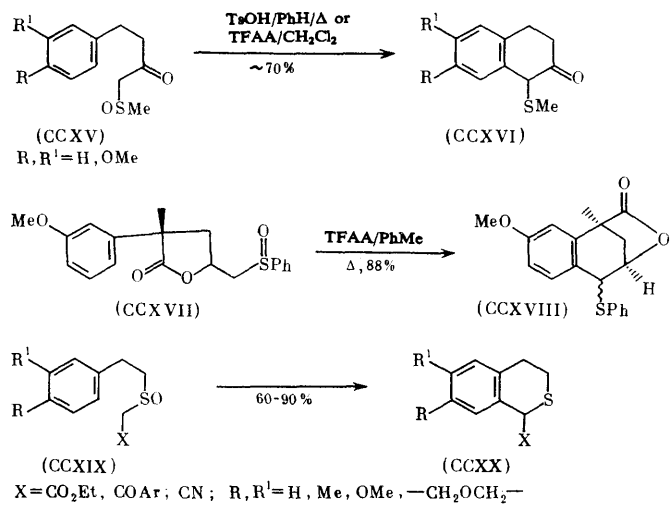
The results of cyclisation of sulphinyl derivatives of enamides by the Pummerer reaction, such as the reactions of (CCXI)[142–145] and (CCXIII)[146] to the erythrinan (CCXII) and pyrrolizidine (CCXIV) respectively, indicate that an increase in nucleophilic capacity of an internal C=C bond is not always accompanied by an increase in the efficiency of the process (Scheme 26).

Scheme 26



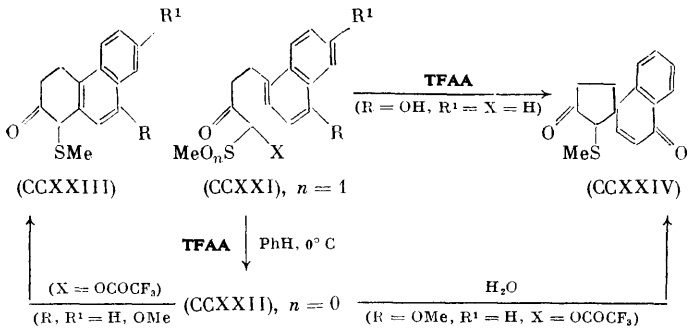
In addition to those reactions considered above, a large number of possible variants of the intramolecular stabilisation of PIs generated by various methods involving a (hetero)aromatic residue of the initial molecule have been reported. Thus, the well-established[147,148] cyclisation of aromatic ketosulphoxides of the type (CCXV) to tetralones (CCXVI) (Scheme 27) has now been considerably extended through examples of the synthesis of related five-, six-, and seven-membered bi- and tri-cyclic structures.[149–153] In particular, the conversion of the phenyl sulphoxide (CCXVII) to the tricyclic lactone (CCXVIII) is used as the basis of the enantio-controlled synthesis of (+)-aphanorphine.[153] The series of benzothiopyrans (CCXX) is prepared in a similar manner from sulphoxides (CCXIX) and a number of their derivatives.[154–158]

Scheme 27



In principle, cyclisation of the above ketosulphoxides induced by carboxylic anhydrides can occur, as a result of equilibrium (*4*) (Scheme 1), with the involvement of *gem*-acyloxysulphides of the type (V) (Z = OCOR) as kinetically independent species. This is quite extensively used (c.f. Section III) for the formation of a C–C bond based on stable *gem*-derivatives of this series,[159,160] and in particular for the two-stage preparation of these cyclisation products.[112–122,136–141] During the direct cyclisation of keto-sulphoxides, *gem*-derivatives of the type (V) can sometimes be isolated[136–141] or detected spectroscopically. Thus, in Scheme 28,[149] analysis of a mixture of (CCXXI) (X = H) and TFAA by NMR spectroscopy indicates that there is a rapid formation of the sulphide (CCXXII) (X = $OCOCF_3$), which is then slowly converted to the tricyclic product (CCXXIII). It is worth noting that treatment of the reaction mixture at this stage with 1 mole equivalent of H_2O gives the spirodiketone (CCXXIV), as does the addition of TFAA in benzene to (CCXXI) (R = OH, R^1 = X = H).

Scheme 28

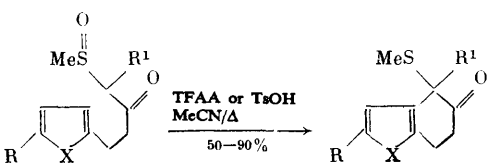


(CCXXIII) (CCXXI), $n = 1$ (CCXXIV)

(CCXXII), $n = 0$

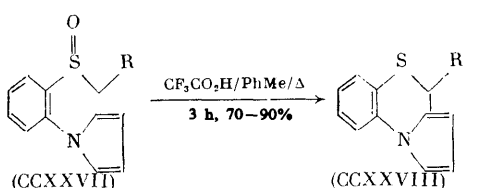
The application of this approach to the synthesis of condensed pyrrole and thiophene derivatives is demonstrated (Scheme 29) by the cyclisation of the precursors (CCXXV) to ketosulphides (CCXXVI) on treatment with different "activating" agents.[161] Similarly, heating of sulphoxides (CCXXVII) with CF_3CO_2H in toluene gives the tricyclic sulphides (CCXXVIII) in high yield.[162]

Scheme 29



(CCXXV) (CCXXVI)

X = NH, S; R = H, Ph; R¹ = H, CONHPh,

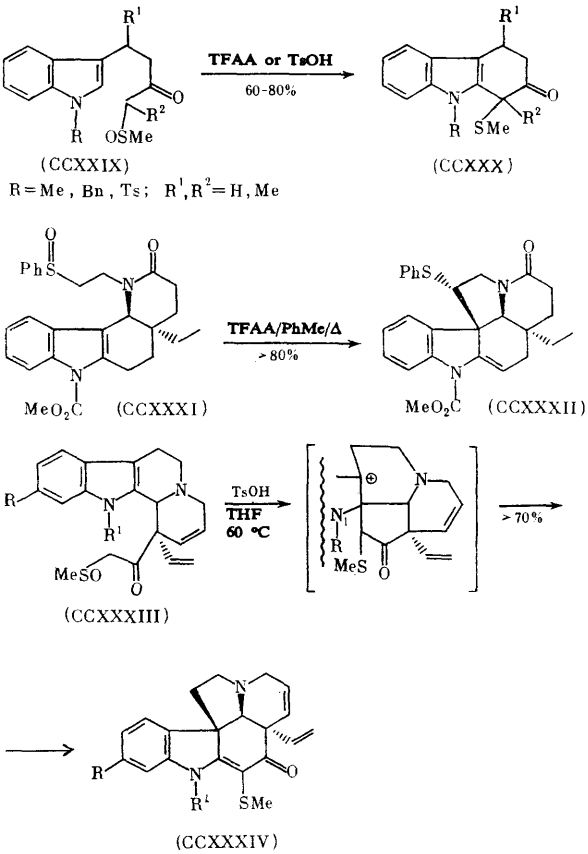


(CCXXVII) (CCXXVIII)

R = CO_2Et, Bz, CN.

The use of the PR for the stereoselective synthesis of polyheterocyclic structures such as indole alkaloids has proved extremely productive. As an illustration, Scheme 30 shows the preparation from the bicyclic precursor (CCXXIX) and tetracyclic precursors (CCXXXI) and (CCXXXIII) of the corresponding tricyclic compound (CCXXX) and pentacyclic compounds (CCXXXII) and (CCXXXIV), which act as key products in the total synthesis of olivacine and ellipticine,[161,163] (±)-8-oxotabersonine,[164] vindorosine, and vindoline.[165,166] These reactions have been used as the basis for the recently developed strategy for the total synthesis of other pentacyclic indole alkaloids.[167–171]

Scheme 30



R = H, OMe; R¹ = Me, CH_2OMe

Thus, sulphoxides can be successfully used in the PR for the intra- and inter-molecular variants of forming a C–C, C–N, C–O, and C–S bond, which is difficult to achieve by other methods.

Thus, the PR at the present time is a powerful tool in fine organic chemistry, making it possible to obtain in different ways from various primary and secondary sulphoxides functionalised linear, carbocyclic and heterocyclic sulphides, sulphonium salts, carbonyl compounds, and other classes of organic compounds.

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Translated from *Uspekhi Khimii* 60 1283–1317 (1991) U.D.C. 547.92

The synthesis of brassinosteroids, a new class of plant hormones

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ABSTRACT. Data on methods of synthesis of brassinosteroids are correlated. In view of their extremely low reported content in nature, the role of chemical synthesis from other natural steroids as the main source of obtaining these hormones for detailed study and practical use is assessed.

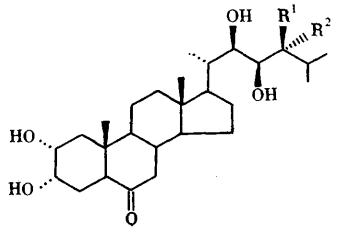
The bibliography contains 224 references.

Contents

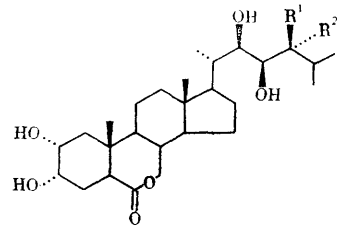
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I. Introduction

Hyopotheses have been expressed many times on the possible hormonal function of steroids in plants because of the numerous functions of steroidal compounds as hormones in man and the higher animals,[1,2] insects[3,4] and certain fungi,[5] and also of their wide distribution in the plant world.[1,3] The first real confirmation of the role of steroids as hormones in higher plants was obtained in 1979 when American scientists established the structure of brassinolide (VIII), a powerful growth stimulant, isolated from rape pollen.[6] Subsequently several compounds, structurally and functionally related to brassinolide, called the brassinosteroids (BS),[7–9] were isolated from various sources and identified, and heralded a new group of phytohormones. Some of these compounds, which today number close to 30, are given below.[10] The ecdysteroids are the closest in structure of the brassinosteroids.[3,4]



brassinone, $R^1=R^2=H$ (I)
castasterone, $R^1=Me$, $R^2=H$ (II)
epicastasterone, $R^1=H$, $R^2=Me$ (III)
homocastasterone, $R^1=Et$, $R^2=H$ (IV)
dolichosterone, $R^1R^2=CH_2$ (V)
homodolichosterone, $R^1R^2=CHMe$ (VI)



norbrassinolide, $R^1=R^2=H$ (VII)
brassinolide, $R^1=Me$, $R^2=H$ (VIII)
epibrassinolide, $R^1=H$, $R^2=Me$ (IX)
homobrassinolide, $R^1=Et$, $R^2=H$ (X)
dolicholide, $R^1R^2=CH_2$ (XI)
homodolicholide, $R^1R^2=CHMe$ (XII)

Features of the chemical structure of BS are the presence of 2α,3α- and (22*R*, 23*R*) diol groupings, a *trans* junction of rings A and B, and a 6-keto group [compounds (I)–(VI)] or a lactone function in ring B [compounds (VII)–(XII)]. Certain compounds do not contain some of the above groupings and are probably biosynthetic precursors of the corresponding BS with a complete set of functions. Compounds with an additional methyl group at C-25 have also been isolated.

In view of the extremely low BS content reported in plants (10^{-5}–10^{-12}%) and the short period in which they have been investigated, it must be assumed that the inventory of natural products of this type is far from complete. For the same reason it is difficult to judge at present the real distribution of BS in various plants. At the same time it follows quite unequivocally from the available data that the method of isolation from natural raw material cannot be considered as a practical route for providing the BS required for their study and possible use in plant culture. Individual attempts to make this approach of practical value have not changed the overall position.[11–13] This explains the wide range of investigations on BS synthesis begun in various countries directly after establishment of the brassinolide structure. Up to the present time several schemes have been developed for the partial synthesis of BS from other groups of natural steroids. Total synthesis is obviously only of theoretical interest since it requires the formation of the exceptionally complex stereochemistry of these considered compounds which contain 11–13 chiral centres in the molecule. It must be emphasised that even a partial synthesis is an extremely complex task particularly when forming the polyfunctional side chain.

Widespread investigations on the synthesis of BS have led to the publication of a large number of papers devoted to this problem, including several reviews.[7,8,14–28] In addition the rapid

accumulation of new information and the limited availability of the majority of foreign reviews, coupled with the lack of them in the domestic literature, has made preparation of the present review urgent.

II. General principles characteristic of syntheses of the natural brassinosteroids

Any scheme for the synthesis of BS may be divided provisionally into two parts, (a) the formation of the structural elements of the tetracyclic nucleus characteristic of BS and (b) construction of the side chain of the molecule. For the first time investigators have encountered the need to construct a polyfunctional side chain containing 4 asymmetric carbon atoms (a task only known in the case of the steroids, however that is simpler) and the traditional steroid chemistry methods developed during investigations on ecdysone synthesis may be used to functionalise the cyclic portion of the molecule.

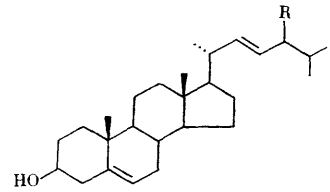
When solving problems of the strategy and tactics of BS synthesis, particularly for practical use, it is necessary to consider several circumstances, primarily the level of growth stimulating activity of a BS, its relative synthetic availability and sources of steroid raw material. The most acceptable starting materials are the available natural steroids containing a Δ^{22}-bond in the side chain, such as stigmasterol (XVI) and ergosterol (XVII). The available cholesterol (XVIII) and β-sitosterol (XIX), which do not contain such a bond, enable the preparation only of BS analogues with a non-functional side chain, possessing as a rule comparatively little activity. The use of 22-dehydrocampesterol (XIV) and brassicasterol (XV) is extremely attractive. These have recently become commercially available due to the development of efficient methods for their isolation.[29–33] Other possibilities are linked with the use as starting materials of cholic acid derivatives such as hyodeoxycholic acid (XX) and steroids of the pregnane series, particularly pregnenolone (XXI) which is used in the pharmaceutical industry for making drugs.

Depending on the starting materials used and the target products all the synthetic schemes may be divided into two large groups:

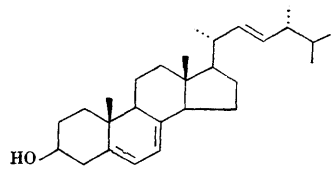
— syntheses retaining the native carbon skeleton of the starting material,

— syntheses forming new carbon–carbon bonds in the side chain.

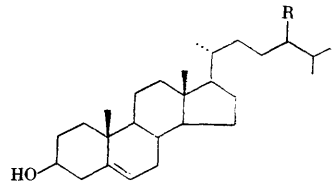
It is obvious that syntheses of the first group are simpler and more economical since no changes are required in the carbon skeleton. In addition the possibilities of using this approach are limited by the availability of sterols having the required carbon skeleton and functionality enabling construction of all the structural elements of the desired compound to be effected. For example the comparative availability of ergosterol and stigmasterol requires only direct functionalisation of the starting material, without breaking and forming new C–C bonds, in syntheses of epibrassinolide and homobrassinolide respectively. At the same time due to the limited availabity of 22-dehydrocampestrol (XIV), which possesses the appropriate carbon skeleton, the main method for the synthesis of brassinolide is still the conversion of stigmasterol into the 22-aldehyde [for example compounds (XXII) and (XXIII)] by fission of the $C_{22}-C_{23}$ bond and subsequent introduction of the $C_{23}-C_{28}$ fragment. Depending on the starting material, other variants of constructing the side chain of brassinolide include the introduction of $C_{22}-C_{28}$ or $C_{24}-C_{28}$ fragments (in the case of initial steroids of the pregnane series or the C_{23} series respectively)



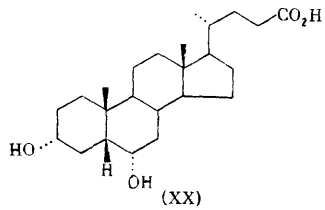
22-dehydrocholesterol, R = H (XIII)
22-dehydrocampesterol, R = α-Me (XIV)
brassicasterol, R = β-Me (XV)
stigmasterol, R = α-Et (XVI)



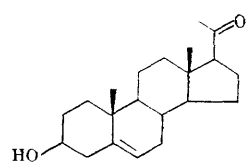
(XVII)



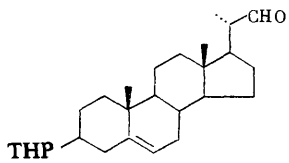
R = H (XVIII)
R = α-Et (XIX)



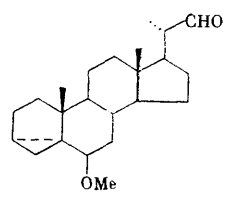
(XX)



(XXI)



(XXII)



(XXIII)

THP = tetrahydropyran-2-yl

An optimum choice of the sequence of transformations to be carried out in the cyclic portion and the side chain is absolutely essential for the provision of an efficient synthetic scheme, since in many cases the overall yield and number of stages is linked directly to it. Although the choice of variants for constructing structural fragments of the BS molecule is comparatively large, the sequence of using them in a synthetic scheme has paramount importance for the achievement of the maximum positive effect overall. A general illustration of the features and efficiency of the schemes developed for BS synthesis is given in Table 1.

Table 1. Syntheses of the most important natural BS.

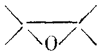
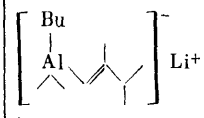
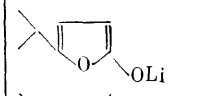
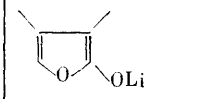
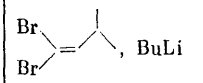
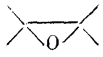
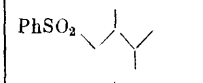
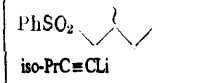
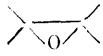
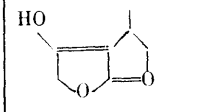
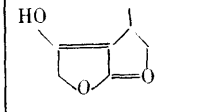
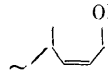
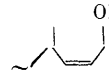
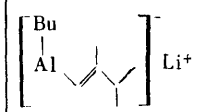
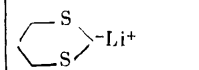
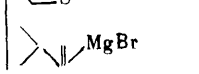
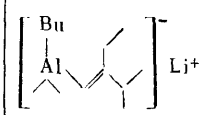
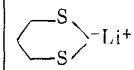
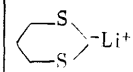
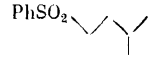
BS	Starting material	Type of synthesis	Method of forming side chain			No. of steps	Overall yield, %	Refs.
			carbon atoms introduced	substrate functional group	reagent			
(VIII)	(XXII)	S → B_k → A → B_l	1) C_{23}–C_{27}	–CHO	iso-PrC≡CLi	23	2.5	[34]
			2) C_{28}		$HCN-Et_3Al$		3.6	[35]
(VIII)	(XXIII)	»	C_{23}–C_{28}	–CHO		12	–	[36]
(VIII)	(XXIII)	»	C_{23}–C_{28}	–CHO		–	–	[37]
(VIII)	(XXIII)	»	C_{23}–C_{28}	–CHO		–	–	[37]
(VIII)	(XX)	»	C_{23}–C_{28}	–CHO	$Me_2CH_2COCHAsPh_3$	–	–	[38]
(VIII)	(XIV) + (XV)	B_k → A → S → B_l	–	–		10	0.9	[39]
(VIII)	(XVI)	»	1) C_{23}–C_{27}	–CHO		15	7	[40]
			2) C_{28}		Me_3Al, BuLi	16	3	[41–45]
(VIII)	(XVI)	»	C_{23}–C_{26}	–CHO		19	1.3	[46–47]
(VIII)	(XVI)	B_k → S → A → B_l	C_{23}–C_{28}	–CHO		20	7.8	[48]
(VIII)	(XVI)	B_o → S → B_k → A → B_l	1) C_{23}–C_{27}	–CHO	iso-PrC≡CLi	15	8.5	[49–51]
			2) C_{28}		Me_3Al, BuLi			
(VIII)	(XXI)	»	C_{22}–C_{28}	=CO		25	7	[52, 53]
(VIII)	(XXI)	B_k → A → S → B_l	C_{22}–C_{28}	=CO		25	10.5	[54–56]
(VIII)	(XXIII)	S → B_k → A → B_l	1) C_{23}–C_{27}	–CHO	iso-PrC≡CMgBr	9	2.5	[57]
			2) C_{28}		$MeC(OEt)_3$			
(VIII)	(XXIII)	»	1) C_{23}–C_{24}	–CHO	HC≡CLi	24	5.3	[58–60]
			2) C_{28}	–C=CH	MeI, BuLi			
			3) C_{25}–C_{27}		$EtC(OEt)_3$			
(XI)	(XVI)	B_k → A → B_l → S	C_{23}–C_{28}	–CHO		18	1.5	[42, 61–62]
(XI)	(XVI)	»	1) C_{23}	–CHO		20	7.6	[63, 64]
			2) C_{24}–C_{28}	–CHO				

Table 1 (continued).

BS	Starting material	Type of synthesis	Method of forming side chain: carbon atoms introduced	Method of forming side chain: substrate functional group	Method of forming side chain: reagent	No. of steps	Overall yield, %	Refs.
(IX)	(XVII)	$B_k \rightarrow A \rightarrow S \rightarrow B_l$	–	–	–	10	4.6	[65, 66]
(IX)	(XVII)	»	–	–	–	9	<2	[67]
(IX)	(XVII)	»	–	–	–	9	13	[68]
(IX)	(XVII)	»	–	–	–	9	4	[69]
(IX)	(XV)	»	–	–	–	5	20	[70]
(IX)	(XV)	»	–	–	–	7	–	[39]
(X)	(XVI)	»	–	–	–	8	–	[71, 72]
(X)	(XVI)	»	–	–	–	8	2.6	[73]
(X)	(XVI)	»	–	–	–	15	6.8	[74, 75]
(X)	(XVI)	»	–	–	–	11	<1	[76]
(X)	(XVI)	»	–	–	–	13	3.7	[76]
(X)	(XVI)	»	–	–	–	12	8.8	[77, 78]
(XII)	(XVI)	$B_k \rightarrow A \rightarrow B_l \rightarrow S$	–	–	–	12	1.4	[79]
(XII)	(XVI)	»	$C_{22}-C_{28}$	–CHO		18	2.6	[42, 80, 81]
(VII)	(XIII)	$S \rightarrow B_k \rightarrow A \rightarrow B_l$	–	–	–	9	4.3	[82–84]
(VII)	(XXII)	»	1) C_{23}	–CHO				
			2) $C_{24}-C_{27}$	–CHO	iso-BuMgBr	10	4.2	[82–84]
(VII)	(XXII)	»	$C_{23}-C_{27}$	–CHO	iso-PrC≡CLi	13	6.4	[35, 82]
(VII)	(XVI)	$B_k \rightarrow A \rightarrow B_l \rightarrow S$	1) C_{23}	–CHO				
			2) $C_{24}-C_{27}$	–CHO	iso-BuMgBr	20	9.8	[62]
(VII)	(XVI)	$B_k \rightarrow S \rightarrow A \rightarrow B_l$	$C_{23}-C_{27}$	–CHO		–	–	[85, 86]

Note. A denotes ring A with preformed functionality; B_o, B_k and B_l denote ring B with 6-hydroxy-, 6-keto- or with the 7-oxa-6-ketc functions respectively; S denotes preformed side chain.

Brassinosteroids belonging to the 6-keto steroid series with a saturated side chain are, in the majority of cases, direct synthetic precursors of the corresponding lactones since Baeyer-Villiger oxidation is particularly convenient after forming all the remaining structural fragments of the molecule. The only exceptions are the $\Delta^{24(28)}$-brassinosteroids in which lactonisation must be effected in one of the synthetic stages before construction of the unsaturated side chain. However, as in the first case, the preparation of steroids of this group, such as dolichosterone (V) [42,63] and homodolichosterone (VI),[42,87,88] differs from the synthesis of the corresponding 7-oxa derivatives (XI) and (XII) only in the absence of the lactonisation stage. The 24(28)-unsaturated BS containing an additional 25-methyl substituent, particularly 25-methyldolichosterone and 25-methyl-2,3,-diepidolichosterone have been obtained by a similar scheme.[89,90]

The synthesis of 6-desoxobrassinosteroids also includes the obligatory stage of obtaining the 6-keto derivatives, the carbonyl function being removed by hydrogenolysis in the concluding stage of the synthesis (in the case of saturated BS) or at the stage preceding the introduction of the unsaturated side chain [in the case of $\Delta^{24(28)}$-BS].[42,91] An example of the first approach in the synthesis of 6-deoxocastasterone[42] by the Huang-Minlon reduction of castasterone (II), and of the second is the preparation of 6-deoxo-dolichosterone via removal of the keto group of the intermediate 2α,3α-diacetoxy-20-methylpregnan-6-one by conversion into the ethylenedithioketal and desulphurisation of the latter with Raney nickel.[42]

The synthesis of the epimers and related 2-deoxy derivatives differs insignificantly from the preparation of 6-ketobrassinosteroids of the 2α,3α-dihydroxy series. In the case of typhasterol[35,49,58,59]

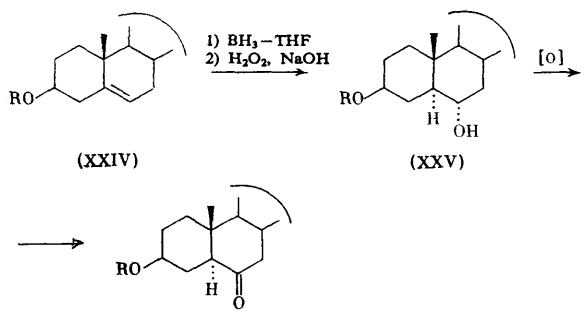
and teasterone[49,58,59,92] for example the 3-substituted 6-ketones are used directly.

III. Formation of functions characteristic of the cyclic portion of the brassinosteroid molecule

As already mentioned, the main starting materials used for BS synthesis are sterols and derivatives of pregnane and bile acids. In the majority of these compounds there is 3β-OH group and a Δ^5-bond or 5,7-diene system. The presence of the structural elements indicated limits the number of possible methods of forming BS functionality and determines the choice of corresponding transformations of the initial compound.

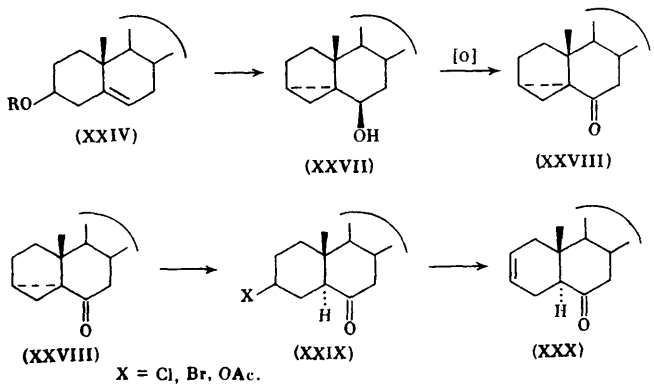
The methods usually used for creating 2α,3α-dihydroxy-6-keto functionality are known from classical steroid chemistry[1] and were later developed and improved during work on the synthesis of ecdysones.[3,4,93] They include as a rule the sequential introduction of the 6-keto group, a Δ^2-bond and its hydroxylation.

One of the methods of obtaining 6-ketones widely used in BS synthesis consists of hydroboration of Δ^5-derivatives (XXIV) with the BH_3–THF complex, oxidation of the resulting trialkylborane with alkaline hydrogen peroxide and subsequent conversion of alcohol (XXV) into ketone (XXVI).[34–36,52–56,82,83]



(XXIV) (XXV) (XXVI)

Another more efficient and universal method, distinguished by its simplicity, consists of using the rearrangement, which is specific for Δ^5-steroids, of the 3-tosyloxy- or 3-mesyloxy derivatives (XXIV) into the cyclic alcohols (XXVII), which are then oxidised to the cycloketones (XXVIII).[39–47,49–51,57–62,65–81,84–87,90,94–95] The presence of a cyclopropane fragment in the latter molecule affords the possibility of conversion into the corresponding 3-substituted 6-ketones (XXIX), for example by fission of the propane ring by hydrochloric,[57,67,96] hydrobromic,[97–102] or by a mixture of acetic and sulphuric acids.[39,49,59,60]



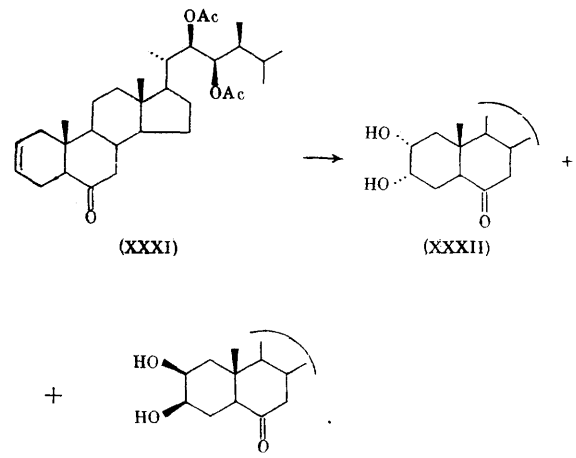
(XXIV) (XXVII) (XXVIII) (XXIX) (XXX)

Subsequent elimination of HX from the molecule of (XXIX, X = Cl, Br) gives the unsaturated ketones (XXX). A similar route comprising fission of the elements of TsOH or MsOH from (XXIX, X = OTs, OMs) may also be used.[39] However it is frequently used in syntheses including hydroboration of the Δ^5-bond.[34–36,52–56,82,83,103]

Recently the one-step transformation of the cycloketones (XXVIII) into Δ^2-steroids (XXX) has gained wide usage in syntheses of BS. The method is similar to that developed by Barton[104,105] and later used by other authors in BS synthesis[46,70,71] for the isomerisation of (XXVIII) by TsOH into the sulpholane. Examples are isomerisation by pyridinium hydrobromide,[106] and by sodium[50,107] or lithium[108,109] bromide in the presence of TsOH on boiling in DMF and also the recently proposed method[110] for thermal isomerisation by heating cycloketones in toluene with pyridinium tosylate. A possible mechanism for the reaction has been discussed.[111]

The introduction of 2α,3α-dihydroxy functionality into compound (XXX) is effected by hydroxylation of the Δ^2-bond by a catalytic or equimolar amount of osmium tetroxide[112–114] providing a high yield of α-diols (XXXII).[114]

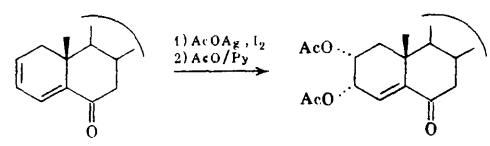
However, the formation of significant quantities of the isomeric dervatives (XXXIII) has been reported in certain cases. For example, diols (XXXII) and (XXXIII) were obtained in 77 and 14% yield respectively on hydroxylation of the enone (XXXI) with a catalytic amount of OsO_4.[49]



(XXXI) (XXXII)

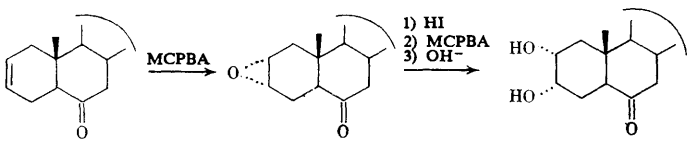
(XXXIII)

Methods of forming 2,3-dihydroxy functionality in ring *A* without using the expensive and toxic osmium tetroxide are of interest. One of them[115–125] is based on the Woodward hydroxylation of the $\Delta^{2,4}$-6-ketones (XXXIV). The formation of 2α,3α-dihydroxy derivatives, and not their 2β,3β-epimers,. occurs in contrast to the corresponding Δ^2-6-ketones.

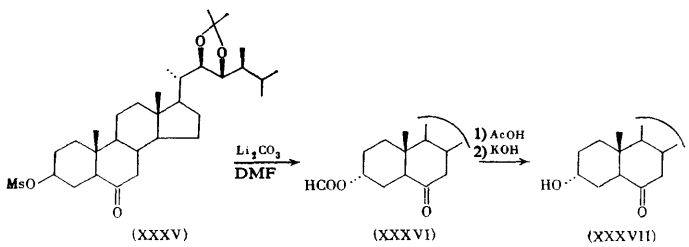


(XXXIV)

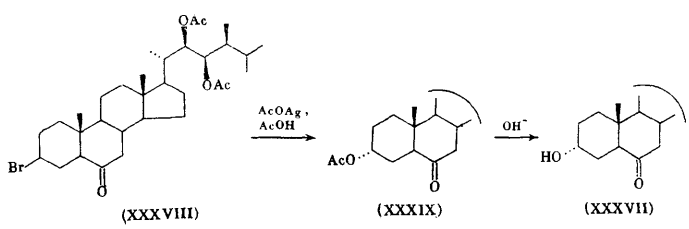
The second method consists of epoxidation of Δ^2-6-ketones with m-chloroperbenzoic acid (MCPBA) and subsequent transformation of the epoxide into the diol.



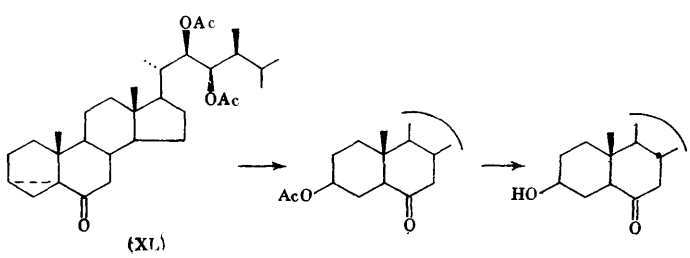
The usual method of obtaining BS of the 2-deoxy series consists of nucleophilic replacement of 3β-mesyloxy- or 3β-bromo-6-keto derivatives with the aim of reversing the configuration at C-3. Treatment of the sulphonate (XXXV) with lithium carbonate in DMF with subsequent boiling of the resulting 3α-formate (XXXVI) in aqueous acetic acid and hydrolysis with aqueous methanolic alkali leads to typhasterone (XXXVII) in 22% yield calculated on (XXXV).[35,59,60]



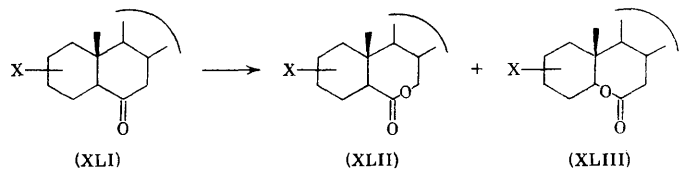
A more effective method, using reaction of the bromide (XXXVIII) with silver acetate in acetic acid and subsequent hydrolysis of the triacetate (XXXIX), gave triol (XXXVII) in 46% overall yield.[49]



The formation of 2β-6-keto functionality in the synthesis of teasterone was achieved by simple fission of the propane ring in compounds of type (XL) by a mixture of acetic and sulphuric acids[49,59,60] and subsequent alkaline hydrolysis of the acetate group.

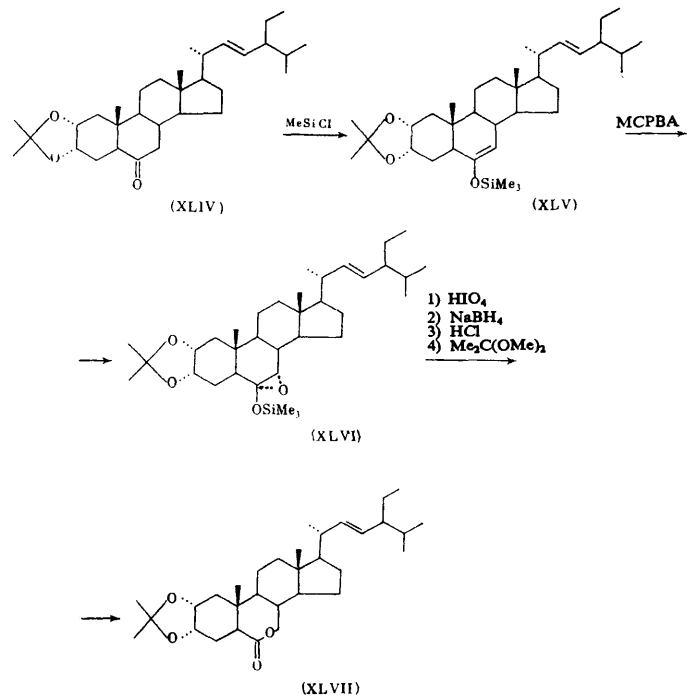


The standard method of introducing a lactone function into ring *B* is the Baeyer-Villiger oxidation of the 6-ketones (XLI) with trifluoroperacetic acid.[7,8,127–130] Since the ratio of the isomers (XLII) and (XLIII) formed depends appreciably on the nature and stereochemistry of the substituents in ring *A* [131] and is greatest in the case of 2α,3α-disubstituted derivatives, the oxidation is carried out, as a rule, as the final step of the synthesis being also linked with the relative lability of the lactone ring.

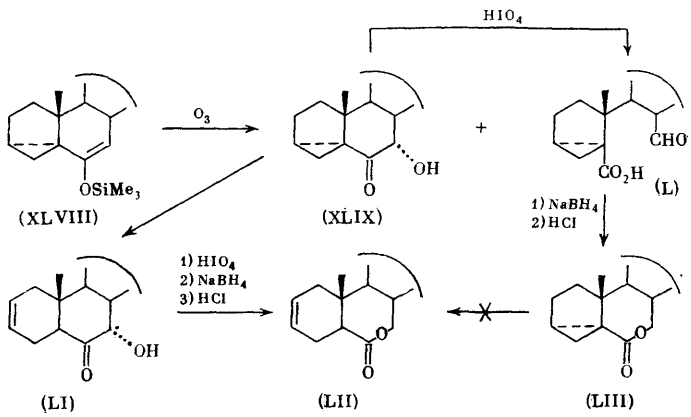


Although the fraction of the required lactones (XLII) is maximal for 2α,3α-diols, protected derivatives (acetates or acetonides) are usually used in the oxidation as a result of which a higher yield of products is achieved and separation of the regioisomers is facilitated. In addition, according to patent data,[132] good results may also be achieved on oxidation of unsubstituted 2α,3α(22*R*,23*R*)-tetraols with trifluoroperacetic acid in the presence of sodium trifluoroacetate. The application of MCPBA as a reagent for obtaining lactones according to Baeyer-Villiger has been reported.[72,79,133]

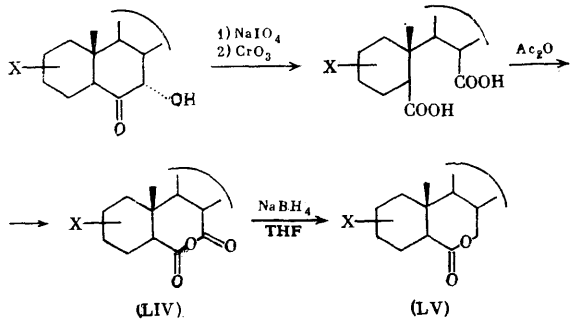
An alternative means of lactonising ring *B* through the silylated enol ether (XLV) obtained from the ketone (XLIV) was developed by Japanese workers in the synthesis of dolicholide.[42] Treatment of ether (XLV) with MCPBA gives epoxide (XLVI) (53%) together with a certain quantity of the 7α-hydroxy-6-ketone (17%). Oxidative fission of the epoxide (XLVI) with periodic acid, subsequent reduction and relactonisation with restoration of the protecting grouping in ring *A* led to lactone (XLVII).



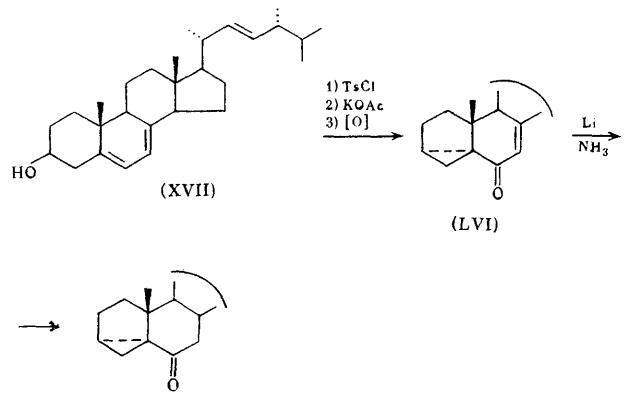
A modification of this approach is the recently proposed method[134] of forming the cyclic portion of brassinolide using ozonolysis of the silylated enol (XLVIII) which leads to a mixture of 7-hydroxy ketones (XLIX) and *B*-seco derivative (L) (depending on the reaction conditions the latter may not be formed). Fission of the hydroxyketones (XLIX) with periodic acid gives the aldehydoacid (L) in quantitative yield, which is then converted by borohydride reduction and acid treatment into the cyclic lactone (LIII). Since all attempts to transform (LIII) into the Δ^2-steroid (LII) proved to be unsuccessful, the latter was synthesised from the unsaturated ketol (LI) by a similar sequence of conversions in 79% yield calculated on ketol (XLIX).



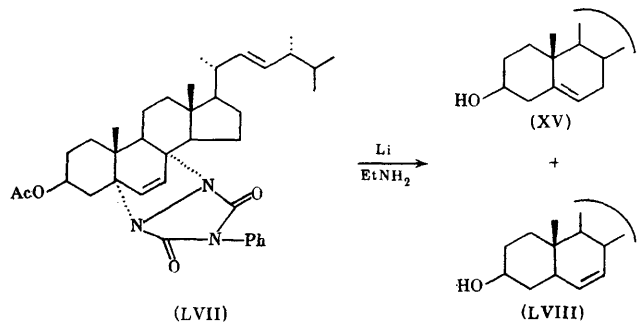
It must be noted that the principle of constructing the lactone fragment by the oxidative degradation of α-ketols of the (XLIX) type into *B*-seco derivatives and subsequent ring closure was proposed for the first time in a study[135] where a related sequence of conversions was carried out and the exceptionally high regioselectivity of the reduction of a carbonyl group in ring *B* of the anhydride (LIV) was shown to provide a high yield of the lactone (LV).



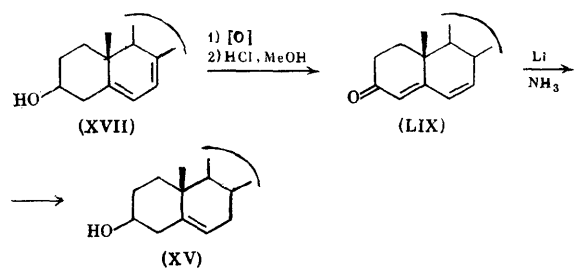
In conclusion it is necessary to mention the features of constructing the cyclic portion of the BS molecule when ergosterol (XVII) acts as starting material. The presence of an additional Δ^7-bond in its ring *B* requires an additional stage for its reduction with subsequent construction of the AB portion of the BS molecule by one of the means considered above. Thus reduction of the cyclic enone (LVI) was effected with lithium in liquid ammonia.[65]



According to another method[67] brassicasterol (XV) was obtained by the reduction of the adduct (LVII) with lithium in ethylamine. The adduct (LVII) was obtained from ergosterol acetate by Diels-Alder addition of 4-phenyl-1,2,4-triazolin-3,5-dione. The resulting mixture of 5,22- and 7,22-dienes (XV) and (LVIII) (3 : 2) was used for the following stage without separation. Different variants of the direct reduction of the ergosterol 5,7-diene system with dissolved metals (Li, Na, K) have been proposed,[69,105,136] and in the second of them attempts were undertaken to clarify the differences in the isomeric content of the products depending on the reaction conditions and the character of the substituent at position 3 of the ergosterol molecule from a mechanistic point of view. The formation of a mixture of Δ^5- and Δ^7-sterols is a drawback to the method described above for the reduction of ergosterol.



A sequence of reactions has been proposed[137] enabling brassicasterol to be obtained without admixture of its Δ^7-analogue. The Oppenauer oxidation of the hydroxydiene (XVII) and subsequent acidic isomerisation of the $\Delta^{4,7}$-3-ketone leads to the $\Delta^{4,6}$-3-ketone (LIX) which gives brassicasterol (XV) on reduction with Li in liquid ammonia.



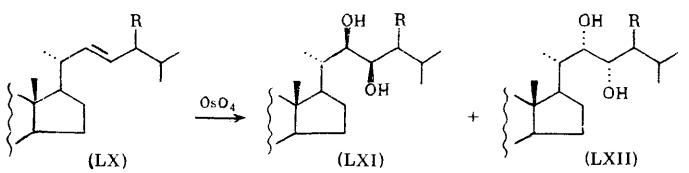
In spite of the fact that there is no information in the literature to data on the use of ergosterol in the synthesis of BS by alternative means, i.e. not by reduction but through the *trans*-formation of the Δ^7-bond, such an approach would seem to be extremely interesting.

IV. Construction of the side chains of brassinosteroids

The construction of the side chains of BS is a fairly complex problem for the solution of which it is necessary to develop original methods in addition to using known general principles.[3,4,93,138–140] Depending on the desired and the initial compounds the construction of the chain may be effected without changing or by changing the carbon skeleton of the initial molecule. In the latter case the key step of introducing the chain is usually a nucleophilic addition reaction of a suitable carbanion to a C-22, C-23 or C-24 carbonyl derivative of a steroid. The few examples to date of the use of other reactions to obtain a C–C bond may also be classified according to the number of the atom forming the new bond.

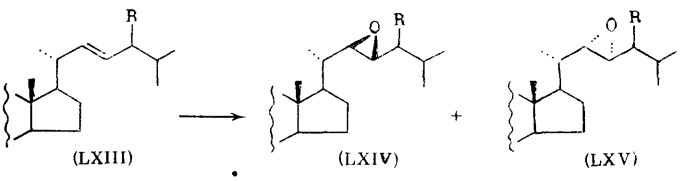
1. Syntheses retaining the carbon skeleton

When a side chain with a preformed carbon skeleton is present the problem of obtaining the BS reduces to the construction of the 22,23-diol grouping. The simplest method of introducing this is hydroxylation of a Δ^{22}-bond with osmium tetroxide.



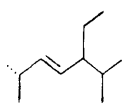
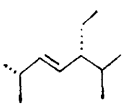
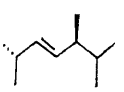
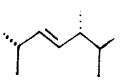
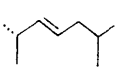
In all cases the reaction leads to the formation of both possible diols (LXI) and (LXII) the ratio of which depends on the size and configuration of the substituent R at C-24 (Table 2). Although the ratio of isomers, as a rule, proves to be unfavourable for the synthesis of the natural BS this route was used repeatedly for their preparation, particularly in the early period of investigations. In addition the method is used widely in the synthesis of the (22*S*,23*S*) analogues of the natural brassinosteroids[39,46,57,97–101,141–149] and is also used in the recently proposed process of isolating[150] 22,23-dihydroxycyclostigmastanones, intermediates for BS, from the mixture of phytosterols of sugar cane. Consideration of the mechanism of hydroxylation and the reasons for the preferential formation of isomers of type (LXII) has been undertaken.[77]

Other stereochemical results were observed in the oxidation of the Δ^{22}-bond with peracids leading to (22*R*,23*R*)-epoxide as the main reaction products.[138,143,151–153] For example on epoxidation of the dehydrocholesterol derivative (LXIII, R = H) the ratio of epoxides (LXIV) and (LXV) was 2:1,[143] and on oxidation of the related derivatives of campesterol (R = α-Me) and stigmasterol (R = α-Et) the ratios of the pairs of isomers (LXIV) and (LXV) were 1.5:1 [46] and 1.1:1 [76] respectively.



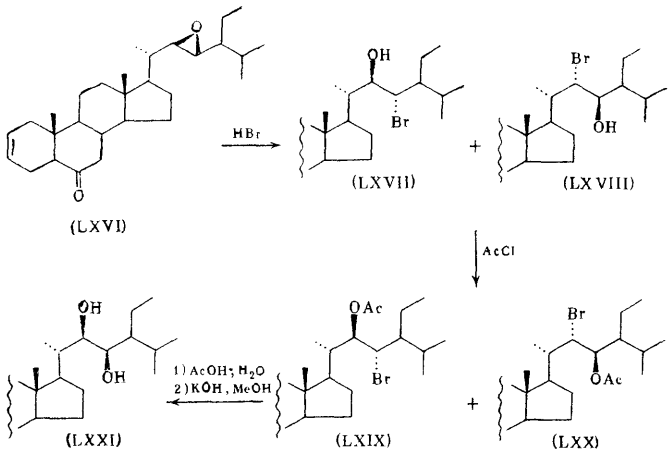
The resulting epoxides differ in chromatographic mobility, the (22*R*,23*R*) derivatives being usually less polar. It was shown[154] that ^{13}C NMR spectroscopy may serve as a convenient method for assigning configuration at the C-22 and C-23 centres.

Table 2. Ratio of isomeric diols on hydroxylation of Δ^{22}-steroids with osmium tetroxide.

Side chain structure	Ratio (LXI):(LXII)	Refs.
	1:6.7	[133]
	1:2.0	[134]
	1:4.6	[133]
	1:6.5	[57]
	1:1.0	[67, 133]
	1:2.7	[69]
	1:2.4	[112]
	1:2.3	[133]
	1:2.5	[135]
	1:2.3	[133]

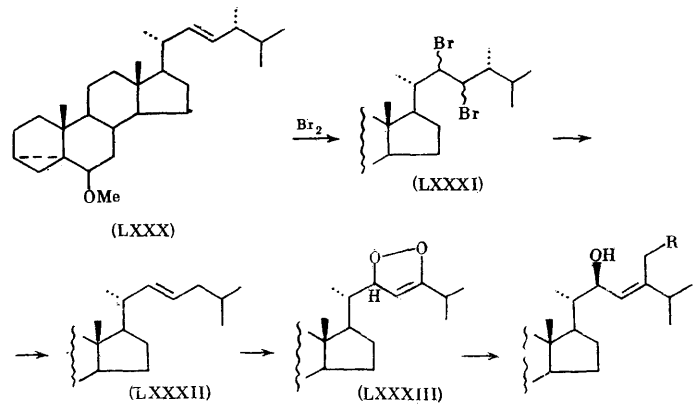
The predominant formation of (22*R*,23*R*)-epoxides on reacting Δ^{22}-steroids with peracids enabled a route to be proposed for the synthesis of (22*R*,23*R*)-diols which is more efficient than hydroxylation with OsO_4 and is based on a transformation of the epoxide ring.[46,47,74–78,155] Thus, in order to form the homobrassinolide (X) side chain, the epoxide (LXVI) was treated with HBr giving a mixture of the bromohydrins (LXVII) and (LXVIII). Treatment with acetic anhydride in pyridine led to the acetates (LXIX) and (LXX) the hydrolysis of which with 80% acetic acid at

90–100 °C proceeds with the inversion of the configuration of the carbon atom linked to bromine. The diol (LXXI) was obtained by subsequent deacylation of the hydroxy-acetates.[74,75] The application of this approach provides a fairly efficient route to brassinosteroids of the natural type.

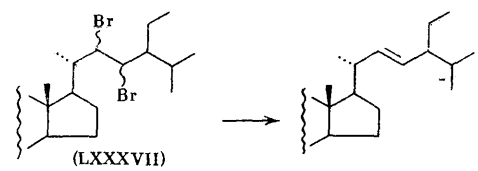


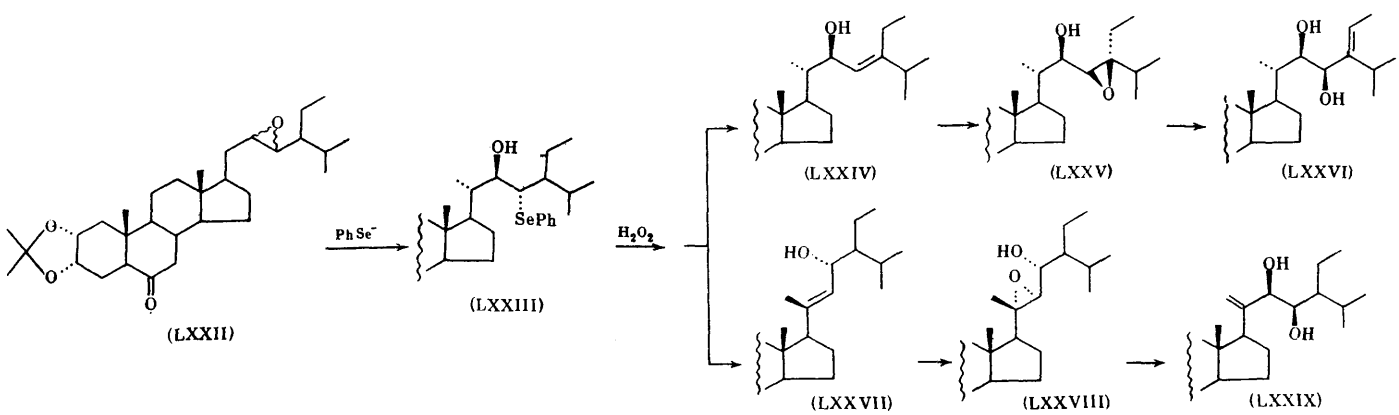
The formation of the C-24 centre with retention of the carbon skeleton of the initial steroid has been described with few examples. This route is used particularly to obtain homodolicholide (XII) and homodolichosterone (VI) from stigmasterol (XVI) through 22,23-epoxides of the (LXXII) type.[79,87] Fission of the epoxide ring of (LXXII) by the phenylselenyl anion, obtained from diphenyl diselenide and sodium borohydride, led to the alcohol (LXXIII) mixed with its regioisomer. Treatment of the mixture with hydrogen peroxide gave an inseparable mixture of the allylic alcohols (LXXIV) and (LXXVII) the epoxidation of which with subsequent treatment of the epoxides (LXXV) and (LXXVIII) with aluminium isopropoxide gave a mixture of the diols (LXXVI) and (LXXIX). After separation of the mixture the diol (LXXVI) was converted into homodolicholide (XII). A similar means of constructing the side chain was used in the synthesis of dolicholide (XI).[156]

A method of converting the side chain of ergosterol into the 23-ene-22α-hydroxy derivative (LXXXVI), a key intermediate in the synthesis of brassinolide (VIII),[36] has been proposed.[136] It comprises the bromination of the methyl ether (LXXX), subsequent conversion of the dibromide (LXXXI) into diene (LXXXII), treatment of a solution of the diene in pyridine with molecular oxygen and fission of the epoxide (LXXXIII) by hydrogenation over Lindlar catalyst. Removal of the OH group at C-28 in the alcohol (LXXXIV) was effected by conversion of it into the mesylate with subsequent reduction of (LXXXV) with lithium aluminium hydride.



It is interesting that the dibromide (LXXXVII) of the stigmasterol series undergoes debromination under dehydrobromination conditions[157] and this may be used for the protection of the Δ^{22}-bond.[98]

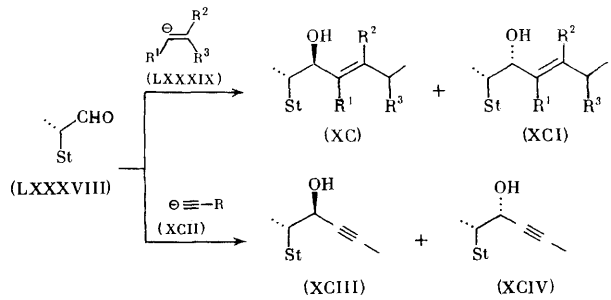




2. Construction of the side chain with the formation of new carbon–carbon bonds

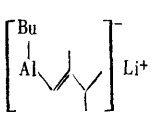
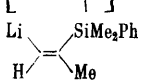
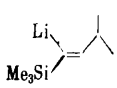
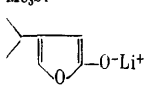
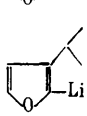
a) Syntheses with the participation of the C-22 centre

The presence of a Δ^{22}-bond in the stigmasterol molecule enables reconstruction of the carbon skeleton to be carried out in the following way. The missing portion of the chain containing the centres C-24, C-25 and C-23 in final form or accessible to the final form is added to a C_{22} fragment (22-aldehyde) obtained for example by ozonolysis of a sterol derivative with a protected Δ^5-bond. In the majority of cases vinyl (LXXXIX) [36,42,61,62,80,81,158–159] or ethynyl (XCII) [34,35,40–45,49–51,57–60,82,160–163] carbanions, obtained from the corresponding organometallic compounds, were used as nucleophiles for addition to the aldehyde (LXXXVIII). In all cases a mixture of the 22α-OH-(XC), (XCIII) and 22β-OH-(XCI), (XCIV) isomers was formed by the reaction



St = steroidal skeleton

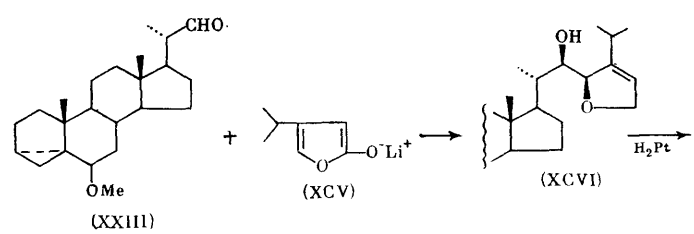
Table 3. Comparative efficiency of reagents in the nucleophilic addition to the 22-aldehyde.

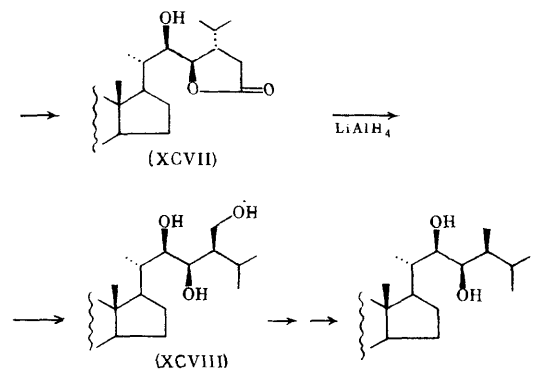
Reagent	Overall Yield, %	Ratio of isomers 22α-OH:22β-OH	Refs.
Li–C≡CPr-iso	76	1:1	[34]
	76	3:2	[35]
	68	1.1:1	[42]
	54	8.5:1.5	[36]
	64	3:1	[158]
	97	10:1	[159]
	90	8:1	[37]
	96	4.5:1	[164]
	99	7:3	[165]
$Me_2CHC{\equiv}CSnBu_3$	78	9:1	[163]

The ratios, yield and the route of further transformations into the desired products is determined by the structure of the nucleophile. Attempts have been undertaken in the course of investigations on the synthesis of BS to optimise the key stage (aldol reaction) by choice of reagent. The comparative efficiency of some of these is given in Table 3.

Among the reagents studied the heterocyclic derivatives provide a high yield and good stereoselectivity for the process and seem extremely promising. In addition the adducts formed in these cases enabled, as a rule, ready transformation into the desired compound through the minimum number of stages. Thus the use of the anion of 3-isopropylbut-2-enolide (XCV) in the reaction with the aldehyde (XXIII) enabled the formation of centres C-22 and C-23 simultaneously with a high stereoselectivity.[37]

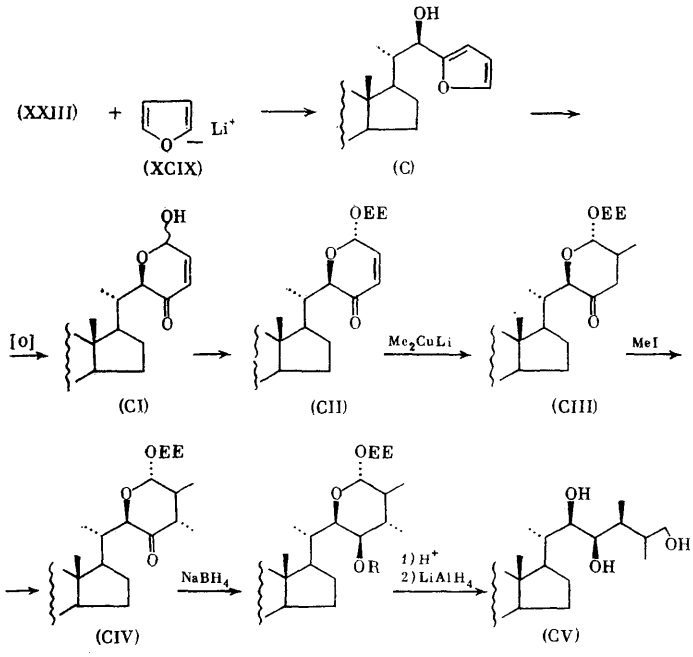
Subsequent reduction of the butenolide intermediate (XCVI) also occurred selectively leading to the (24*S*)-isomer in 78% yield. The reductive fission of lactone (XCVII), protection of the dihydroxy grouping in the trihydroxy derivative (XCVIII), oxidation of the hydroxyl at C-29 into the ketone and decarbonylation completed the formation of the side chain of brassinolide with an overall yield of 32% calculated on aldehyde (XXIII).





A related method of constructing the brassinolide side chain through the lactone (XCVII) obtained by the transformation of adducts of aldehyde (XXIII) with 3-isopropyl-2-lithiofuran has been used.[164] It is characterised by high yield and good selectivity at the addition stage, however it requires a large number of stages for the subsequent transformation into the desired product.

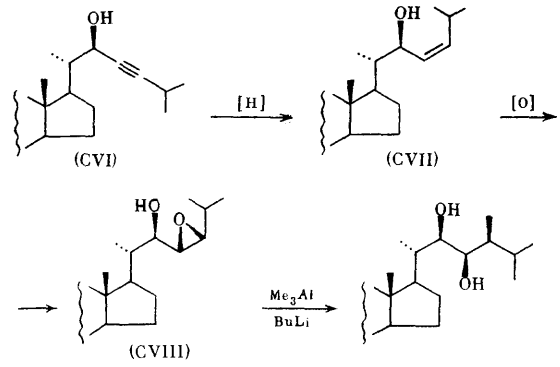
The route based on the use of the 2-lithiofuran (XCIX) is similar to those considered.[165]



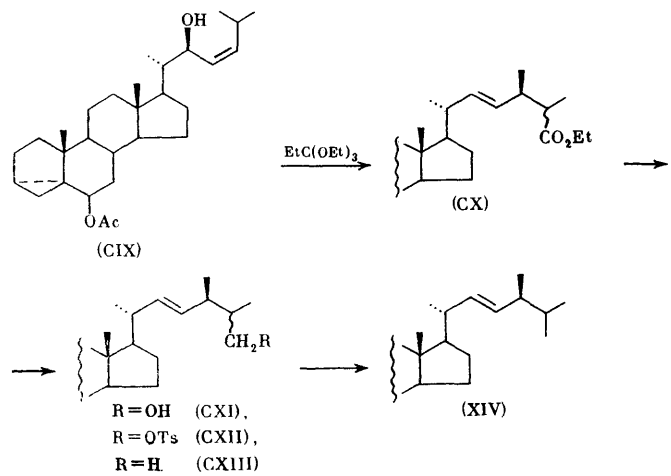
The adduct (C) formed in this case was oxidised with *N*-bromosuccinimide to the lactone (CI) as an unseparable mixture of anomers which was converted into a mixture of the corresponding ethoxyethyl ethers with (CII) predominating. The sequence of stages of conjugated addition of lithiummethylcuprate to the enone (CII), α-methylation of ketone (CIII), sodium borohydride reduction of the carbonyl group in the dimethyllactone (CIV) and ring opening gave the triol (CV). Protection of the *vic*-diol grouping and removal of the 27-hydroxy function by hydride reduction of the corresponding mesylate led to the formed side chain of brassinolide in an overall yield of more than 40% calculated on (XXIII).

In the syntheses based on the use of the acetylenic alcohols (CVI) the comparatively low stereoselectivity of the stage of adding the acetylides may be partially compensated by converting the by-product 22β-alcohol into the 22α-alcohol by the sequence of stages of oxidation to the ketone and hydride reduction,[35,42] leading to inversion of the configuration at C-22. The usual route of the subsequent conversions includes hydrogenation of the acetylenic alcohols (CVI) over Lindlar catalyst[34,35,57,160] or Raney nickel in the presence of ethylenediamine[42,44] to the *cis*-olefin (CVII), epoxidation of the latter with t-butyl hydroperoxide in the presence of vanadyl acetylacetonate[34–36] or by the action of MCPBA [40–42] and ring opening of the epoxide (CVIII) with trimethylaluminium in the presence of n-butyllithium.[40–45,49–51]

The accomplishment of the last stage is, however, linked with distinct practical difficulties[35] since introduction of the methyl group at position C-24 is sometimes carried out by a complex multistage synthesis[25–34] comprising hydrocyanation of the epoxide (CVIII) and subsequent transformation of the CN group on C-24 into methyl.



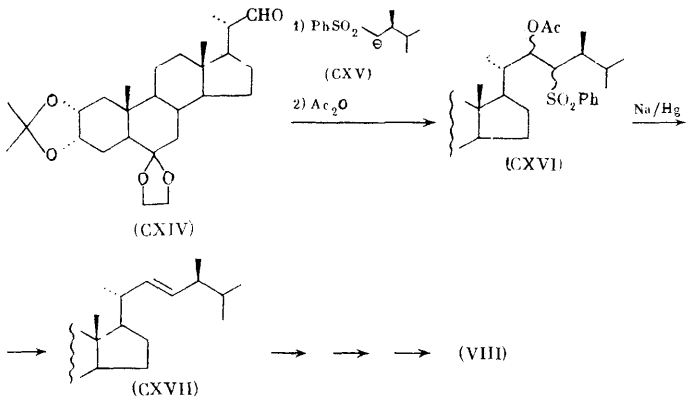
Another route for transforming the allylic alcohols (CVII) to the brassinolide side chain is the application of the Claisen rearrangement.[57,58,160] Thus rearrangement of the alcohol (CIX) using triethyl orthopropionate gave a mixture of epimers at C-25 of the ester (CX), the reduction of which led to the corresponding alcohol (CXI). Subsequent tosylation of (CXI) and reduction of the tosylate (CXII) with lithium aluminium hydride gave the cyclic alcohol (CXIII) which was then isomerised into 22-dehydrocampesterol (XIV).[160]



A drawback of this approach to BS synthesis is the need to apply to compound (XIV) the methods considered above for the functionalisation of a side chain with a preformed carbon skeleton which leads to a comparatively low yield of final product with a significant total number of steps (more than 20).

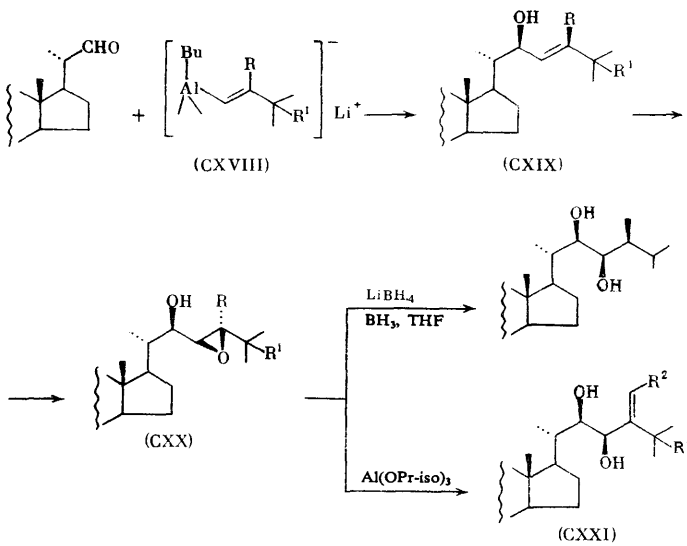
The formation of only one centre at C-24 at the first stage of making the Δ^{22}-derivatives has been used[46–48] and is based on the reaction of anion (CXV), generated from the corresponding sulphone, with aldehyde (CXIV). Acetylation of the product and reduction of the acetoxysulphone (CXVI) with sodium amalgam leads to compound (CXVII), which has the side chain of

22-dehydrocampesterol, and was converted into brassinolide (VIII) through the 22,23-epoxide.



Similar principles may be used to obtain the 28-nor analogues of BS containing no chiral centre at C-24.[48,85]

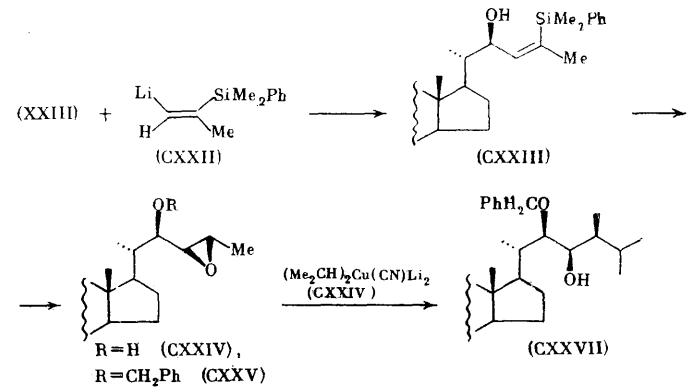
Among the methods using vinyl carbanions the most used are reactions with the lithium alkylaluminium derivatives (CXVIII)[36,42,61,62,80,81] leading to the formation of the Δ^{23}-derivatives (CXIX) as in the case of the allylic alcohols (CVII) considered above.



R=Me, Et; R^1=H, Me; R^2=H, Me

Further transformation is effected by conversion into the 22,23-epoxide and subsequent reductive fission of the oxide ring of (CXX) contrary to the Markownikoff rule leading to the brassinolide side chain.[36] Isomerisation of the epoxides (CXX) on boiling in toluene with aluminium isopropoxide is a convenient method of obtaining the diols (CXXI),[42,61,62,80,81] which are intermediates for 24(28)-unsaturated brassinosteroids.

The vinylsilanes (CXXII) have been shown to be useful in the reaction with the aldehyde (XXIII).[158] Epoxidation of the adduct (CXXIII) with subsequent removal of the dimethylphenylsilyl grouping gives the epoxide (CXXIV). Interaction of the benzyl ether (CXXV) with the mixed cuprate (CXXVI) and subsequent fission of the ether (CXXVII) with lithium in liquid ammonia leads to a diol with a complete brassinolide side chain.

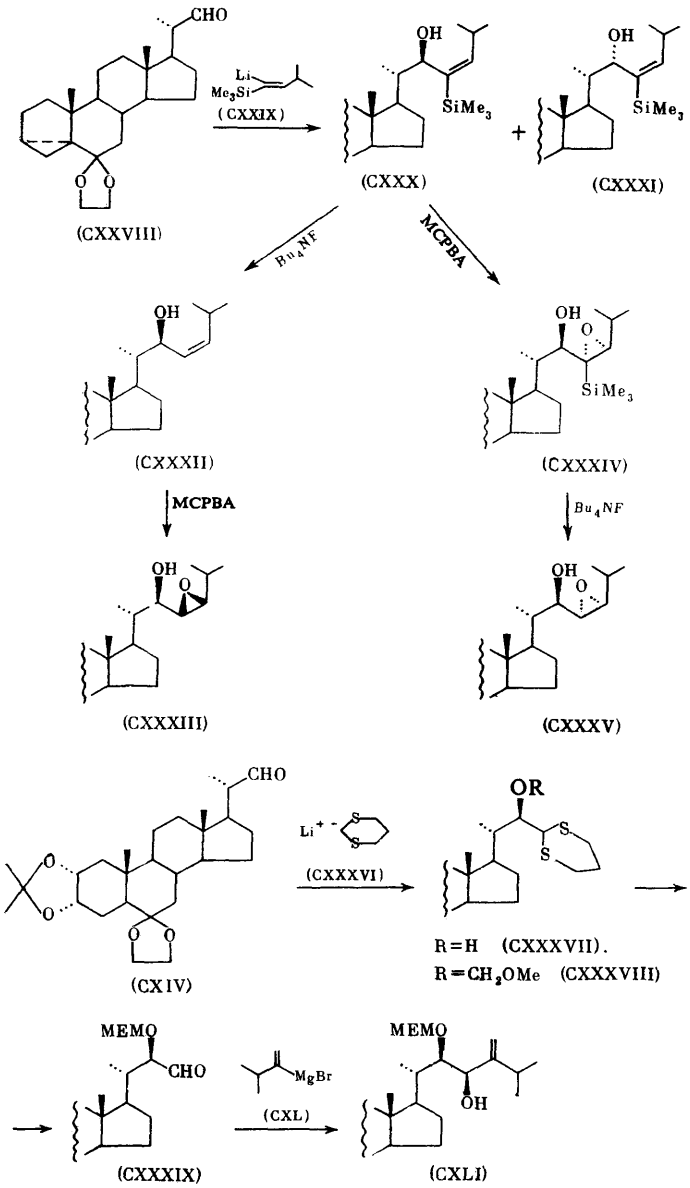


A method of forming the brassinolide side chain using vinylsilanes of type (CXXIX) has been proposed.[159] The presence of a bulky substituent stabilising the carbanion and bonded directly to the anionic centre of the nucleophile enabled a significant increase in the stereoselectivity of the reaction and in the yield of adduct. Thus addition of the anion (CXXIX) to the aldehyde (CXXVIII) proceeds with the formation of the alcohols (CXXX) and (CXXXI) in a ratio of 10:1 in 97% overall yield.

Desilylation of (CXXX) and subsequent epoxidation of (CXXXII) led to the epoxide (CXXXIII) from which the brassinolide side chain may be constructed by the methods described above.[40–45,49–51] A change in the reaction sequence [epoxidation of (CXXX) and then desilylation of (CXXXIV)] led to the isomeric epoxide (CXXXV).

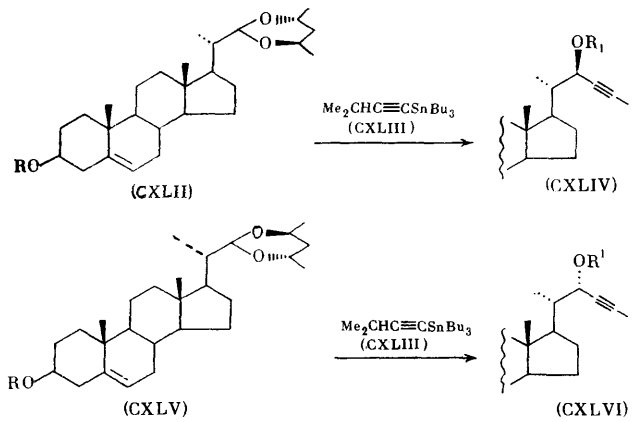
Treatment of the aldehyde (CXIV) with the lithium salt of the dithiane (CXXXVI) in tetrahydrofuran at −20 °C and subsequent protection of the hydroxy group in the adduct (CXXXVII) with chloromethyl methyl ether led to the dithiane (CXXXVIII) in 85% yield. Its dethioacetalation proceeds quantitatively without epimerisation at C-22 and gives the aldehyde (CXXXIX) which was then used for the stereoselective formation of the C-23 centre in the synthesis of dolicholide (XI) and dolichosterone (V)[63,64] by reaction with the Grignard reagent (CXL) obtained from 2-bromo-3-methyl-1-butene. Conversion of the alcohol (CXLI), formed selectively in 73% yield, into the corresponding diol was achieved by the sequential stages of protecting the 23-hydroxy group as the acetate,

hydrolysis with dilute hydrochloric acid, acetylation and saponification of the diacetate with potassium hydroxide solution.



28-Norbrassinolide was synthesised by a similar route using isobutylmagnesium bromide.[63,82,84] The selective addition of vinylstannanes to the 23-aldehyde has been described.[166]

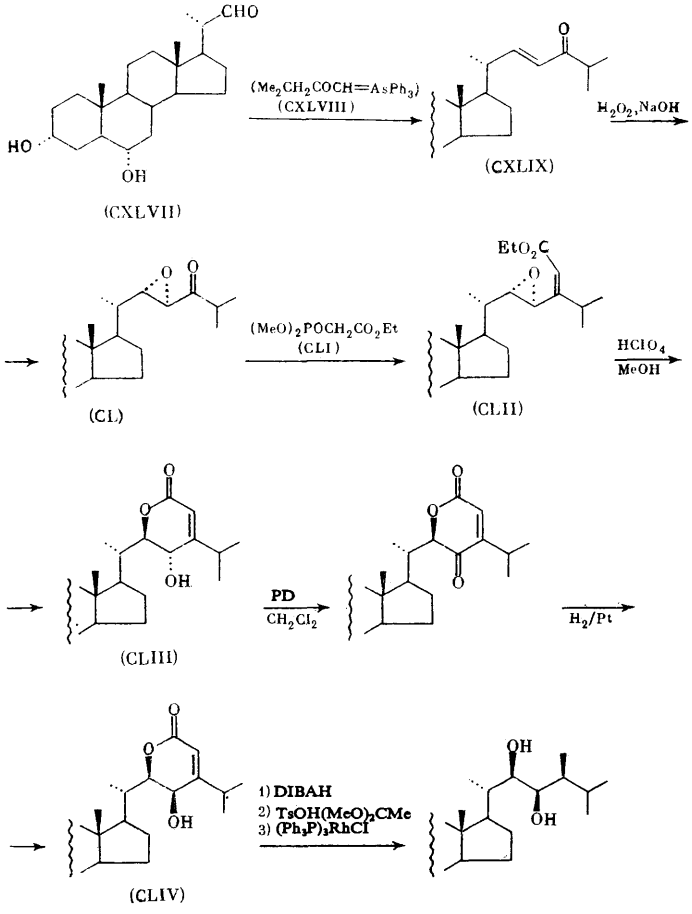
According to patent literature[167,168] an efficient means of influencing the stereochemistry of 22-hydroxy derivatives consists of the use in the addition reaction of the stereoisomeric acetals (CXLII) and (CXLV), which correspond to the aldehyde with added 2-methylpentane-2,4-diol. Their reaction with the acetylide (CXLIII) occurs with high stereoselectivity, leading to an epimeric mixture of the acetylenic derivatives (CXLIV) and (CXLVI) in a ratio of 95:5 and 11:89 for (CXLII) and (CXLV) respectively.



Organoarsenic compounds have been used to form the brassinolide side chain.[169] The aldehyde (CXLVII) obtained from hyodeoxycholic acid (XX) was treated with the ylid (CXLVIII) with the formation of α,β-unsaturated ketone (CXLIX).

Epoxidation of (CXLIX) with alkaline hydrogen peroxide gave the epoxyketone (CL) which, by Wittig-Horner reaction with compound (CLI), was converted into the epoxyester (CLII). The lactone (CLIII) was obtained by acid treatment of (CLII). The natural stereochemistry of the substituent at C-22 was thus formed. Inversion of the configuration at C-23 was achieved by sequential oxidation and reduction of the 23-hydroxyl group. Reduction of (CLIV) with diisobutylaluminium hydride (DIBAH), treatment of the resulting hemiacetal with 2,2-dimethoxypropane and

decarbonylation completed construction of the brassinolide side chain.

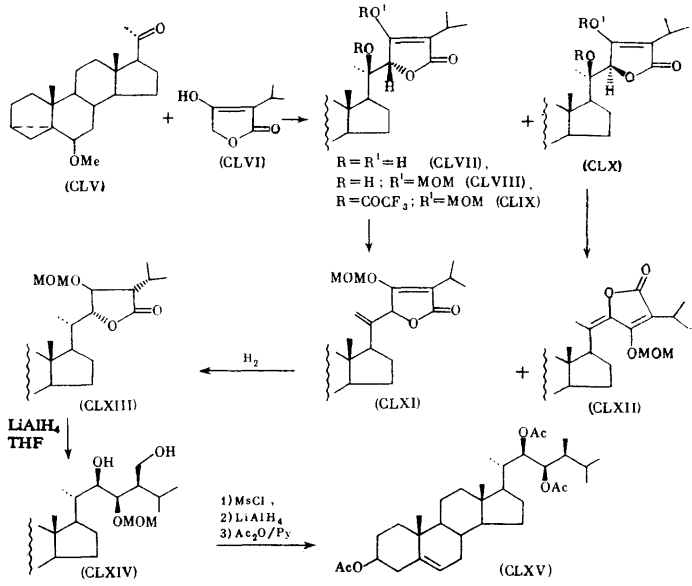


PD = pyridinium dichromate

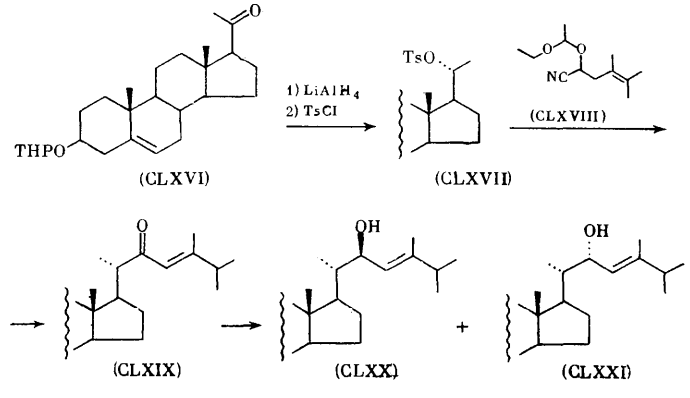
b) Syntheses with the participation of the C-20 centre

The main part of this section consists of syntheses the key stage of which is the nucleophilic addition reaction of the 3-isopropyltetronic acid anion (CLVI) to a C-20-ketone of the pregnane series (CLV).[52–55] It is interesting to note that the addition succeeds only for the derivatives (CLVII) with an unprotected hydroxyl group and the reaction does not take place in the case of the corresponding methoxymethyl ether. The diol (CLVII), obtained together with a little epimer (CLX) in a ratio of 91:9 in 84% overall yield, is used for further conversions. Protection of the secondary hydroxy group in compound (CLVII) as the methoxymethyl ether and subsequent treatment of (CLVIII) with trifluoroacetic anhydride in the presence of triethylamine and 4-pyrrolidinopyridine led to the acetate (CLIX), which on boiling in benzene with 1,8-diazabicyclo[5,4,0]undec-7-ene gave a mixture of the 5-ylidenetetronates (CLXI) and (CLXII) in a ratio of 82:18 in 73% overall yield. The saturated lactone (CLXIII) was obtained as the main product by catalytic hydrogenation of the main isomer (CLXI). Reductive fission of the ring in compound (CLXIV), removal of the 28-hydroxy group by conversion of the alcohol (CLXIV) into the 28-mesyloxy derivative with subsequent reduction with lithium aluminium hydride and acetylation led to the triacetate (CLXV) in 29% yield [based on (CLV)] which has the brassinolide side chain with protected hydroxyl groups.[52–56] A similar sequence of reactions for the tetronate (CLXII) enabled preparation of a side chain with a 22(*S*),23(*S*),24(*R*) configuration of substituents.

Another route using the 20-ketopregnanes to construct the brassinosteroid side chain, which has been suggested[170] includes conversion of the 20-keto group of pregnenolone (CLXVI) into a (20*R*)-tosyl (CLXVII) and subsequent alkylation of the tosylate (CLXVII) with the protected cyanohydrin (CLXVIII). Reduction of the resulting enone (CLXIX) with diisobutylaluminium hydride leads to the formation of a mixture of the allylic alcohols (CLXX) and (CLXXI) in a ratio of 97:3. Further construction of the brassinolide side chain from allylic alcohol (CLXX) was carried out similarly to that described previously.[136]

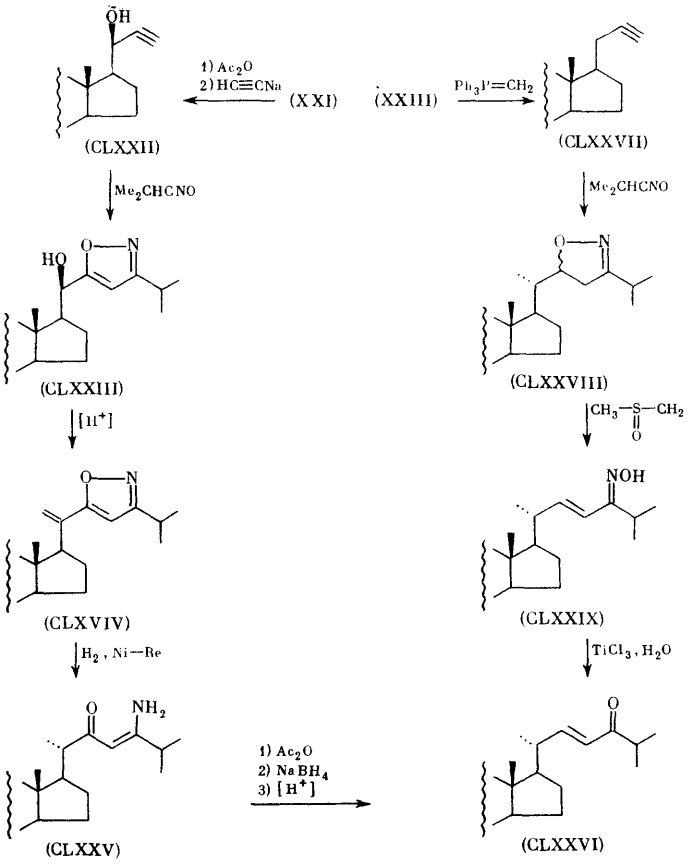


MOM – methoxymethyl



The method of constructing steroidal side chains using the nitrile oxide approach[171–181] possesses great potential and may be used successfully in the synthesis of brassinosteroids. Two means of obtaining the Δ^{22}-24-ketone (CLXXVI) from pregnenolone (XXI)

are shown below. The first method comprises the addition of isobutyronitrile oxide to the acetylenic alcohol (CLXXII), dehydration of the alcohol (CLXXIII), hydrogenation of (CLXXIV) and conversion of the enaminoketone (CLXXV) into the Δ^{22}-24-ketone (CLXXVI) by sequential acetylation, borohydride reduction and acid hydrolysis. The route to (CLXXVI) through the isoxazoline (CLXXVIII), obtained from the olefin (CLXXVII) and isobutyronitrile oxide by a 1,3-dipole cycloaddition reaction, is more convenient. Isomerisation of the isoxazoline (CLXXVIII) by base leads to the α,β-unsaturated oxime (CLXXIX), treatment of which titanium trichloride gives (CLXXVI). The use of Δ^{22}-24-ketones in the synthesis of brassinosteroids has been demonstrated[169,182,183]



In addition to the approaches discussed it is also necessary to mention the recently proposed improved methods of obtaining starting and intermediate compounds for the synthesis of BS, including the 20-formyl-[184–186] and 20-carboxypregnanes,[181,187,188] the 22,23-diols and their derivatives[150,189] and a new method of forming the side chain through 17(20)-pregnenes.[190,191]

Simultaneously with the development of investigations on the synthesis of the natural brassinosteroids attempts have been undertaken to obtain biologically active analogues of them differing in the structure of the side chain or of the cyclic portion of the molecule. In some cases as, for example, in the synthesis of epibrassinolide (IX), preparation by the synthetic route[39,69–70] preceded detection of the hormone in nature. The same methods are generally used to make modified BS as for the natural compounds. Up to the present the synthesis of a large number of derivatives has been effected, including compounds with a transformed side chain,[39,46,57,61,97–101,133–140] a modified cyclic fragment[145,192,217–222] or containing modification in both portions of the molecule.[192,207,209–215,223,224] As might be expected compounds are found among the analogues synthesised which are comparable in activity with the natural hormones. This shows the prospect of further search in this direction.

The methods discussed for forming the cyclic portion and the side chains of BS encompass data published up to the present in the scientific and patent literature. In addition investigations in this region continue to develop vigorously which affords the promise in the very short term of original approaches and of a wider application of methods and reactions known and used in other classes of natural products to the synthesis of BS.

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Translated from *Uspekhi Khimii* 60 1318–1342 (1991) U.D.C. 547.466

Acetylenic amino acids

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ABSTRACT. The methods of synthesis, application, and mechanisms of the biological action of α- and γ-amino acids containing an acetylene residue in the molecule that gives rise to the specific ability of these compounds to deactivate irreversibly certain enzymes are reviewed.

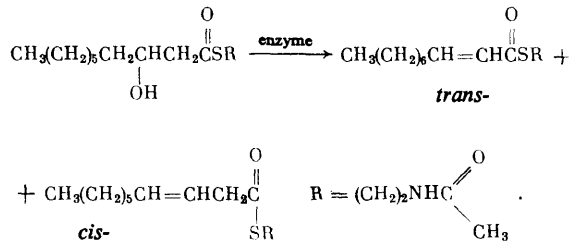
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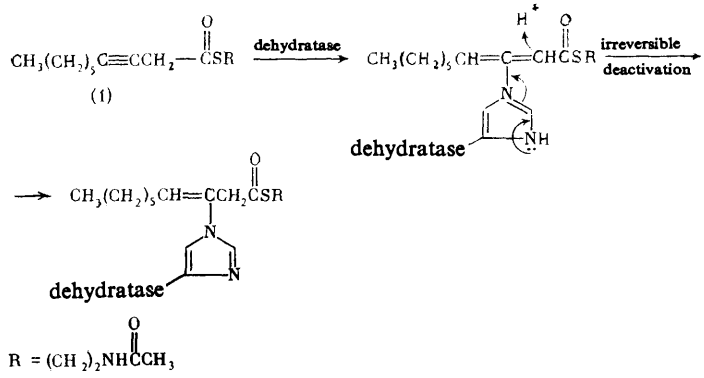
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I. Introduction

The growing interest in unsaturated amino acids is stimulated by their potential biological activity as specific irreversible enzyme inhibitors. A study of the action mechanism of these inhibitors shows that they contain functional groups which when treated with enzymes form new highly reactive groups. The latter immediately interact with nucleophiles in the active sites of the enzymes, as a result of which covalent compounds are formed between inhibitors and enzymes, leading to inhibition of the activity of the latter. Thus, the enzymes catalyse their own deactivation, which is also known as "suicidal" deactivation, while the compounds that cause the suicidal deactivation are called "suicide substrates".[1–5] It is found that compounds that contain carbon–carbon triple bonds act on enzymes that catalyse isomerisation, oxidation, elimination, and transamination. Thus acetylenic ketones inhibit dehydrogenases and aldolases, acetylenic amines inhibit monoamine oxidases bound to flavin, and acetylenic hydroxyacids inhibit lactate dehydrogenases.[4,6] The fundamental chemical principles of the action of acetylenic compounds appear to be mainly derived from the fact that they can be converted enzymically to conjugated allenes. The latter are strong Michael acceptors, whereas the former are not very chemically reactive.[7] A typical example of highly specific deactivation of this type is the irreversible suppression of β-hydroxydecanoyl thioester dehydratase by 3-decynoyl *N*-acetylcysteamine (1). This enzyme plays an important part in the synthesis of unsaturated fatty acids and catalyses the reversible conversion of hydroxydecanoyl thioesters to α,β-*trans*- and β,γ-*cis*-unsaturated compounds:



On treatment with the enzyme, amide (1) isomerises to an allene which reacts with histidine at the active site of the enzyme, causing the irreversible deactivation of the latter.[8]



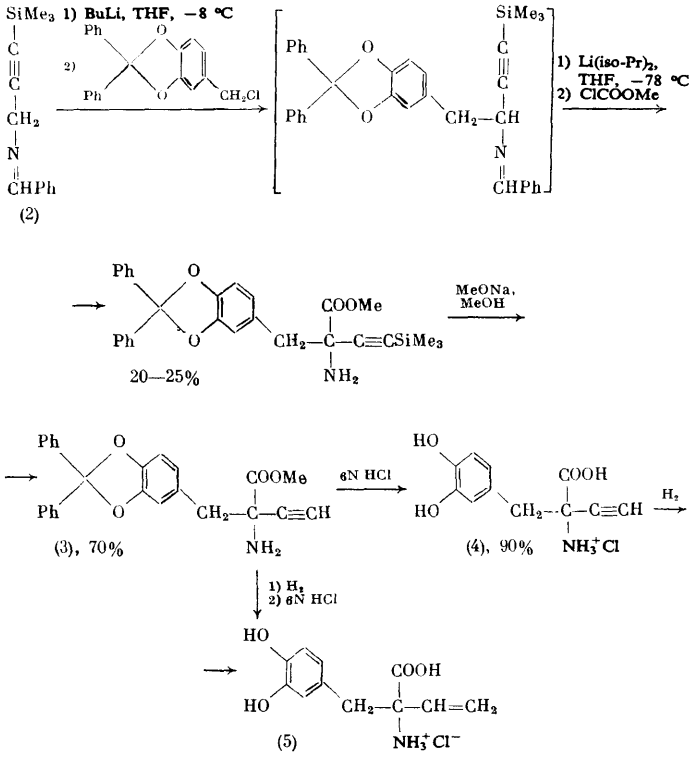
II. α-Amino acids

1. α-Ethynyl-α-amino acids

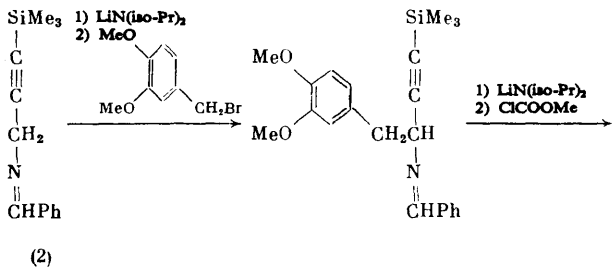
In 1977 α-ethynyl-3,4-dihydroxyphenylalanine (4) and α-vinyl-3,4-dihydroxyphenylalanine (5), which were the first examples of α-substituted α-amino acids with an unsaturated function on the quaternary α-carbon atom, were synthesised.[9] These analogues of dihydroxyphenylalanine (DOPA) proved to be inhibitors of DOPA decarboxylase.

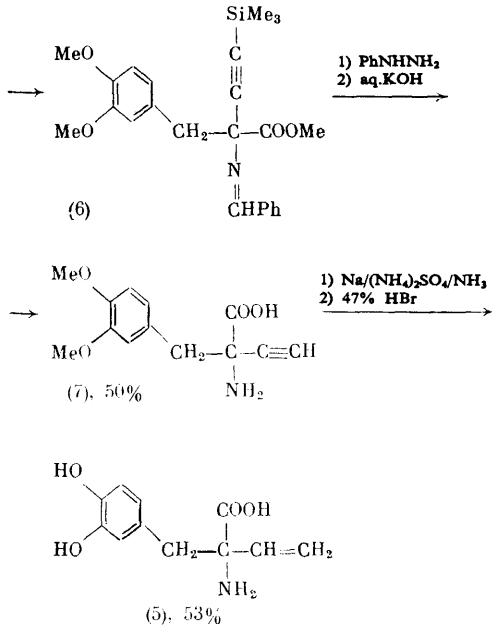
In order to obtain amino acids (4) and (5), Taub and Patchett[9] alternately introduced protected 3,4-dimethoxyphenylmethyl and carboxyl functions into the propargyl synthon (2). A diphenylmethylene group, which is stable during chromatography on silica gel but is readily removed by mild acid treatment, was used to protect the base-sensitive catechol function. After removal of the

protecting groups the acetylenic amino acid (4) was obtained with an overall yield of 13–16% [based on the initial synthon (2)]. On partial hydrogenation of the protected amino ester (3) followed by acid hydrolysis as in the case of (3) → (4) it was possible to obtain the hydrochloride of α-vinyl-α-amino acid (5) with a yield of about 70% [based on amino ester (3)].



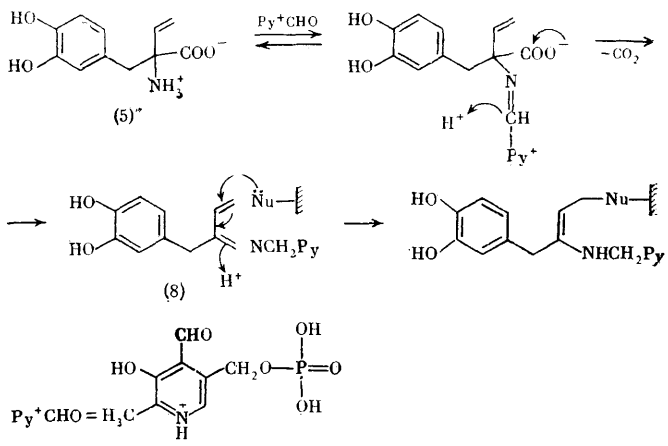
At almost the same time Metcalf and Jung reported[10] their own variant of the synthesis of amino acids (4) and (5), which differed from the above in that the regioselective alkylation of aldimine (2) was carried out with 3,4-dimethoxybenzyl bromide. In order to generate an anion from aldimine (2) use was made of lithium diisopropylamide, which can avoid the dialkylation that occurs to a considerable degree when n-butyllithium is used as the base. The benzyl and trimethylsilyl protecting groups were removed by successive treatment of the imine ester (6) with phenylhydrazine and an aqueous solution of potassium hydroxide. The acetylenic amino acid (7), which was obtained with a 50% overall yield based on 3,4-dimethoxybenzyl bromide, was subsequently reduced with sodamide and treated with 47% hydrobromic acid, and after neutralisation α-vinyl-DOPA (5) was isolated.





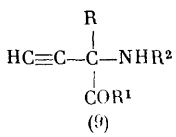
By using 3,4-isopropylidenedioxybenzyl bromide instead of 3,4-dimethoxybenzyl bromide for the regioselective alkylation of aldimine (2), it was possible to obtain the acetylenic amino acid (4) with an overall yield of 24%.

Metcalf and Jung[10] examined the possible mechanism of deactivation of DOPA decarboxylase by β,γ-unsaturated α-amino acids in the case of α-vinyl-DOPA (5). The process is initiated with the formation of a Schiff base between the amino acid and the coenzyme of the decarboxylase—pyridoxal phosphate. After decarboxylation of the Schiff base the vinylimine (8) is formed, which reacts with the nucleophile of the active site of the enzyme to form a strong covalent bond, resulting in irreversible deactivation of the latter. The authors assumed that α-acetylene-DOPA also deactivates the carboxylase by the same mechanism.



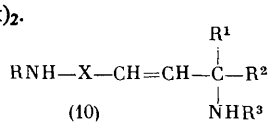
By successive alkylation and acylation of the carbanions obtained from 3-trimethylsilylpropyne-2-ylbenzaldimine (2) with various electrophilic reagents, Metcalf et al.[10–24] obtained a large number of α-ethynyl-α-amino acids and their esters, amides, thioesters, thioamides, lactams, and other derivatives (9),[10–16] (10),[17–19]

and (11),[20–24] which can be used as reagents to combat pathogenic viruses, bacteria, and fungae, as stimulants of the nervous systems, antidepressants, tranquillisers, agents for treating Parkinsonism, rheumatoid arthritis, carcinoid syndromes, bronchospasmatic conditions in asthmatics, manic disorders, and other conditions induced by high levels of 5-hydroxytryptamine and other polyamines that play an important part in cell division and growth, since compounds (9)–(11) are irreversible inhibitors of the decarboxylases that participate in the formation of polyamines from the corresponding amino acids.



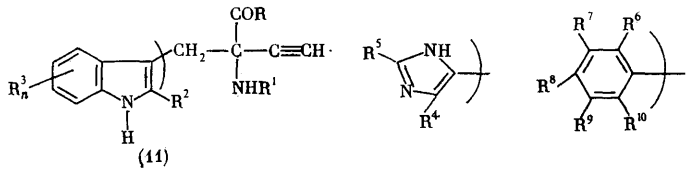
(9)

R = $MeS(CH_2)_2$, $PhCH_2S(CH_2)_2$, (*S*)-(5-desoxyadenosynyl-5)-*S*-methylthionethyl, $H_2NC(=NH)NH(CH_2)_3$, $R^3NH(CH_2)_n$, $n = 3,4$, R^3 = H, Alk, CO_2Alk, $C(O)CH(NH_2)R^4$, R^4 = H, Alk, CH_2Ph; R^2 = H, C(O)Alk, CO_2Alk; R^1 = OH, OAlk, CO_2Alk, NH_2, $N(Alk)_2$.



(10)

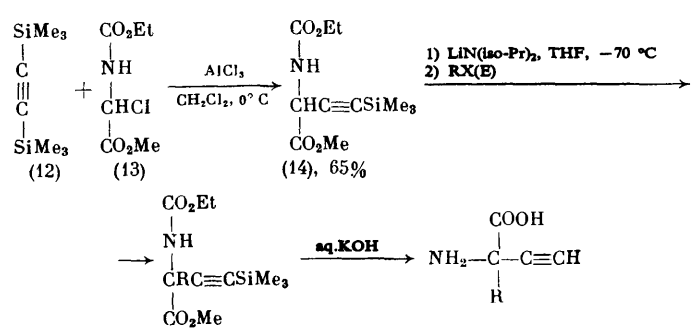
X = CH_2, $(CH_2)_2$, CH=CH, CHMe; R = H, $C(=NH)NH_2$, CO_2Alk, $C(=O)CHR^4NH_2$; R^1 = $CH=CH_2$, C≡CH; R^2 = H, CO_2H, CO_2Alk; R^3 = H, C(=O)Alk, CO_2Alk; R^4 = H, Alk, CH_2Ph, $CH_2C_6H_4$—OH-*n*.



(11)

R = OH, OAlk, NH_2, R^1 = H, C(=O)Alk, CO_2Alk; R^2 = H, Me; R^3 = H, OH, OAlk, CO_2Alk, Hal, Me; $n = 1,2$; R^4, R^5 = H, Hal, $Alk(C_{1-4})$; R^6–R^{10} = H, Me, Et, t-Bu, Cl, F, OR^{11}, R^{11} = H, $Alk(C_{1-8})$, $C(=O)Alk(C_{1-6})$, C(=O)Ph, $C(=O)Alk(C_{1-6})Ph$.

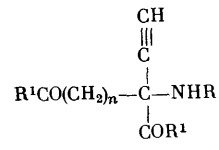
As a continuation of studies on the synthesis and properties of derivatives of α-acetylenic α-aminoacids, Casara and Metcalf[25] developed another general method for their synthesis by regioselective alkylation of a common synthon—the urethane (14), which was readily obtained in 65% yield by amidoalkylation of bis(trimethylsilyl)acetylene (12) under conditions of the Friedel–Crafts reaction.



(12) (13) (14), 65%

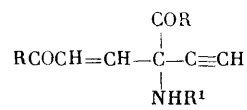
R = CH_2Ph (75%), $CH_2CH=CH_2$ (70%), $(CH_2)_5Me$ (60%).

By changing the initial amide (13) and varying the electrophiles (E), Metcalf et al.[26–29] increased the number of amino acids and their derivatives synthesised by the same method to include (15) and (16), which irreversibly inhibit glutamic acid decarboxylase, stimulate the activity of the nervous system, and have bactericidal activity.



(15)

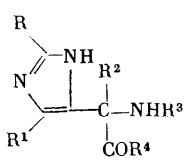
R = H, R^2CO; R^2 = $Alk(C_{1-4})$, $OAlk(C_{1-4})$, H_2NCHR^3CO; R^3 = H, Alk, CH_2Ph, $CH_2C_6H_4$—OH-*n*; R^1 = OH, OAlk, NR^4R^5; R^4 = R^5 = H, Alk, $NHCHR^6CO_2H$; R^6 = H, Alk, CH_2Ph, $CH_2C_6H_4$—OH-*n*; $n = 1 \div 3$.



(16)

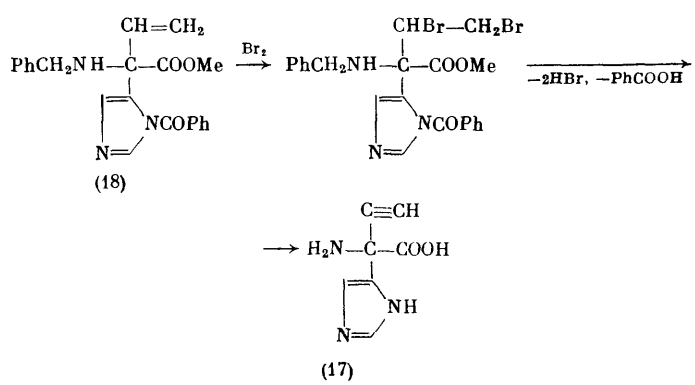
R = OH, OAlk, NR^2R^3(R^2, R^3 = H,Alk), $NHCHR^4CO_2H$(R^4 = H, Alk, $CH_2C_6H_4$—OH-*n*); R^1 = H, Alk, CH_2Ph, $CH_2C_6H_4$—OH-*n*.

In synthesising the amino acid derivatives (17), which exhibit antihistamine activity, Metcalf and Jung[30,31] introduced the acetylene function by successive bromination and didehydrobromination of histidine derivatives of amino acids with protected amine and acid functions (18).



(17)

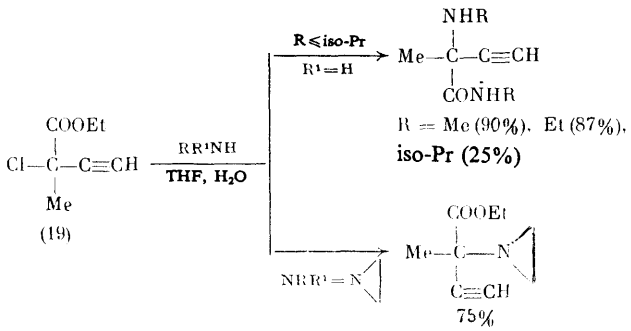
R = R^1 = H, F, Cl, Br, I, $Alk(C_{1-4})$; R^2 = $CH=CH_2$, C≡CH; R^3 = H, CO_2R^5(R^5 = Alk (C_{1-4})); NH_2CHR^6CO(R^6 = H, $Alk(C_{1-4})$, $CH_2C_6H_5$, $CH_2C_6H_4$—OH-*n*); R^4 = OH, OAlk. (C_{1-8}), NR^7R^8(R^7, R^8 = H, $Alk(C_{1-4})$, $NHCHR^9CO$(R^9 = H, $Alk(C_{1-4})$, $CH_2C_6H_4$—OH-*n*))



(18)

(17)

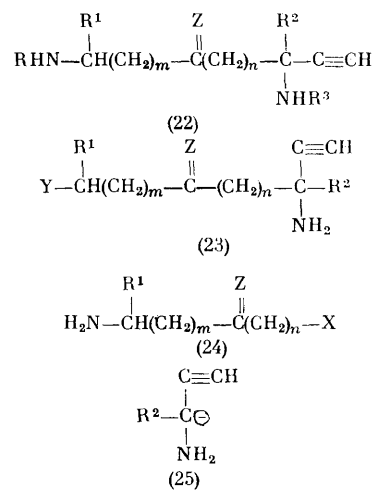
In 1983 Dugat and Verny[32] suggested another approach to derivatives of α-ethynyl-α-amino acids starting from ethyl 2-chloro-2-methyl-3-butynoate (19).



The simplest α-ethynyl-α-amino acid — 2-amino-3-butynoic acid (20), which Metcalf and Jung were not able to obtain[10] — was first isolated by Kuroda et al.[33] in its *L*-form from a cultural liquid of *Streptomyces*, and it is produced by the microorganisms *Streptomyces catenulae*. It appeared to be unstable in aqueous solution so it was isolated and determined by the authors as its acetyl derivative (21).[34] It is an antibiotic that is active towards Gram-positive bacteria and inhibits alanine racemase.

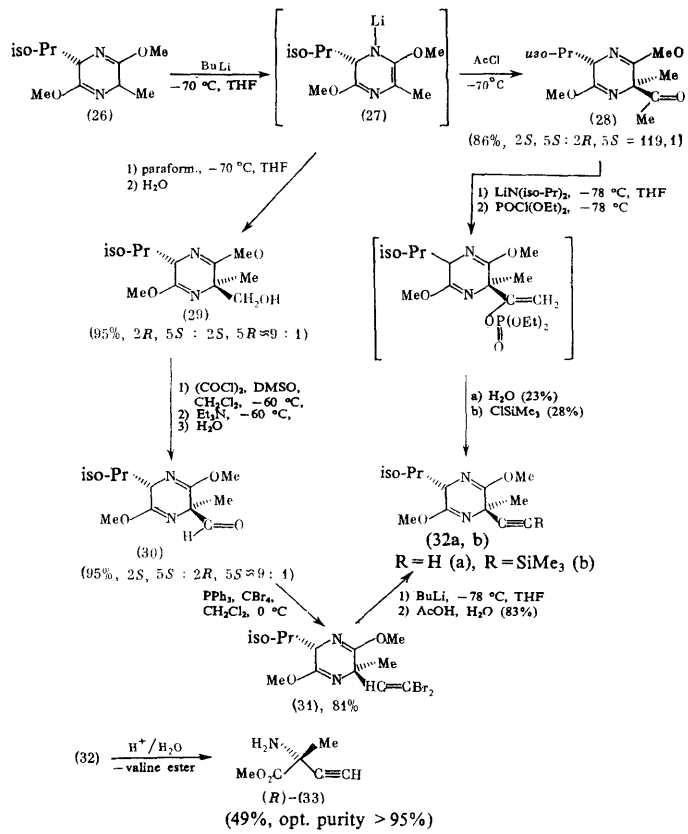


α,δ-Diamino-α-ethynyl-α-amino acids and their derivatives (22), which deactivate amino acid decarboxylase, have been proposed by Gerhard and Van Dorsselaer as antitumour agents.[35]



R = H, $R^4C=O$ (R^4 = Alk, Ph, Ph—Alk), residue of *L*-amino acid, R^1 = H, Alk; *m*, *n* = 0, 1 (*m*+*n* = 1); Z = O, CH_2; R^2 = H, $R^5C=O$ (R^5 = OH, when R = R^3 = H, R^5 = OAlk, NR^6R^7, where R^6, R^7 = H, Alk, residue of *L*-amino acid); R^3 = H (R = H, R^3 = H), $R^4C=O$; Y = Br, Cl, I, TsO, MsO; X = Br, Cl, I.

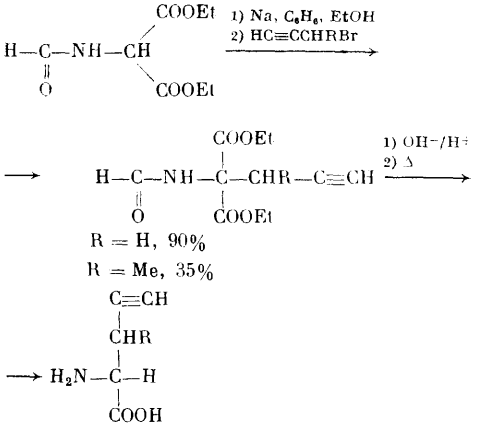
Compound (22) was obtained by either amination of the phthalimide derivatives of compounds (23) with hydrazine or methylamine followed by treatment with strong acid or reaction of amines (24) with the carbanion (25). At the same time the acetylene and amino groups in (23)—(25) were protected in a suitable manner.



In 1988 Schöllkopf et al., starting from the cyclic bislactim diether of *L*-valine and alanine (26), carried out the asymmetric synthesis of (*R*)-α-ethynylalanine (33) — a potential suicidal inhibitor of glutamic acid decarboxylase — in two ways.[36] A key stage of the first method was the regio- and stereo-selective acetylation of the *N*-lithiated ether (27) to the 2-acetyl-2,5-dihydropyridine (28) with a 90% excess of the (2*S*, 5*S*)-enantiomer. Compound (28) was converted by phosphorylation and subsequent hydrolysis or trimethylsilylation to 2-ethynyldihydropyrazines (32a, b), acid hydrolysis of which gave (*R*)-α-ethynylalanine (33) with an overall yield of 10—12% based on the initial ether (26). In the second method treatment of the lithiated bislactim ether (27) with paraformaldehyde followed by hydrolysis gave the alcohol (29) with an optical purity of 90%, which was oxidised with a mixture of oxalyl dichloride and dimethyl sulphoxide to the aldehyde (30). A Wittig reaction of the latter with triphenylphosphine dibromomethylene gave the 2-dibromoethylene-2,5-dihydropyrazine (31), which was converted by dehydrobromination and acid hydrolysis to the 2-ethynyldihydropyrazine (32a) in higher yield but with slightly lower stereoselectivity than in the first case. When the other enantiomer of the initial bislactim ether (26) is used it is possible to obtain the (*S*)-enantiomer of α-ethynylalanine in a similar manner.

2. α-Propargyl-α-amino acids

The first known example of α-propargyl-α-aminoacids was propargylglycine (34a), which was prepared in 1949 by Gershon et al.[37] from sodium formamidomalonate during research on active bactericidal agents amongst glycine analogues. The same authors subsequently reported the propargylglycine homologue—2-amino-3-methylpentynoic acid (34b).[38]



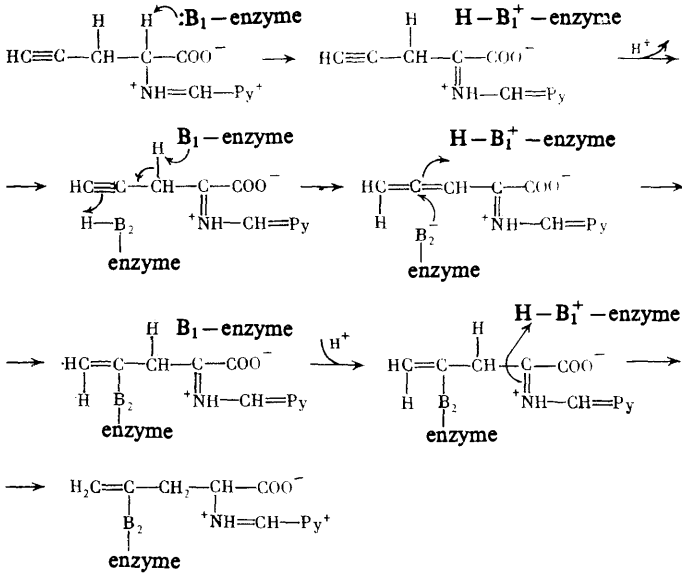
(34a, b)

R = H (a), 89%

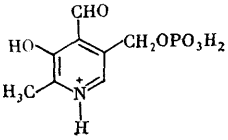
R = Me (b), 71%

It transpired that both amino acids (34a, b) actively inhibit the growth of yeast *Saccharomyces cerevisiae* and mould *Ercherihia* [Eschericia?] *coli* microorganisms.

In 1971 Scannel et al.[39] found that *L*-propargylglycine can be obtained microbiologically from cultivation of *Streptocetes*. As a result of fundamental biochemical studies by Walsh, Abeles, Marcotte, et al.,[40–45] it was established that inhibition of the growth of bacteria[41,43] and fungae[45] by propargylalanine is caused by its ability to deactivate irreversibly the enzymes bound to pyridoxal phosphate as the coenzyme—γ-cystathionase,[40,42] cystathionine γ-synthetase, methionine γ-lyase,[43] *L*-alanine transaminase, and others[44]—which take part in the biosynthesis or metabolism of the corresponding amino acids, and hence to disrupt the growth and development of cells, tissues, and complete organisms. As a result of a study on the suicidal deactivation of rat liver γ-cystathione with α-propargylglycine labelled with ^{14}C, ^{2}H, and ^{3}H isotopes, a mechanism for the process was put forward.[40,42] According to this mechanism, after bonding of the amino group of propargylglycine with the aldehyde group of the coenzyme, one of the bases (B_1) of the active site of γ-cystathionase by reacting alternately with the hydrogen atoms of the α- and β-carbon atoms of propargylglycine catalyses the isomerisation of the Schiff base and rearrangement of the acetylene residue to a highly reactive allene.[40,42] The authors assume that one of the acid groups of the active site of the enzyme ($H-B_2$) assists the formation of the allene by protonating the δ-carbon atom of the propargylglycine residue. It is very probable that after deprotonation, a base (B_2) adds to the allene, forming a covalent bond between enzyme and deactivator. A study of the hydrolysis products of the adduct between deactivator and enzyme showed that cysteine and tyrosine residues in the active site of the enzyme act as nucleophiles (and bases) forming a covalent bond with the deactivator. However, the authors do not exclude the possibility that the number of bases involved in the process may in fact amount to more than two.

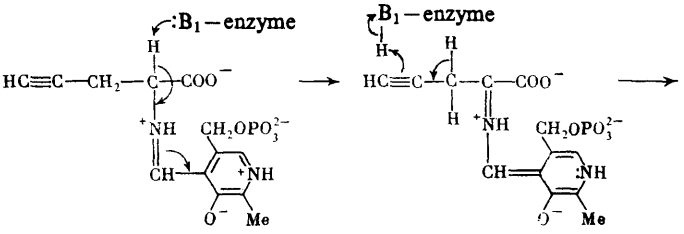


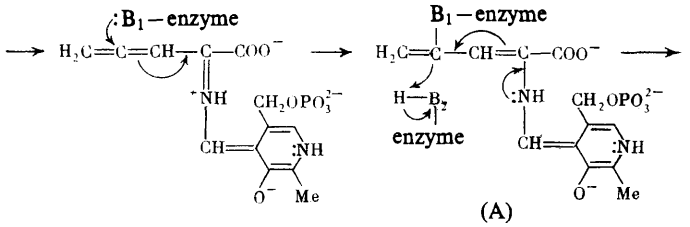
where Py^+-CHO is pyridoxal phosphate bound to the enzyme:

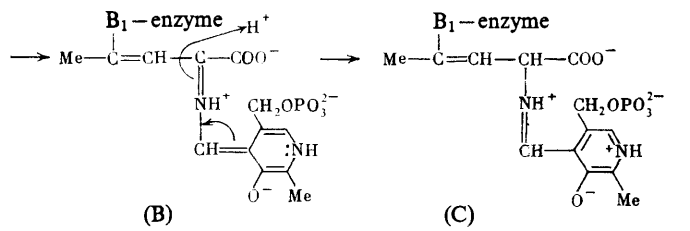


and B_1 and B_2 are bases (or nucleophiles) at the active site of the enzyme.

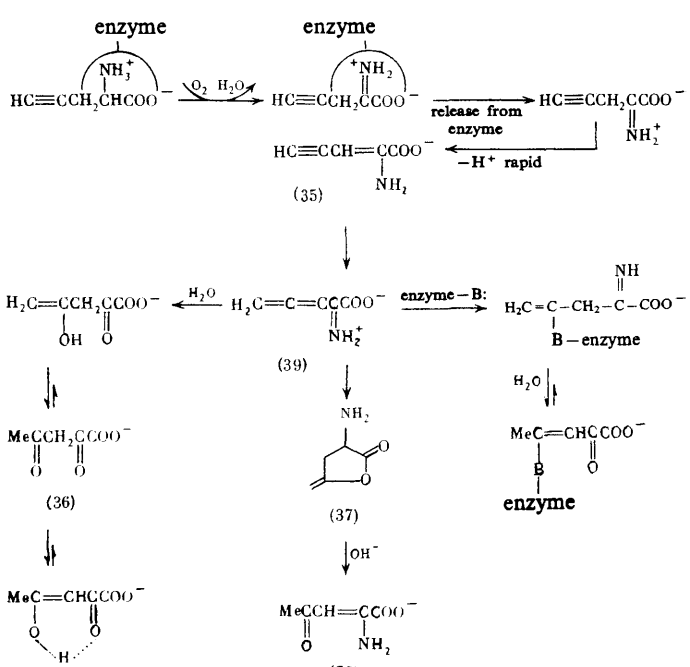
It is possible that the sequence of action of bases B_1 and B_2 is somewhat different to that described above. Johnston et al.[43] put forward a modified mechanism for the deactivation by *L*-propargylglycine of two enzymes—cystathionine γ-synthetase and methionine γ-lyase—from different types of bacteria. The main stages of this mechanism are the same as for the above, namely: reaction of propargylglycine with the coenzyme (pyridoxal phosphate), isomerisation of the acetylene residue of bound propargylglycine to an allene group with the participation of a minimum of two bases (or nucleophiles: B_1 and B_2) in the active site of the enzyme, and final protonation of the α-carbon atom of the deactivator, possibly through proton exchange with the solvent. The main difference from the previous mechanism is that Johnston et al.[43] assume that isomerisation of the γ,δ-double bond of the deactivator in adduct (A) to a β,γ-double bond occurs. As a result the final adduct mainly has structure (B) (according to the visible absorption spectra of the adduct between methionine γ-lyase and the deactivator) or (C) (in the case of cystathionine γ-synthetase.





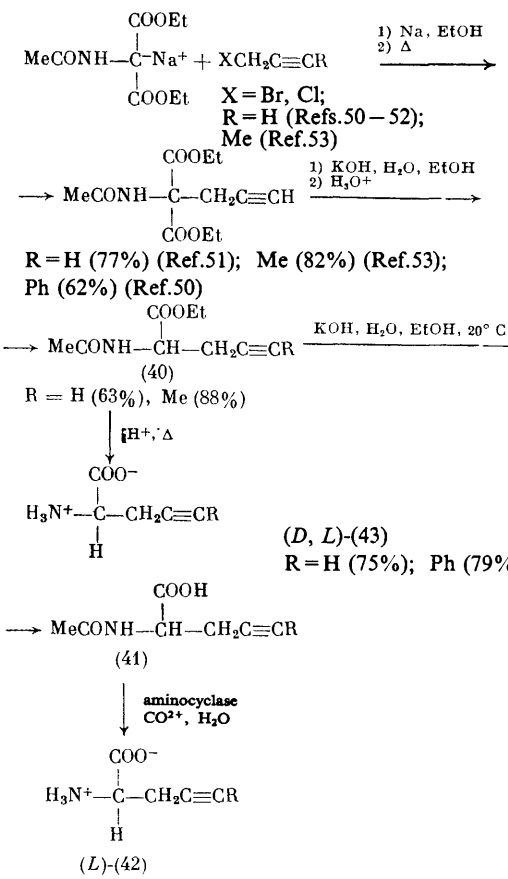


The action of *D*- and *L*-propargylglycine on *D*- and *L*-amino acid oxidases bound to flavin as the coenzyme has been studied in detail.[46–49] It was established that *D*-propargylglycine is oxidised by a *D*-oxidase to the 2-aminopent-2-en-4-ynoate (35), which is then converted to acetopyruvate (36) or to the iminodiene lactone (37), and the latter after treatment with alkali gives 2-amino-4-oxo-2-pentenoate (38). Compounds (35) and (38) form charge transfer complexes with a *D*-amino acid oxidase and act as noncovalent inhibitors. However, after oxidation of propargylglycine the activity of the oxidase is not completely regenerated by the usual methods. Therefore, it was assumed by the authors that the enzyme undergoes not only reversible modification but also irreversible (covalent) modification as a result of the reaction of a nucleophilic residue (B:) in the active site of the enzyme with a highly reactive metabolite of propargylglycine, which may be the conjugated allenimino acid (39).



B—nucleophile of active site of enzyme

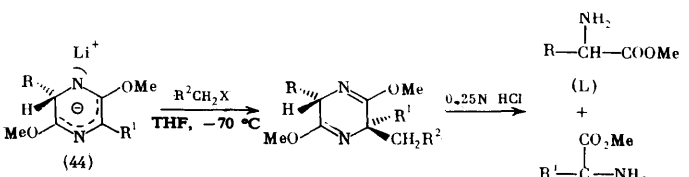
In biochemical studies use is made not only of *L*-propargylglycine obtained microbiologically[39] but also of racemic *D,L*-propargylglycine synthesised by the Gershon method modified by different authors.[50–53] Stereospecific hydrolysis of the acetamide group of the *D,L*-acetamide (41) by pig kidney aminoacylase in the presence of cobalt acetate or chloride gives *L*-propargylglycine (42). The *D*-form of the ethyl ester of the amino acid acetamide (41) is isolated from the filtrate.[53]



R=H (80%) (Ref.52); Me (86%) (Ref.53).

On conventional acid hydrolysis of the racemates of the acetamide ethyl esters (40), the corresponding amino acids (43) are obtained in a racemic form.

Diastereoselective alkylation of the lithiated bislactim ethers (44) followed by hydrolysis of the resulting intermediates was carried out by Schöllkopf et al.[54–59] for the asymmetric synthesis of the methyl esters of (*R*)-α-propargylglycine (45a) and certain other β-acetylenic α-amino acids (45b–d).



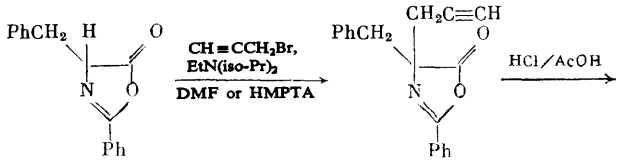
(45a–d)

Amino ester (45)	R	R^1	R^2	Yield, %	Optical Purity, %	Refs.
a	iso-Pr	H	C≡CH	52	60–65	[54]
a	t-Bu	H	C≡CH	59	95	[55–58]
b	iso-Pr	H	C≡CPh	86	95	[54–57]
c	iso-Pr	Me	C≡CH	–	95	[56–58]
d	iso-Pr	$(CH_2)_2PO(OEt)_2$	C≡CH	83	95	[59]

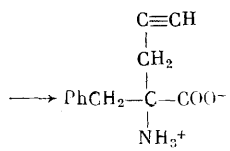
In 1984 O'Donnell et al.[60] demonstrated the possibility of obtaining α-propargylglycine (34a) in good yield (68%) by propargylation of the Schiff base of ethyl glycinate with diphenyl ketone in acetonitrile in the presence of potash and tributylammonium bromide as a phase transfer catalyst.

Propargylglycine is not used solely as a suicidal inhibitor of enzymes:[40–41] it has been used to establish the chemical structure of the active sites of enzymes[61,62] and also to synthesise tritium-labelled norleucine-containing peptides[52,53] and other novel peptides.[63]

The original synthesis of α-propargylphenylalanine (47) by reaction of propargyl bromide with the oxazoline (46) in the presence of a tertiary amine in dimethylformamide or hexamethylphosphoric triamide has been reported.[64]

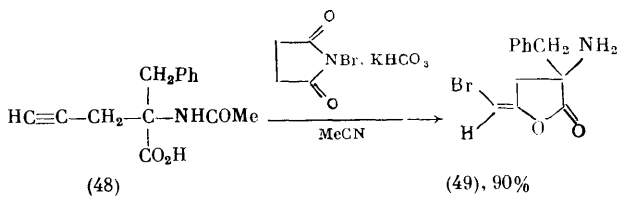


(46)

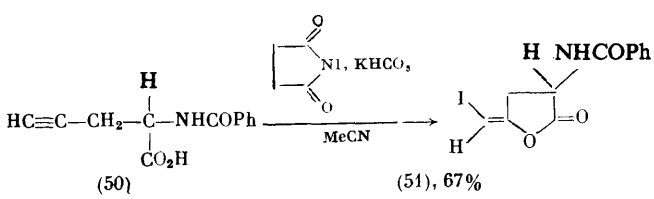


(47) 25%

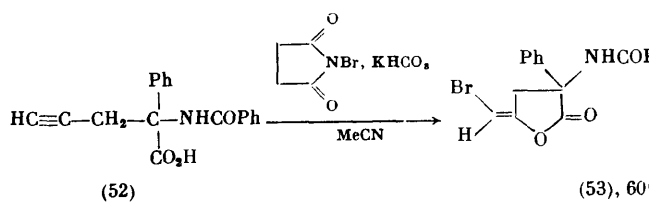
Katzenellenbogen et al.[65] subsequently used amides of propargylphenylalanine (48), propargylglycine (50), and propargylphenylglycine (52) for the synthesis of the five-membered lactones (49), (51), and (53), which proved to be inhibitors of serine protease.[65]



(48) (49), 90%

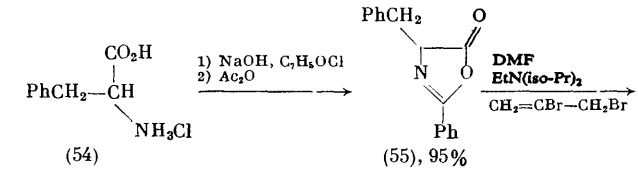


(50) (51), 67%

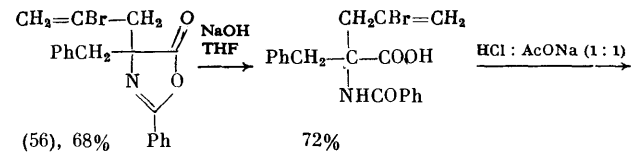


(52) (53), 60%

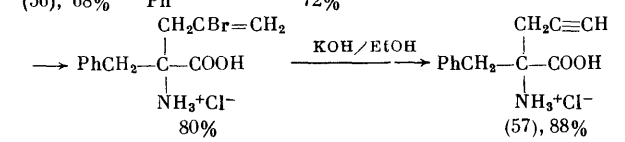
The synthesis of propargylphenylalanine was carried out by the authors in three ways. In the following scheme is depicted the method in which the 2-bromo-2-propenyl group, which was introduced into the 2-benzyloxazolone (55) obtained by reaction of phenylalanine hydrochloride with benzoyl chloride, was used as the propargyl synthon. After three-stage hydrolysis of the alkylated oxazoline (56) in different media propargylphenylalanine (57) was isolated with a total yield of 33% [based on phenylalanine (54)].



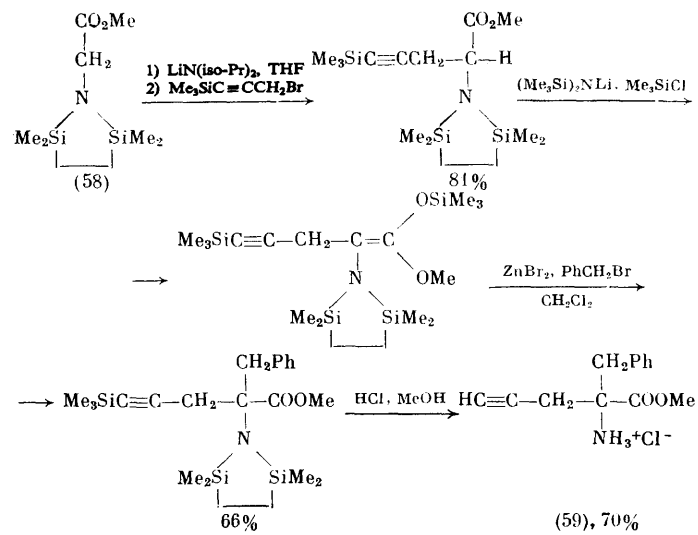
(54) (55), 95%



(56), 68% 72%



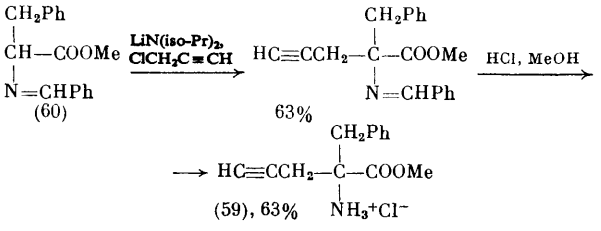
Alternative approaches to propargylphenylalanine (57) include the selective alkylation of the suitably protected α-amino acid derivatives (58) and (60). In the first method the adduct of methyl glycinate and 1,1,4,4-tetramethyldichlorosilylethylene (58) was first alkylated with 1-bromo-3-trimethylsilyl-2-propyne in the presence of lithium diisopropylamide and then benzylated under Friedel–Crafts conditions. After acid hydrolysis the methyl ester of propargylphenylalanine hydrochloride was isolated with an overall yield of 37%.



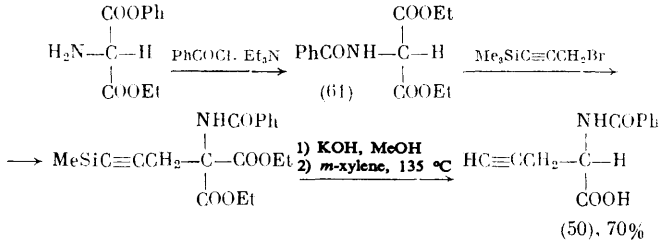
(58) (59), 70%

In the second method the benzylidenimine of phenylalanine methyl ester (60) after treatment with lithium diisopropylamide at −78 °C was alkylated with 1-chloro-2-propyne. After removal of the benzylidene protecting group by acid hydrolysis, the methyl ester

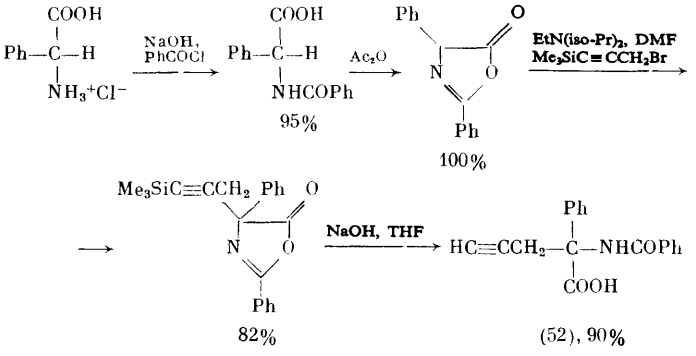
of propargylphenylalanine hydrochloride (59) was isolated with a total yield of 38%.



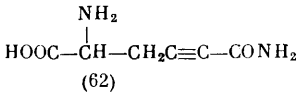
Sofia et al.[65] used the method of Gershon for the synthesis of propargylglycine benzamide (50), namely, diethyl malonate benzamide (61) was alkylated with 1-bromo-3-trimethylsilyl-2-propyne:



The benzamide of propargylphenylglycine (52) was synthesised using the methods described above in the following way:

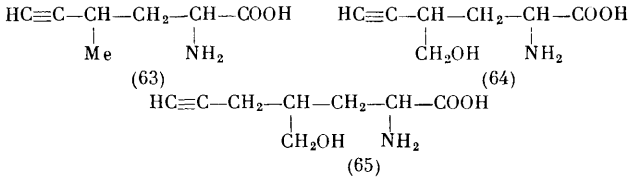


The carbamoyl derivative of propargylglycine—2-amino-5-carbamoyl-4-pentynoic acid (62)—has been isolated by Japanese biochemists from a cultural liquid of *Streptomyces* bacteria, which are capable of producing this antibiotic.[66]

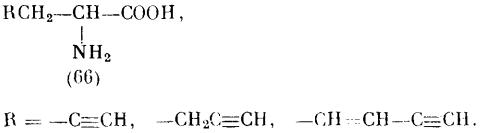


3. γ-Ethynyl-α-amino acids

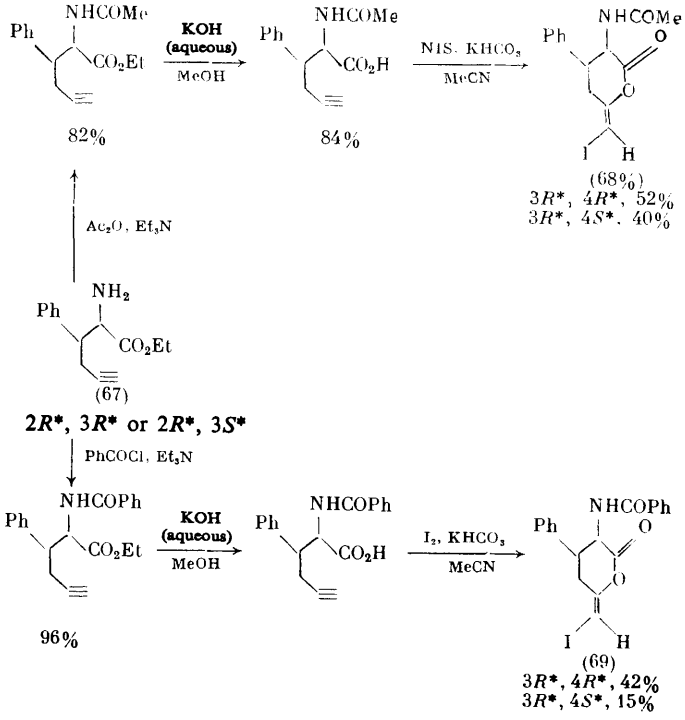
Information about γ-ethynyl-α-amino acids is limited. The isolation of two γ- and one δ-ethynyl-α-amino acids (63)–(65) from seeds of *Euphoria longan* plants was reported.[67]

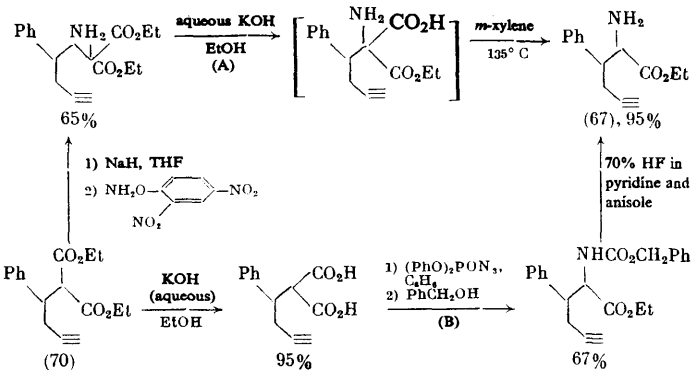


Several acetylene-containing amino acids of the type (66) were later isolated by extraction from a culture of *Basidomycetes* (for example, *Amanita Pseudoporphria*).[68]



In synthesising the iodomethylidenetetrahydro-2-pyranones (68) and (69), which, like the five-membered lactones (49), (51), and (53) described above,[65] act as irreversible inhibitors of serine protease, Sofia and Katzenellenbogan[69] used as the starting compound ethyl 2-amino-3-phenyl-5-hexynoate (67), which after protection of the amine group with acetyl or benzoyl functions underwent hydrolysis and iodolactonisation.



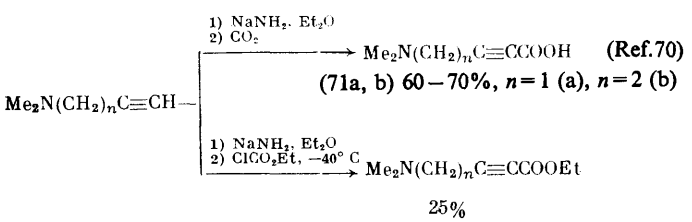


The γ-ethynyl-α-amino acid ethyl ester (67) was synthesised from the substituted malonate ester (70) either by successive amination and decarboxylation (route A) or by a modified Curtius rearrangement (route B).[69]

III. γ-Amino acids

1. α-Acetylenic γ-amino acids and their derivatives

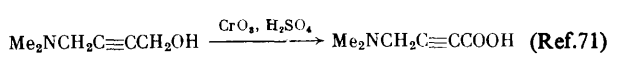
The first syntheses of α-acetylenic γ-, δ-, and ε-amino acids date back to the late 1950s when Olomucki and Marszak[70–74] put forward several methods for the preparation of 4-dimethylamino-2-butynoic acid (71a), its homologues, and esters, without touching on the question of their possible biological activity.



(Ref.70)

(71a, b) 60–70%, $n=1$ (a), $n=2$ (b)

25%

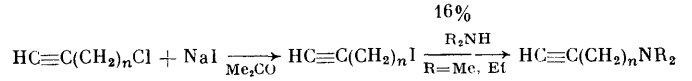


(Ref.71)

50–60%

$Me_2NH + ClCH_2C{\equiv}CCOOH \rightarrow Me_2NCH_2C{\equiv}CCOOH$ (Ref.72)

16%

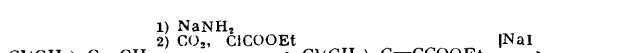


(Ref.73)

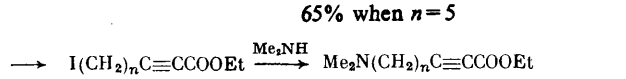


(Ref.73)

$n = 1, 3$, 70%

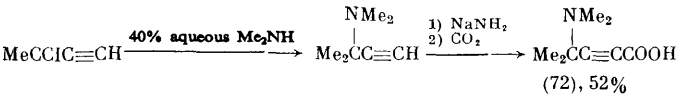


80% when $n=3$;
65% when $n=5$



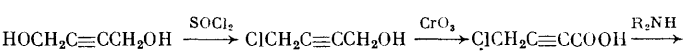
(Ref.74)

Subsequently Hennion and Perrino,[75] in studying the synthesis and conversions of certain α-acetylenic tertiary amines, obtained 4,4-dimethyl-4-dimethylamino-2-butynoic acid (72).

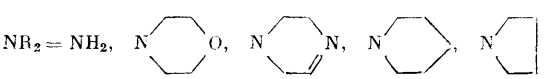


(72), 52%

Bert and Johnston[76] in 1972 were the first to consider the biological activity of α-acetylenic γ-amino acids. They synthesised 4-aminotetrolic acid (73) and some of its derivatives as simple conformationally strained analogues of the neuromediator—γ-aminobutanoic acid (GABA)—in order to establish a correlation between the structure and activity of γ-amino acids.

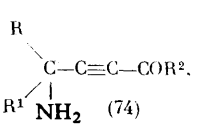


(73)



All of the γ-amino acids (73) that were synthesised proved to be inhibitors of the stimulation of central neurons, but they were weaker than GABA.

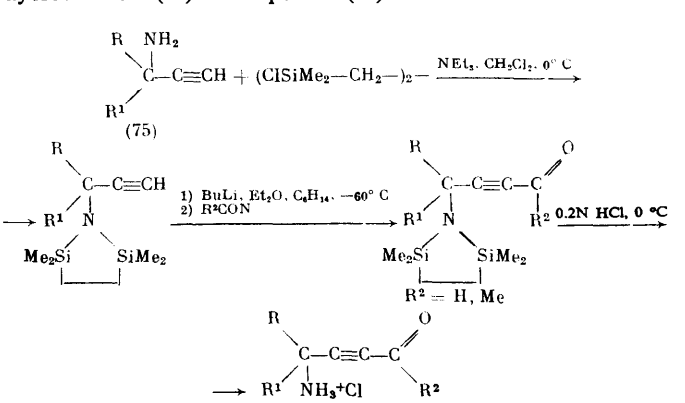
In the middle of the 1980s the aminoacetylenecarbonyl compounds (74), amongst which were amides of γ-carbon atom-substituted analogues of γ-aminobutynoic acid, were proposed[77] for the therapeutic treatment of alcoholism.



(74)

R and R^1 are hydrocarbon or heteroatomic hydrocarbon groups, R + R^1 is a cycloalkylene or heterocycloalkylene group, R^2 = H, Alk, NH_2.

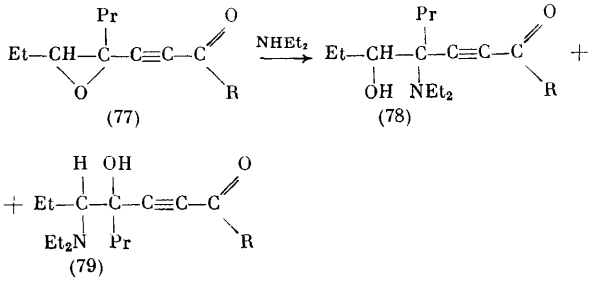
They were synthesised from the acetylenic amines (75), by replacing the acetylenic hydrogen with an aldehyde, carbonyl, or amide function after initial protection of the amino group. Subsequent acid hydrolysis under mild conditions gave the hydrochlorides (76) of compounds (74).



(76)

Some of the hydrochlorides (76) exhibited antitumour properties.[77]

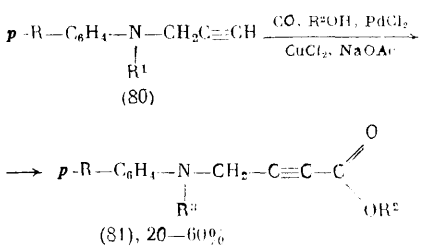
By aminating the epoxyacetylenic acid derivatives (77), Larionov et al.[78] in 1985 synthesised certain esters and amides of α-acetylenic hydroxyamino acids (78) and (79). The biological activity of the latter was not studied.



(77) (78) (79)

R = OMe, NEt_2

It was recently demonstrated by the present authors that for the synthesis of *N*-substituted α-acetylenic γ-amino acid esters in sufficient yield for preparative purposes, it is possible to utilise the oxidative alkoxycarbonylation of acetylenic amines (80) with carbon monoxide in alcohols under conditions of homogeneous catalysis by palladium chloride.[79,80]



(80) (81), 20–60%

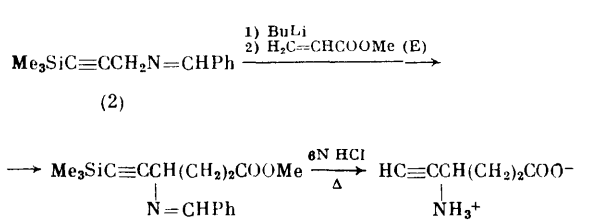
R = H, Cl; R^2 = Me, Et; R^3 = Me, $CH_2C{\equiv}CCOOMe$.

The amino esters (81) exhibit weak fungicidal and antistaphylococcal activity.

2. γ-Ethynyl-γ-amino acids

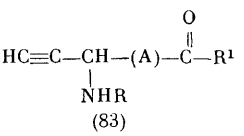
γ-Ethynyl analogues of GABA have attracted the attention of research workers because they have proved to be active inhibitors of GABA α-ketoglutarate transaminase from mammalian brain. Therefore they have very considerable potential for application in therapy as psychotropic agents. Metcalf and Jung[81,82] put forward a possible mechanism of their action which is similar to that described above for other irreversible enzyme inhibitors containing an acetylene function.[40,42,43]

The first example of this class of amino acids—4-amino-5-hexynoic acid (82) was obtained by alkylation of the protected aldimine (2), used subsequently for the synthesis of α-ethynyl-α-amino acids.[9,10]



(2) (82), 53%

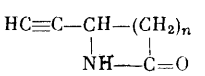
By varying the electrophilic reagent (E), Metcalf and Jung[83–86] obtained a large group of γ-amino acids (83) and their lactams (84) in racemic and enantiomerically pure forms. Some of these compounds had a beneficial effect in the treatment of functional disorders of the nervous system caused by Parkinsonism, chorea, epilepsy, alcohol syndrome, psychoses related to schizophrenia, manic depression, and hyperkinesia. Other compounds had hypothermal, myorelaxant, cholinergic, antibacterial, anticonvulsive, analgesic, sedative, and tranquillising activity.



(83)

R = Alk, $C(O)Alk(C_{1-4})$, $OC(O)Alk(C_{1-4})$, $C(O)CHR^2$, NH_2

R^2 = H, $Alk(C_{1-4})$, CH_2Ph, $CH_2C_6H_4OH$-*p*;



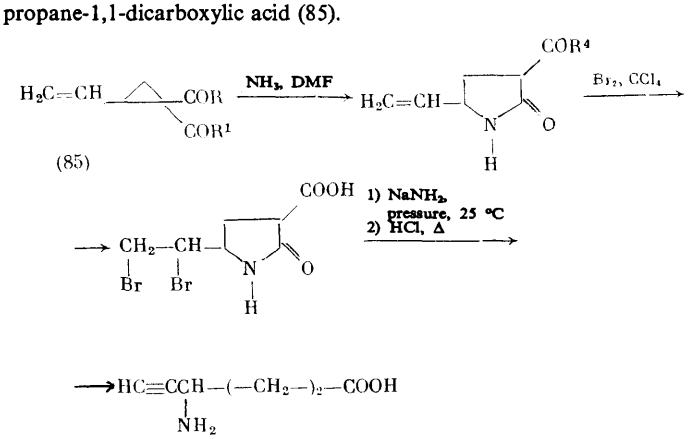
(84) *n* = 2, 3

R^1 = H, $AlkO(C_{1-8})$, NR^3H, R^3 = $Alk(C_{1-4})$, $NHCHCOOH$ (R^4);

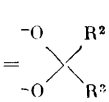
R^4 = H, $Alk(C_{1-4})$, CH_2Ph,

$CH_2-C_6H_4-OH$-*p*; A = $-CH(R^5)-$, R^5 = H, $Alk(C_{1-4})$, Ph, *o*-, *m*-, *p*-$C_6H_4-R^6$, R^6 = Hal, $OAlk(C_{1-4})$, $Alk(C_{1-4})$.

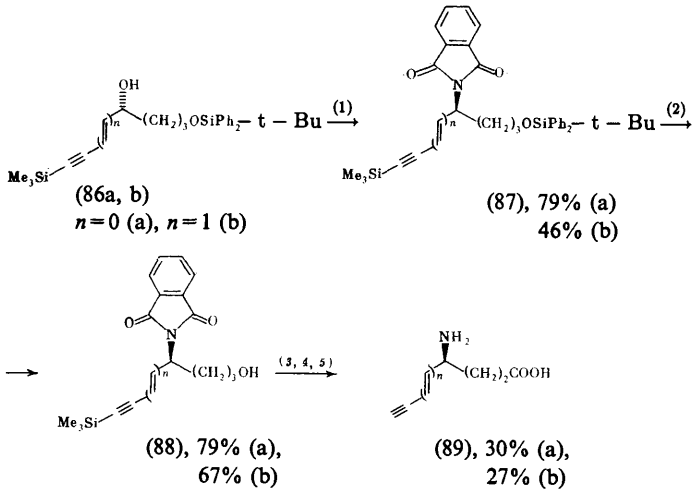
Gittos and Letertre proposed another route for the synthesis of 4-amino-5-hexynoic acid (82)—from derivatives of 2-vinylcyclopropane-1,1-dicarboxylic acid (85).



(85) (82)

R, R^1 = $OAlk(C_{1-4})$, R + R^1 =  , R^2, R^3 = $Alk(C_{1-4})$.

R^4 = OH, NH_2, **O–Bu-t.**



(*1*) Ph_3P, phthalimide, diethyl azodicarboxylate, THF, room temperature, 19 h;
(*2*) HF–pyridine (3 equiv.), THF, room temperature, 19 h;
(*3*) $(COCl_2)$, DMSO, Et_3N, CH_2Cl_2, −78 °C, then Jones reagent (2 equiv.);
(*4*) $H_2N-NH_2.H_2O$, EtOH, refluxing, 10 min;
(*5*) $Bu_4N^+F^-.3H_2O$, THF, −10 °C, 20 min.

In 1989 Tabor et al.[88] carried out the enantioselective synthesis of (*S*)-γ-acetylene-γ-aminobutyric acid (89a) and its vinyl analogue—(*S*)-*trans*-γ-butenynyl-γ-aminobutyric acid (89b)—with greater than 95% enantiomeric purity by phthalimide substitution of the homochiral alcohols (86a, b) followed by desilylation of the imides (87a, b), oxidation of the imidoalcohols (88a, b), and removal of the phthalimide and trimethylsilyl protecting groups.

IV. Various mono- and poly-acetylene -containing amino acids

In addition to the information given above on the synthesis and biological properties of α- and γ-amino acids, there are separate reports in the literature on the preparation of certain other acetylenic and polyacetylenic amino acids.

Dumont et al.[89] synthesised the diacetylenic amino acids (90) by reaction of acetylenic amines or amides with haloacetylenic acids.

$$R^1R^2N(CH_2)_n-C\equiv CH + BrC\equiv C(CH_2)_n-COOH \xrightarrow[EtNH_2]{Cu^I} \longrightarrow R^1R^2N(CH_2)_nC\equiv CC\equiv(CH_2)_m-COOH,$$

R^1 = H, Me, COH; R^2 = H, Me; n = 1–6; m = 2, 4. (90)

When this reaction was carried out with primary amines, the amino group was first protected by formylation, and after formyl derivatives (90) were obtained, R^1 = HCO, R^2 = H, they were deformylated with caustic soda to the corresponding amino acids (90), $R^1 = R^2 = H$.[89]

Acid hydrolysis of nitriles of *N*-alkynylamino acids (91) gave the corresponding amino acids (92) in 90% yield.[90]

$$R-\underset{\displaystyle R^1}{\overset{\displaystyle C\equiv CH}{\overset{|}{C}}}-NH-(CH_2)_2-CN \xrightarrow{HCl,\ Et_2O} R-\underset{\displaystyle R^1Cl^-}{\overset{\displaystyle C\equiv CH}{\overset{|}{\overset{+}{C}}}}-NH_2-(CH_2)_2-COOH,$$

(91) (92), 90%

R = R^1 = Me, Et; R = Me, R^1 = Et.

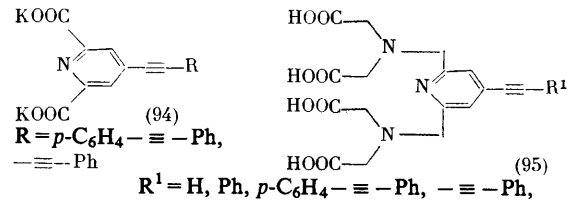
Ahmed et al.[91] isolated the polyacetylenic amino acids (93) from cultures of *Fayodia bisphaerigera* fungae. The structure of the acids was reliably established by a range of physicochemical studies and by counter-synthesis.

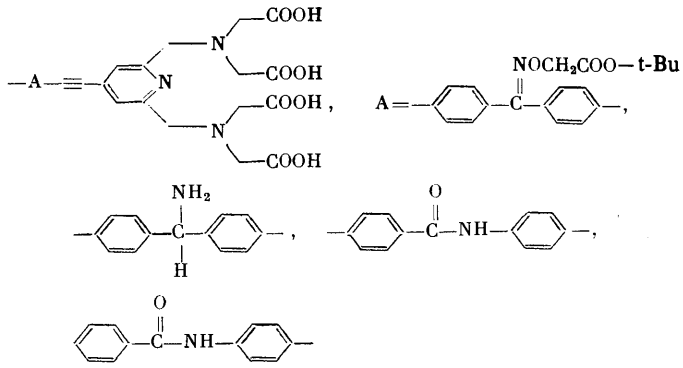
trans-HO–CH_2–CH=CH–$(C\equiv C)_3$–COX, (93)

X = OMe, NHCHRCOOMe, R = H, Me.

In recent years amino acid derivatives containing an acetylene residue in the molecular structure have attracted the attention of research workers as complexing agents and as synthons for the derivation of novel compounds with interesting and useful properties.

Takalo, Hänninen, et al.[92–94] in a multistage synthesis obtained a number of polyconjugated derivatives of ethynylated pyridinecarboxylic acids (94) and pyridinaminocarboxylic acids (95) in order to study the spectroscopic properties of their metal complexes.



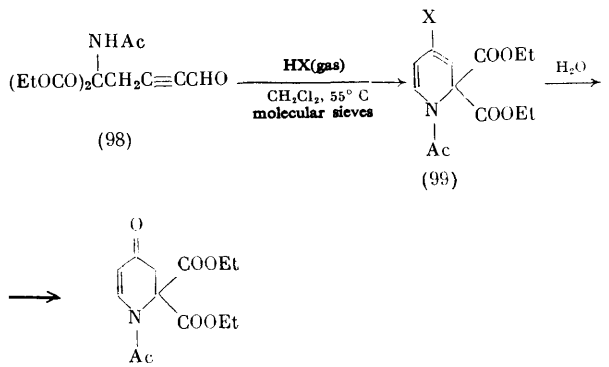


The alkyl esters of *N*-propargyl-*N*-alkoxycarbonylglycine (6) were used[95] to obtain 1-propargyl-2,4-dioxoimidazolidine (97)—an intermediate in the synthesis of pyrethroid insecticides and acaricides

$$HC\equiv CCH_2-\underset{\displaystyle (96)}{\overset{\displaystyle CH_2COOR^1}{\overset{|}{N}}}-COOR + NH_3 \xrightarrow[atm.pressure]{0-100^\circ C} \longrightarrow HC\equiv CCH_2\overset{\displaystyle CH_2COOR^1}{\overset{|}{N}}-COOR \xrightarrow[2)\ H^+,\ H_2O]{1)\ NaOMe,\ \Delta}$$

$$\longrightarrow HC\equiv CCH_2N\begin{array}{l}C(=O)\\ \\ NH\end{array}\!\!-\!\!\!-\!\!\!-\!

It was found by Roduit and Wyler[96] that the propargylacetylaminomalonic acid derivatives (98) readily cyclise, forming dihydropyridines (99), which are then hydrolysed to trihydropyridones (100). Dihydropyridines are known to be widely used in pharmacology and in biological studies.



(100), up to 85%

X = Cl, Br

This review of information in the literature on amino acids of various structures that contain an acetylene residue in the molecule, obtained by both chemical and microbiological methods, provides an indication of the extensive possibilities of using these compounds as biologically active agents whose specific physiological action is mainly due to their ability to modify irreversibly the active sites of certain enzymes by disrupting the chain of biochemical reactions of vital amino acids. Acetylenic amino acids are also used as synthons for the preparation of various compounds that have properties with useful practical applications.

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Translated from *Uspekhi Khimii*, **60** 1346–1367 (1991) U.D.C. 541.64:541.124;541.127;541.128

Characteristic features of radical polymerisation occurring under the influence of non-traditional initiators

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ABSTRACT. The kinetics of free radical polymerisation processes during which macromolecules grow stepwise are examined. A general approach suitable for the calculation of the molecular weight distribution of the products of the polymerisation initiated by various classes of non-traditional initiators is formulated. The effectiveness of this theoretical approach is illustrated in numerous examples of the solution of specific practical problems.

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I. Introduction

A common feature of a large proportion of radical polymerisation processes is a decrease in molecular weight with increase in the concentration of traditional initiators, which imposes fundamental limitations on the increase in the productivity of the corresponding processes. This is associated with the fact that the length of the material chain in the absence of transferring agents is equal either to the length of the kinetic chain or to twice its length respectively in cases where the termination reaction proceeds via a combination or disproportionation mechanism. An increase in the rate of polymerisation as a result of an increase in the rate of initiation in the processes considered therefore leads to a simultaneous decrease in the length of the kinetic chain and hence to a decrease in molecular weight.

This undesirable effect can be avoided by employing non-traditional radical polymerisation initiators whereupon the material chain consists of several elementary chains whose number increases continuously in the course of the process. An increase in the molecular weight of the polymer with conversion and a narrowing of its molecular weight distribution are then observed. These features are qualitatively different from those noted in the usual processes.

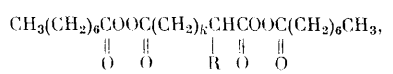
This review deals with questions concerning the quantitative description of such pseudolive radical polymerisation initiated by non-traditional compounds of two classes. The first includes polyfunctional initiators, for example, polyperoxides, containing more than one labile group in each molecule. The second contains so called "inferters" participating in chain transfer and termination reactions apart from initiation. A characteristic feature of both classes of these non-traditional initiators is that during polymerisation processes with their participation macromolecules capable of further reactivation and chain propagation are formed.

II. Polyfunctional initiators

1. Introduction

In conformity with their name, the molecules of polyfunctional initiators contain two or more functional groups capable of forming free radicals on decomposition. These groups are characterised by the chemical nature of the labile interatomic bond present in them, for example, the bond in the azo- and peroxy-groups. A fairly large number of chemically different types of polyfunctional initiators are now known. Information about the structure and method of synthesis of these compounds can be found in reviews.[1–6] Polyperoxides, in relation to which the general theoretical postulates will be illustrated below, have been most thoroughly investigated among them (to a large extent as a result of the fundamental research by Ivanchev and co-workers[7–16]).

The molecules of polyfunctional initiators can differ by the number of labile groups of various types. The simplest among initiators of this kind, such as, for example, diacyl diperoxide



(I)

contain two labile groups. For a sufficient length of the methylene bridge separating them, when the number k of the CH_2 units exceeds 6–8, both these groups decompose independently.[12,15] The entire discussion below will refer solely to polyinitiators with similar kinetically independent labile groups.

Generally speaking, the peroxy-groups in the diperoxide (I) have different thermal stabilities, since one of them contains an unsubstituted acyl group while the other has an α-substituted acyl group. The difference between the rate constants for the decomposition of these groups may be very appreciable depending on the nature of the substituent R. Thus Ivanchev and co-workers[9,10,12,15] determined the kinetic parameters of the thermolysis of a large number of different polyperoxides which they synthesised and also established the dependence of these parameters on the length k of the bridge, the nature of the substituent R, and the number of peroxy-groups in the molecules. Some data concerning the parameters, indicated above, of the decomposition of polyfunctional initiators have also been presented in communications by other investigators (see, for example, Refs. 17–20).

It has been established[12,18] that polyperoxides with independent peroxy-groups are most suitable for practical application. The rate of polymerisation initiated by such compounds will evidently be identical, under the conditions of the applicability of the Flory principle,[21] with the rate of polymerisation under the influence of traditional monofunctional initiators containing the same peroxy-groups and present at the same overall concentrations in both systems mentioned above.[22,23] The task of the quantitative theory of homopolymerisation with participation of polyfunctional initiators is therefore only the calculation of the molecular weight distribution (MWD) and of its statistical moments while for joint polymerisation it also includes the calculation of the composition distribution of the products formed.

2. The polymerisation mechanism

The main feature of the polymerisation in the presence of polyfunctional initiators consists in the formation, during the process, of macromolecules containing labile groups in the main chain (within it and/or at its ends). The mechanism of the formation of such macromolecules is illustrated schematically in Fig. 1 for the simplest case of the synthesis of monomers of the type of polystyrene under the influence of a diperoxide with the same peroxy-groups. The decomposition of any of the peroxy-groups results in the formation of a pair of free radicals each of which recombines, after the readdition in the course of its growth of a certain number of monomers, with one of the other similar macroradicals, generating macromolecules of the "dead" polymer. The latter contain only the elementary polymer chain and differ by the number of terminal peroxy-groups whose subsequent decomposition leads to the formation of a pair of polymeric radicals capable of further growth and recombination.

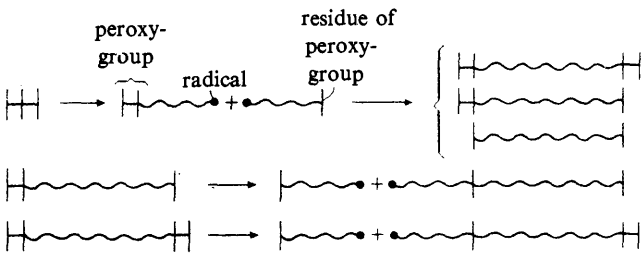


Figure 1. Schematic illustration of the formation of the polymer chain during polymerisation initiated by a symmetrical diperoxide.

The set of such parallel-consecutive reactions characterises the polymerisation-recombination mechanism of the formation of macromolecules in the presence of polyfunctional initiators discussed here.[1,23] Naturally, if the molecules of the initiators include more than two labile groups, then the molecules of the macroinitiator formed during polymerisation may contain these groups not only at the edge but also within the main chain. The structure of such macromolecules, formed during the consecutive decomposition of peroxy-groups and of the recombination of macroradicals, may be complex (Fig. 2). An arbitrary polymer chain may consist of any number m of elementary chains separated by peroxide clusters containing one, two, three, etc. peroxy-groups. The term "cluster" implies here a sequence of peroxy-groups bounded either by two elementary chains or by an elementary chain and the end of the macromolecule. In the former case, the cluster is referred to as closed and in the latter as semi-open.

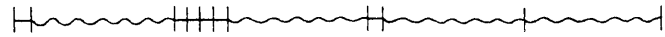


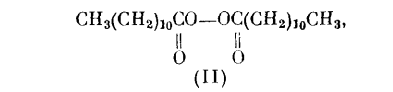
Figure 2. Schematic illustration of one of the polymer chains formed during the process presented in Fig. 1.

For polyinitiators with independent functional groups, the thermal stability of each of them should not depend on the cluster to which it belongs and on the site where it is located. The decomposition constant for any such peroxy-groups will then be identical with the constant characterising it in the molecule of the initial polyinitiator.

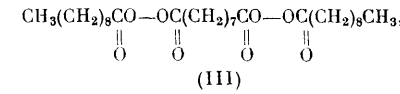
Examples of similar polyperoxides are well known.[1–3,5] The rate of polymerisation W initiated by such compounds should not evidently depend on their functionality for the same overall concentration C of peroxy-groups in the reaction system and is described by the usual formula

$$W = k_p M (I/k_t)^{1/2}, \text{ where } I = 2fk_dC, \quad (1)$$

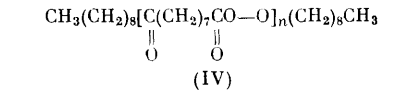
used in the traditional theory of radical polymerisation with participation of monofunctional initiators.[21] The following notation is used here and henceforth: I and f are the rate and efficiency of initiation, M is the concentration of the monomer, and k_d, k_p, and k_t are respectively the rate constants for the elementary reactions involving the decomposition of the peroxy-groups and chain propagation and termination. In conformity with the Flory principle, these constants do not change on passing from monofunctional to polyfunctional initiators, which has been confirmed in relation to the peroxides



(II)



(III)



(IV)

by the experimental data presented in Fig. 3.

In contrast to the kinetics, the traditional theory of radical polymerisation cannot be used for the calculation of the molecular weight characteristics of the polymer. Thus even the simplest formula of this theory[21]

$$P'_N = \frac{2}{1+\lambda}\nu, \text{ where } \nu = \frac{W}{I}, \ \lambda = \frac{k_{td}}{k_t}, \ k_t = k_{td} + k_{tc}, \quad (2)$$

which relates the number-average degree of polymerisation P_N of the macromolecules for the initial conversions to the length of the kinetic chains ν and also to the constants of elementary reactions

involving chain termination by the combination (k_{tc}) and the disproportionation (k_{td}) of the radicals, proves to be invalid. Contrary to Eqn. (2), the average molecular weight begins to increase from the very beginning of the polymerisation, provided that it is initiated by polyfunctional compounds.[1-3,5] This result follows naturally from the polymerisation-recombination mechanism of the formation of macromolecules (Fig. 1), because the formation in the polymer of one or two new elementary chains, depending on whether the kinetic chain is terminated by combination or disproportionation, corresponds to each effectively decomposed labile bond.

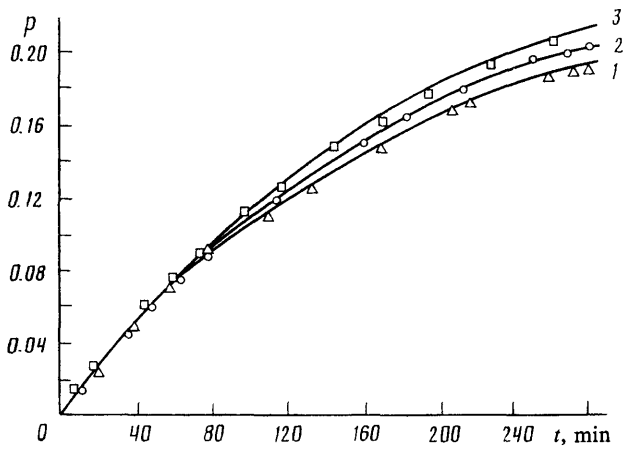


Figure 3. Kinetic curves for the polymerisation of styrene in bulk at T = 80 °C and at a peroxy-group concentration $C^0 = 2.5 \times 10^{-3}$ M for initiation by monoperoxides (curve *1*), diperoxides (curve *2*), and polyperoxides (curve *3*) containing 18 peroxy-groups.[23]

3. The superposition principle

For the calculation of the molecular weight distribution of the products of polymerisation initiated by polyperoxide, it is convenient to distinguish the macromolecules in terms of the number m of elementary chains included in them. The total number $l = l^{(1)} + l^{(2)} + \ldots + l^{(m)}$ of the monomer units in the given macromolecule will determine (neglecting the contribution of the peroxide clusters) its molecular weight. For the calculation of the numerical molecular weight distribution $f_N(l, t)$ of the polymer formed by time t, one can use the expression

$$f_N(l, t) = \sum_{m=1}^{\infty} P_m(t)\, W_m(l), \tag{3}$$

where $P_m(t)$ is the fraction of the macromolecules containing m elementary chains at time t and $W_m(l)$ is the conventional probability that the degree of polymerisation of such a macromolecule is l.

In conformity with the general ideas of the statistical chemistry of polymers, instead of the molecular weight distribution of the polymer one can use its generating function

$$G_N(s, t) = \sum_{l=1}^{\infty} f_N(l, t)\, s^l, \tag{4}$$

ich is fully equivalent to the molecular weight distribution but is more convenient in the calculation of its statistical moments.[24] These characteristics, which determine in particular, the number-average, weight-average, and z-average molecular weights of the polymer, can be calculated as the corresponding derivatives of the generating function $G_N(s)$ at the point $s = 1$. The molecular weight distribution itself can be found from Eqn. (4) by expanding $G_N(s)$ in a power series in terms of s.

For the calculation of the molecular weight distribution, it is necessary to find separately two generating functions:

$$U(x, t) = \sum_{m=1}^{\infty} P_m(t)\, x^m; \quad g(s) = \sum_{l=1}^{\infty} \varphi_l s^l. \tag{5}$$

the first of which corresponds to the distribution $P_m(t)$ of the macromolecules with respect to m elementary chains and the second corresponds to the distribution of these chains with respect to l monomer units in them. The generating function of the molecular weight distribution can then be obtained after substituting the function $g(s)$ in $U(x,t)$ instead of its argument x. One obtains as a result the important relation[23]

$$G_N(s, t) = U(g(s), t), \tag{6}$$

which represents the mathematical formulation of the principle of the superposition of the distributions φ_l and P_m.

The first of these evidently represents molecular weight distribution of the elementary chains, the length of each of which (in the given case $k_{td} = 0$) is made up of two lengths of kinetic chains. Their distribution with respect to length is described by the most probable Flory distribution whose generating function

$$g_k(s) = \frac{(1-a)s}{1-as}, \text{ where } a = 1 - 1/\nu, \tag{7}$$

is determined by the unique parameter a, which depends solely on the average length ν of the kinetic chain [see Eqn. (2)]. Evidently the distribution φ_l of the elementary chains is identical with the molecular weight distribution of the products of polymerisation under the influence of a traditional monofunctional initiator and is described by the generating function $g(s) = g_k^2(s)$. Its substitution in Eqn. (6) yields a solution of the problem of the calculation of the molecular weight distribution of polymer chains subject to the condition that the generating function $U(x, t)$ of the distribution $P_m(t)$ is known.

However, the procedure indicated is valid only in the case where the kinetic parameter ν does not vary during polymerisation as a consequence of the variation of the monomer or initiator concentrations. On the other hand, if such variation does occur then, instead of the function $g(s)$, its average value

$$\langle g(s) \rangle = \int_0^t g(s, t')\, I(t')\, dt' \Big/ \int_0^t I(t')\, dt', \tag{8}$$

should be substituted in Eqn. (6). Here the angular brackets denote averaging with respect to time of the characteristic placed between them.

When traditional monofunctional initiators are used, whereupon each polymer chain consists of one elementary chain, Eqn. (8) evidently describes the molecular weight distribution of the polymerisation products over the entire range of conversions taking into account the consumption of the monomer and initiator during the process. Such consumption may induce a broadening of the

molecular weight distribution with respect to conversion, which is undesirable for practical purposes, and which is characterised by the quantitatively appreciable increase with conversion of the polydispersity coefficient $K' = P'_W/P'_N$ which is equal, by definition, to the ratio of the weight-average and number-average degrees of polymerisation. Eqns. (7) and (8) make it possible to obtain simple formulae for these statistical characteristics:

$$P'_N = 2\langle\nu\rangle, \quad K' = \frac{3\langle\nu^2\rangle}{2\langle\nu\rangle^2}. \tag{9}$$

The effect of the conversion-induced broadening of the MWD indicated can be appreciably diminished if the polymerisation is carried out in the presence of polyperoxides containing a sufficient number of functional groups. This fundamental conclusion follows directly from the general expressions

$$P_N = P'_N P''_N, \quad K = K'' + \frac{(K'-1)}{P'_N}, \tag{10}$$

which can be derived simply from the superposition principle (6) (formulated above) taking into account Eqn. (8). According to Eqn. (10), the molecular weight and the polydispersity coefficient of the polymer obtained depend on similar characteristics: both on the distribution with respect to the lengths of the elementary chains [Eqns. (9)] and on the distribution P_m of the macromolecules with respect to the number m of such chains. The average value $P''_N = \overline{m}$ of this random quantity, which is identical at the end of the polymerisation with the average number of the effectively decomposed labile bonds in the polyperoxide molecule, can be fairly large when the functionality of the polyperoxide is high. In the latter case, the transition from monofunctional to polyfunctional initiators should be accompanied by an appreciable (by the factor P''_N) increase in the average molecular weight and by the simultaneous narrowing of the molecular weight distribution. For sufficiently large values of P''_N, when it is possible to neglect the second term in Eqn. (10) for K compared with the first, the use of polyperoxides makes it possible to suppress completely the conversion factor for the non-uniformity of the molecular weight distribution. The latter can be determined in this case only by the polydispersity coefficient K'' of the distribution P_m, which, as will be seen from the discussion below, is usually not unduly great.

We shall now consider how the superposition principle can be extended to the polymerisation reactions of monomers of the type of methyl methacrylate in which the fraction of the radicals [λ in Eqn. (2)] losing their activity via the disproportionation mechanism is non-zero. As a result of the elementary kinetic chain termination step via this mechanism, the macromolecules lose their activity, being converted into macro-initiator molecules with formation of an additional elementary chain at the end of each of them. However, in contrast to chain termination via combination, its length is equal to the length of not two but only one kinetic chain. Consequently the following formula constitutes an extension of Eqn. (6):

$$G_N(s, t) = U(\langle g_k^2(s)\rangle, \langle g_k(s)\rangle; t), \tag{11}$$

where $U(x, y; t)$ is the generating function of the joint distribution of polymer chains with respect to m and i elementary chains formed respectively by the combination and disproportionation of the radicals. It is easy to obtain from Eqn. (11) a relation, analogous to Eqn. (10), containing the quantities

$$P'_N = \frac{2\langle\nu\rangle}{1+\lambda}; \qquad K' = \frac{(\lambda+1)(3-\lambda)}{2}\frac{\langle\nu^2\rangle}{\langle\nu\rangle^2}. \tag{12}$$

Naturally, with increase in λ, the efficiency of the formation of polyinitiators falls as a consequence of the decrease in the fraction of the combination steps leading to the strengthening of the polymer chains. In order to estimate this effect quantitatively, it is sufficient to find from Eqn. (11) the generating function $U(x, y; t)$.

4. Polyinitiators with labile groups of one type

According to the superposition principle described above, in order to calculate the molecular weight distribution in the case of chain termination via combination, it is sufficient to find the generating function $U(x, t)$ of the distribution $P_m(t)$ of macromolecules with respect to m elementary chains. In order to find $U(x, t)$, the corresponding system of kinetic equations was formulated[23] for this distribution and its exact solution was found. According to the latter, for any initial distribution α_j of polyperoxide molecules with respect to j peroxy-groups, the distribution P_m has the generating function

$$U(x,t) = \frac{(1-\rho)x}{1-\rho x}, \quad P_m = (1-\rho)\rho^{m-1}. \tag{13}$$

The form of the α_j distribution affects only the nature of the time variation of the single parameter ρ:

$$\rho(t) = 1 - \sum_j a_j[1-(1-\theta)^j]\Big/\theta\sum_j ja_j,$$
$$\text{where } \theta = f(1-e^{-\tau}), \quad \tau = k_d t. \tag{14}$$

In the case of function (13), the superposition principle (10) leads to a simple expression for the molecular weight distribution when account is taken of Eqn. (7):

$$f_N(l,t) = \frac{(1-\rho)}{2\sqrt{\rho}}(1-a)\{[a+(1-a)\sqrt{\rho}]^{l-1} -$$
$$-[a-(1-a)\sqrt{\rho}]^{l-1}\}. \tag{15}$$

It is evidently unimodal. The use of Eqns. (10) makes it possible to obtain from Eqn. (13) the formulae

$$P_N = P'_N(1-\rho)^{-1} \text{ and } K = (1-\rho)K' + 2\rho, \tag{16}$$

which are valid over the entire range of conversions when account is taken of Eqn. (9).

According to the first of these formulae, the molecular weight increases during the process from P'_N, obtained when the monoperoxide is used, to a maximum value P_N^{max} which depends on the distribution, α_j, of the peroxy-groups in the polyperoxide molecules and on the efficiency of the initiator f. In the case of polyinitiators with a fairly high functionality, the theory predicts a linear dependence of the molecular weight of the polymer on the conversion over a wide range of the latter. Under these conditions, the slope of the straight line is proportional to the functionality of the polyinitiator, in conformity with Eqns. (14) and (16). These theoretical predictions are satisfactorily confirmed by the experimental data presented in Fig. 4.

An extension of Eqn. (13), taking into account the possibility of chain termination via disproportionation, has been obtained[23] with the aid of the kinetic approach:

$$U(x,y;t) = \frac{V(x,y;t)}{V(1,1;t)}, \quad V(x,y;t) = \frac{(1+dy)^2}{1-b^2x} - 1,$$
$$\text{where } d = \lambda\rho(1-\rho)^{-1}, \quad b^2 = (1-\lambda)\rho. \tag{17}$$

In the case where the length of the kinetic chain ν is large and

constant, the superposition principle (11) makes it possible to find from Eqn. (17) the following expression for the molecular weight distribution of the polymer:

$$f_N(l, t) = \frac{1 - b^2}{2b(d^2 + b^2 + 2d)}\{(d + b)^2 e^{-l/(1-b)\nu} - (d - b)^2 e^{-l/(1+b)\nu}\}, \quad (18)$$

which, like the molecular weight distribution defined by Eqn. (15), is unimodal.

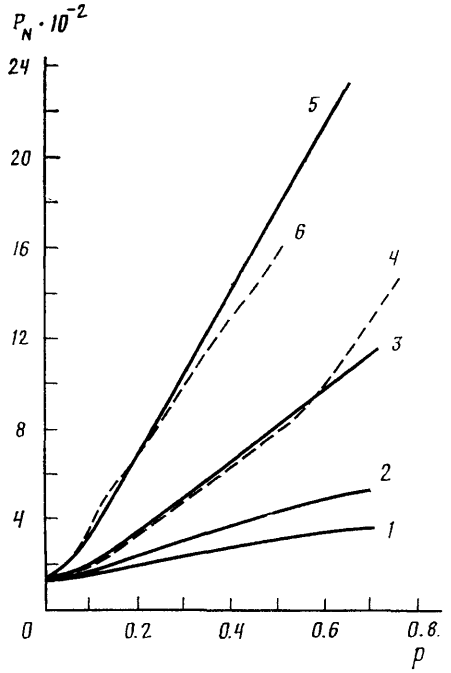


Figure 4. Variation of the number-average molecular weight of polystyrene with conversion in the polymerisation of styrene in bulk in the presence of oligoperoxides with different average numbers of groups; number of groups: *1*, 1; *2*, 2; *3*, and *4*, 4.6; *5*, and *6*, 10.7. Continuous lines—theoretical data; dashed lines—experimental data.[12]

The following formulae serve as extensions of Eqns. (16):

$$P_N = \frac{\lambda + 1}{\lambda + 1 - \rho} P'_N,$$

$$K = \frac{\lambda + 1 - \rho}{\lambda + 1} K' + \frac{(2 - \lambda)^2 \rho (\lambda + 1 - \rho)}{2(1 - \rho + \lambda\rho)}. \quad (19)$$

They demonstrate to what extent the disproportionation reaction eliminates all the advantages of employing polyfunctional initiators. Indeed, regardless of the type of the latter and the kinetic polymerisation parameters, it is impossible, according to Eqns. (19), to increase the molecular weight of the polymer (compared with that which is obtained under the same conditions using the usual monoperoxide) by a factor greater than $(\lambda + 1)/\lambda$. For example, in the polymerisation of methyl methacrylate, where λ is close to 0.5, this factor is close to 3. In such systems, the transition from monoinitiators to polyinitiators is much less effective, as follows from the second Eqn. (19), for the restriction of the increase in the conversion-induced non-uniformity of the polymerisation products. The above factor is one of the fundamental disadvantages of the use of polyperoxides in practice.

5. Polyinitiators with labile groups of several types

The use of polyperoxides containing peroxy-groups with different thermal stabilities leads to extensive possibilities for the molecular design of polymers.[1-6] Under these conditions, questions concerning the dependence of their statistical characteristics on the functionality, composition, and structure of the initial initiating compounds arise. The answers to these questions are provided by the quantitative theory, developed by Ivanov et al.,[31] some of the main results of which are presented below.

The general formulae (3)–(10) for the calculation of the molecular weight and the molecular weight distribution remain valid also on passing to polyinitiators with several types of peroxy-groups. However, the forms of the distribution functions $P_m(p)$ of the macromolecules with respect to m elementary chains are naturally different. In order to find this distribution, it is very convenient to employ a statistical approach according to which any arbitrarily selected macromolecule in the reaction system can be regarded as the realisation of a random process involving conventional motion along the macromolecule.[21,24] It is found that such a random process, describing the products of the homopolymerisation initiated by arbitrary polyperoxides with independent groups, may be a Markov chain. This result is valid for any number r of types of labile groups regardless of the way in which they are distributed among the molecules of the initial polyperoxide. The nature of the distribution will influence only the statistical parameters of the Markov chain; the matrix $\mathbf{Q}$ (with the elements ν_{ij}) of the transitional probabilities and the vector $\vec{v}$ (with the components v_i) of the initial states. In the case considered, the following expression is an extension of Eqn. (13):

$$U(x, t) = \sum_{i=1}^{r} \sum_{j=1}^{r} v_1 x [(\mathbf{E} - \tilde{\mathbf{Q}}x)^{-1}]_{ij} \nu_{j0}, \quad (20)$$

where $\mathbf{E}$ is a unit matrix (with the elements δ_{ij}), $\tilde{\mathbf{Q}}$ the matrix of the transitions (with the elements ν_{ij}, $i \neq 0, j \neq 0$) between r non-return states, and ν_{j0} the probability of the transition from such a jth state to the zeroth state, which is absorbing.

All the parameters of the Markov chain in Eqn. (20) are expressed in terms of the kinetic structural parameters of the initial polyinitiator. The former include the decomposition constants k_{di} and the efficiences of the initiation f_i ($i = 1, \ldots, r$) by all types of peroxy-groups, while the latter include the fractions of the chemically individual polyperoxide molecules with a fixed set of numbers of groups of all types and the order in which they alternate.

The structure of the macromolecules in the given case is similar to that illustrated in Fig. 3 with the sole difference that the peroxide clusters can now consist of groups of different types. In the statistical approach, it is convenient to distinguish (to differentiate arbitrarily) the radicals, elementary chains, and clusters as a function of the mode of their formation. Thus, in the effective decomposition of an ith type labile group, a pair of macroradicals is formed to which the same type i is attributed. Each step involving the recombination of two such macroradicals of types i and j leads to the formation of the elementary chain (ij). The peroxide clusters can

be differentiated in accordance with the same principle in terms of their types as a function of the type of radicals which were formed at one time at the ends of the given cluster. Consequently the elementary chain (ij) is connected to the chain (kl) by a closed cluster of type (jk), while a semiopen cluster of type $(j0)$ or $(0j)$, containing the 0, 1...peroxy-groups, connects the elementary chain to the end or start of the macromolecule. The molecules of the initial polyperoxide are included among the open clusters.

The concentrations N_{ij} of the peroxide clusters of different types (ij) as well as the rates I_i of generation of macroradicals of types $i = 1, ..., r$, i.e.

$$I_i = 2f_i k_{di} C_i, \quad C_i = C_i^0 \exp(-k_{di} t), \quad I = \sum_{i=1}^{r} I_i , \tag{21}$$

are determined by the elements ρ_{ik} and ρ_{kj} of the matrices $\boldsymbol{\rho}$ and $\boldsymbol{\sigma}$:

$$\rho_{ik} = N_{ik} \Big/ \sum_{k=0}^{r} N_{ik} \; (i, k = 1, \ldots r), \quad \rho_{i0} = N_{i0} \Big/ \sum_{k=0}^{r} N_{ik}; \tag{22}$$

$$\sigma_{kj} = \int_0^t \frac{I_k I_j}{I} \, dt' \Big/ \int_0^t I_k dt', \quad \rho_{0k} = N_{0k} \Big/ \sum_{k=1}^{r} N_{0k}, \tag{23}$$

in terms of which all the parameters of the Markov chain in Eqn. (20) are expressed simply by means of the formulae

$$\nu_{ij} = \sum_{k=1}^{r} \rho_{ik} \sigma_{kj} \; (i, j = 1, \ldots r), \quad \nu_{i0} = \rho_{i0} \tag{24}$$

$$v_i = \sum_{k=1}^{r} \rho_{0k} \sigma_{ki} \; . \tag{25}$$

The overall concentration of the polymer molecules Π is equal to the difference between the initial I^0 and current $I(t)$ concentrations of the initiator molecules:

$$\Pi = I^0 - I(t) = I^0 \left[1 - \sum_{\vec{j}} \alpha(\vec{j}) \prod_{i=1}^{r} (1 - \theta_i)^{j_i} \right], \tag{26}$$

where $\alpha(\vec{j})$ is the fraction of the molecules of the initial polyperoxide having a functionality vector $\vec{j}$ with the components $\{j_1, ..., j_i, ..., j_r\}$ equal to the numbers of functional groups of each type. The quantities

$$\theta_i = f_i [1 - \exp(-k_{di} t)] \quad (i = 1 \ldots, r), \tag{27}$$

have the significance of the probability that an arbitrarily selected peroxy-group of the ith type decomposes effectivey at time t.

All the formulae in subsection 3 are valid in the general case considered. Thus the average number of elementary chains in the macromolecule

$$P_N'' = \sum_{i=1}^{r} \sum_{j=1}^{r} v_i [(\mathbf{E} - \tilde{\mathbf{Q}})^{-1}]_{ij} = \sum_{i=1}^{r} C_i^0 \theta_i / \Pi, \tag{28}$$

and hence, according to Eqn. (10), also the number-average molecular weight of the polymer are independent, for the given $\alpha(\vec{j})$ distribution, of the sequence of the peroxy-groups of different types in the polyinitiator molecules. However, the microstructure of the polyperoxide nevertheless exerts an influence on the form of the molecular weight distribution and the degree of its polydispersity K [Eqn. (10)], as follows from the formula

$$K'' = 1 + \sum_{i=1}^{r} \sum_{j=1}^{r} v_i [(\mathbf{E} - \tilde{\mathbf{Q}})^{-2} \tilde{\mathbf{Q}}]_{ij} \Big/ \left\{ \sum_{i=1}^{r} \sum_{j=1}^{r} v_i [(\mathbf{E} - \tilde{\mathbf{Q}})^{-1}]_{ij} \right\}^2 . \tag{29}$$

In the simplest and experimentally most thoroughly investigated case of initiators with two types of peroxy-groups, the general formula (20) reduces to the form

$$U(x, t) = \frac{x(b_1 + b_2 x)}{1 - d_1 x + d_2 x^2}, \tag{30}$$

where

$$b_1 = v_1 \nu_{10} + v_2 \nu_{20}, \quad b_2 = v_1 (\nu_{12} \nu_{20} - \nu_{22} \nu_{10}) + v_2 (\nu_{21} \nu_{10} - \nu_{11} \nu_{20})$$
$$d_1 = \nu_{11} + \nu_{22}, \quad d_2 = \nu_{11} \nu_{22} - \nu_{12} \nu_{21} . \tag{31}$$

When the conditions $b_2 < 0$ and $d_2 > 0$ hold, analysis of Eqn. (30) predicts the possibility of the appearance in the initial polymerisation stage of a bimodal molecular weight distribution, which may then become unimodal as the degree of conversion increases. This nature of the evolution of the molecular weight distribution was in fact observed in certain experiments[5,8,11,12] when the process was initiated by peroxide with two types of labile groups having different thermal stabilities. The polydispersity coefficient K can be easily calculated by Eqn. (10) because Eqn. (29) reduces to the simple form

$$K'' = \frac{4(1 - d_2) - (b_1 + d_1)(3 - d_1 - d_2)}{(2 - b_1 - d_1)^2} \tag{32}$$

when $r = 2$.

In order to find with the aid of the generating function (30) the molecular weight distribution or the polydispersity coefficients (10) and (32), it is necessary to find beforehand with the aid of Eqn. (31) the parameters of the Markov chain, which are fully defined, according to Eqns. (24) and (25), by the matrices $\boldsymbol{\rho}$ and $\boldsymbol{\sigma}$. Their elements can be calculated by Eqns. (22) and (23) provided that the concentrations N_{ik} of the different clusters (ik) are known. Several ways of finding the concentrations N_{ij} for different types of initial polyperoxides have been proposed.[31] The polyperoxides can be both individual chemical compounds and mixtures of molecules differing in the number of peroxy-groups of different types (composition) and their sequence (structure).

Examination of such mixtures is of practical importance because oligomeric initiators are usually synthesised by the polycondensation method.[1-6] As a consequence of the random character of its reactions, the products of this process naturally have a distribution with respect to composition and structure. The latter has been described in many cases[24] by a Markov chain whose non-return states are peroxy-groups of r types and the zeroth absorbing state corresponding to going outside the limits of the molecule. If the matrix of the transition probabilities between the non-return states of this Markov chain is denoted by $\tilde{\mathbf{Q}}^0$ and its initial vector is denoted by $\overleftarrow{v}^0$, when the matrix ρ can be written in the form

$$\boldsymbol{\rho} = [\mathbf{E} - \tilde{\mathbf{Q}}^0 (\mathbf{E} - \mathbf{D})]^{-1} \tilde{\mathbf{Q}}^0 \mathbf{D}, \tag{33}$$

where **D** is a diagonal matrix with the elements $\theta_i\delta_{ij}$. Other parameters in Eqns. (22) and (23) are defined similarly:

$$\rho_{i0} = \sum_{j=1}^{r} \{[\mathbf{E} - \tilde{\mathbf{Q}}^0(\mathbf{E} - \mathbf{D})]^{-1}\}_{ij} v_{j0}^0, \tag{34}$$

$$\rho_{0i} = \frac{I^0}{\Pi} \sum_{j=1}^{r} v_j^0[\theta_j\delta_{ji} + (1-\theta_j)\rho_{ji}], \tag{35}$$

$$\Pi = I^0 - I(t) = I^0\left[1 - \sum_{i=1}^{r} v_i^0(1-\theta_i)\rho_{i0}\right]. \tag{36}$$

Together with Eqns. (10) and (28), Eqns. (34) and (36) provide an exhaustive solution of the problem of the calculation of the number-average molecular weights of the products of polymerisation initiated by polyperoxides with Markov statistics of the sequence of labile groups of different types in them.

The possibility of using a statistical approach to the calculation of the molecular weight distribution of the polyperoxide-initiated polymerisation products is associated with the independent decomposition of all their labile groups. This factor serves as yet another illustration of Flory's idea,[21] which is of general importance for the chemistry of polymers. In the spirit of this idea, the molecular weight distribution functions depend on time only in terms of probability parameters, which in the systems examined here are the elements σ_{kj} [see Eqn. (23)] of the matrix σ and the components θ_i see Eqn. (27) of the vector $\vec{\theta}$.

Rigorous kinetic examination shows that the formulae derived by the statistical method retain their form in systems where the temperature varies during polymerisation. However, the time variation of the probability parameters in these formulae is determined by expressions more general than in the case of an isothermal process. Such an expression, which is an extension of Eqn. (27), is

$$\theta_i(t) = \int_0^t f_i(t')\, k_{di}(t') \exp\left[-\int_0^{t'} k_{di}(t'')\, dt''\right] dt', \tag{37}$$

while in the calculation of the quantities σ_{kj} [see Eqn. (23)], one should take into account the time variation of the kinetic parameters f_i and k_{di} in the functions I_i [Eqn. (21)]. The above explanations make it possible to embrace by the theory described above the polymerisation processes occurring in practice with a programmed increase in temperature, which have a number of advantages compared with isothermal processes.[5]

6. Synthesis of block copolymers

Polymerisation processes with participation of polyinitiators having two types of groups with markedly different thermal stabilities are apparently of greatest practical interest. Such polyperoxides are characterised by decomposition constants $k_{d1} \gg k_{d2}$, which makes it possible to carry out the polymerisation in two stages. In the first stage, carried out at a specific temperature, virtually only the more labile peroxy-groups of the first type decompose with formation of polymer molecules containing peroxide clusters comprising the groups of the second type in the main chain, which are capable of further reactions. After raising the temperature in the polymerisation system, the process goes over to the second stage, during which the less labile groups of the second type are decomposed which is accompanied by the growth of the macroradicals formed and their subsequent recombination. If the monomer is replaced at the end of the first stage, then molecules containing blocks of different monomers are formed during the second stage. This method of synthesis of block-copolymers is extremely simple and promising.[13–15,25–30]

The change in the composition and structure of polyperoxide makes it possible to influence the architecture and statistical characteristics of the block-copolymers formed. In the simplest case, it is possible to select as the initiator an asymmetric diperoxide of the type of, for example, compound (I) with an appropriate substituent R ensuring a sufficient difference between the thermal stabilities of the two peroxy-groups. In particular, the use of a boron atom as R leads to a difference between the decomposition constants k_{d1} and k_{d2} for these groups differing by a factor greater than 20,[12] which guarantees the possibility of carrying out the two-stage synthesis of a block copolymer with participation of the initiator.

The formation during the synthesis of homopolymer molecules as side products in both stages is a disadvantage in this case. It can be eliminated in the first stage by going over from diperoxides to symmetrical triperoxides which contain two identical groups of the first type separated by a central, more stable group of the second type.[10,32] In order to reduce to a minimum the formation of the homopolymer also in the second stage of the process, it is necessary to carry it out in the presence of a polyperoxide with the highest possible functionality and it is desirable to have alternating groups of both types. The latter factor promotes an increase in the uniformity of the compositions of the copolymerisation product, because it ensures a regular alternation in the latter of macromolecular blocks each of which consists in the given instance of a single elementary chain.

In the general case of an arbitrary polyperoxide, selected by guesswork, the block of monomer ith type units in the molecule of the block-copolymer can consist of any number n of elementary chains of the corresponding monomer. The random quantity n has the distribution function $(1-\rho_{ii})\rho_{ii}^{n-1}$, so that the average number of elementary chains in one block is $(1-\rho_{ii})^{-1}$. The distribution of the blocks of the ith monomer with respect to lengths is described by Eqn. (7) and by Eqn. (15) for a constant length ν of the kinetic chain, but in the latter equation ρ must be replaced by ρ_{ii}.

The superposition principle, in a somewhat more general formulation, can also be used for the calculation of the distribution of the block-copolymer with respect to composition. In contrast to the homopolymer, the macromolecules of a binary block-copolymer are characterised by the composition vector $\vec{l}$ (instead of the degree of polymerisation l), whose components l_1 and l_2 are equal to the numbers of monomer units of the first and second type. The corresponding type of elementary homopolymer chain corresponds to each of these types, and the numbers m_1 and m_2 of such chains in the macromolecule can also be regarded as components of the vector $\vec{m}$. When such notation is used, the principal relations (3)–(6) of the superposition principle retain their significance if one goes over in them from the scalar variables l and m to the vector variables $\vec{l}$ and $\vec{m}$. As a result of this, it is sufficient to find a generating function $U(\vec{x}, t)$ of the distribution of polymer chains with respect to the vector $\vec{m}$ characterising them. The solution of the given problem leads to the following expression for this function $U(x_1, x_2)$:[31]

$$\frac{\rho_{01}\rho_{10}x_1 + \rho_{02}\rho_{20}x_2 + (\rho_{01}\rho_{12}\rho_{20} + \rho_{02}\rho_{21}\rho_{10} - \rho_{01}\rho_{22}\rho_{10} - \rho_{02}\rho_{11}\rho_{20})x_1x_2}{1 - \rho_{11}x_1 - \rho_{22}x_2 + (\rho_{11}\rho_{22} - \rho_{12}\rho_{21})x_1x_2}. \tag{38}$$

The subsequent substitution in this formula, instead of x_1 and x_2, of the generating functions $<g_1(s_1)>$ and $<g_2(s_2)>$ of the distributions with respect to the lengths of the elementary chains of each of the two types yields an expression for the generating function $G_N(\vec{s})$ for the required distribution $f_N(\vec{l}, t)$.

The average number $\overline{m}_1$ and $\overline{m}_2$ of the elementary chains of both types per polymer molecule can be calculated simply from Eqn. (38):

$$\frac{\overline{m}_1}{\Pi}=\frac{\rho_{12}+(\rho_{11}+\rho_{21})\rho_{10}}{\rho_{12}\rho_{20}+\rho_{21}\rho_{10}+\rho_{10}\rho_{20}},\quad \frac{\overline{m}_2}{\Pi}=\frac{\rho_{21}+(\rho_{22}+\rho_{12})\rho_{20}}{\rho_{12}\rho_{20}+\rho_{21}\rho_{10}+\rho_{10}\rho_{20}}. \quad (39)$$

They define the average composition of the block-copolymer:

$$\langle\zeta_i\rangle=\langle\nu_i\rangle\overline{m}_i/(\langle\nu_1\rangle\overline{m}_1+\langle\nu_2\rangle\overline{m}_2)\quad (i=1, 2). \quad (40)$$

where $2<\nu_1>$ is the average length of the elementary chain of the i-th type.

The quantities e_1 and e_2, equal to the fractions of the monomer units of each type forming part of the composition of the homopolymers formed during the synthesis as side products, are important process characteristics. Theory yields simple expressions for these quantities:

$$e_i=\Pi\rho_{0i}\rho_{i0}/C_i^0\theta_i(1-\rho_{ii})^2\quad (i=1, 2), \quad (41)$$

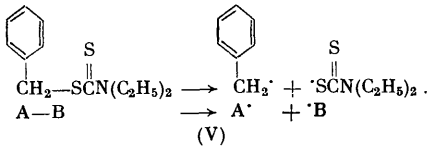
They are suitable for the estimation of the efficiency of the practical employment of various polyinitiators in the synthesis of block copolymers.

III. Iniferters

1. Introduction

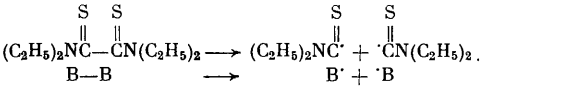
The term "iniferters", proposed first by Otsu and co-workers,[33] is a result of the combination of three words: *Ini*tiator–Trans*fer* agent–*Ter*minator. A characteristic feature of an iniferter is that it participates in all three reactions mentioned above: initiation, chain transfer, and chain termination. Certain features of the polymerisation of monomers such as styrene, methyl methacrylate, methyl acrylate, etc. in the presence of a whole series of such compounds have now been investigated. Among them, mention may be made of various phenylazomethanes, dithiocarbamates, disulphides, etc.[33–50] The studies by Japanese workers and especially those by Otsu and co-workers,[33,34,36,41–52] who discovered a series of characteristics of the polymerisation with participation of iniferters, are outstanding among these investigations. The extensive possibilities of the use of these compounds for the molecular design of polymers synthesised has also been demonstrated.[42,44,45,50–52]

A common feature of all iniferters, regardless of their structure, is the presence in their molecules of labile interatomic bonds capable of decomposing under the conditions of the synthesis with formation of a pair of primary radicals at least one of which is not converted into the polymeric radical although it does participate in chain termination reactions. *S*-Benzyl-*N*,*N*-diethyldithiocarbamate can be quoted as an example of an iniferter:



(V)

It has been used to initiate the photopolymerisation of styrene.[49,55–57] The decomposition of a molecule of this initiator affords two primary radicals, A (benzyl) and B (dithiocarbamyl), with appreciably different chemical reactivities. The primary active radical A is capable of further growth after the addition of the monomer to it, while the second primary radical B hardly reacts with the monomer under the conditions of the synthesis as a consequence of its unduly low reactivity. Apart from such asymmetric compounds, there exist also symmetrical iniferters of the type of tetraethylthiuram disulphide:



(VI)

On decomposition, they afford two identical inactive radicals B. Together with the recombination of radicals of this type with one another at a fairly low concentration, they can combine with the monomer and can thus initiate polymerisation. Depending on what is the main cause responsible for the decomposition of the labile bond, thermo- and photo-iniferters are distinguished. The ability of various chemical compounds to function as iniferters of each of these types has been discussed in a review by Australian workers.[59]

2. The mechanism and kinetics of polymerisation

During the process with participation of an iniferter, polymer chains containing a fairly labile bond at the end are formed. Subsequently each of these bonds can break down under the influence of heat or light with formation of a macroradical and a small radical B, incapable of initiating a new polymer chain. On the other hand, after the addition of a certain number of monomer species, the macroradical recombines with the stable radical B and is converted into a polymeric macroiniferter molecule. The latter decomposes again into a pair of radicals differing significantly in their reactivity, and so on. In conformity with this picture of stepwise polymerisation, each polymer chain exists in succession in two states: the live state (as a macroradical) and the dead state (as a macromolecule). Since the polymer chain lives for a very short time, compared with its inactive state, one can assume that it grows in separate steps. In each such step, the molecular weight increases exactly by one length of the elementary chain.

The characteristic features of the mechanism of radical polymerisation in the presence of iniferters can be understood by resorting to the general kinetic scheme for this process, which assumes the following form, for example, in the case of an asymmetric iniferter I of type (V):

$$\begin{aligned}
&(a)\ \mathrm{I}\xrightarrow{k_d'}\mathrm{A}+\mathrm{B}\ \text{chain initiation}\\
&\left.\begin{aligned}(b)\ &\mathrm{A}+\mathrm{M}\xrightarrow{k_{pA}'}\mathrm{R}(1)\\ (c)\ &\mathrm{R}(l)+\mathrm{M}\xrightarrow{k_p}\mathrm{R}(l+1)\end{aligned}\right\}\text{chain propagation}\\
&\left.\begin{aligned}(d)\ &\mathrm{R}(l)+\mathrm{R}(n)\xrightarrow{k_{tc}}\mathrm{P}(l+n)\\ (e)\ &\mathrm{R}(l)+\mathrm{R}(n)\xrightarrow{k_{td}}\mathrm{P}(l)+\mathrm{P}(n)\\ (f)\ &\mathrm{R}(l)+\mathrm{B}\xrightarrow{k_t'}\mathrm{P}(l)\mathrm{B}\\ (g)\ &\mathrm{B}+\mathrm{B}\xrightarrow{k_t''}\mathrm{BB}\end{aligned}\right\}\text{chain termination}\\
&\left.\begin{aligned}(h)\ &\mathrm{R}(l)+\mathrm{I}\xrightarrow{k_t}\mathrm{P}(l)\mathrm{B}+\mathrm{A}\\ (i)\ &\mathrm{R}(l)+P(n)\,\mathrm{B}\xrightarrow{k_{PB}}\mathrm{P}(l)\,\mathrm{B}+\mathrm{R}(n)\end{aligned}\right\}\text{chain transfer}\\
&(j)\ \mathrm{P}(l)\,\mathrm{B}\xrightarrow{k_d}\mathrm{R}(l)+\mathrm{B}\qquad\text{chain reinitiation}.
\end{aligned}\quad (42)$$

Apart from the usual reactions of traditional radical polymerisation, this scheme includes the reinitiation reaction (*j*), which constitutes the main feature of the process considered. A second important feature of the process is that the chain termination in it is effected solely by reaction (*f*) via the recombination of the polymeric and inactive primary radicals.

Indeed, rigorous analysis of the kinetic equations correpsonding to Scheme (42) has shown[55] that the chain termination reactions (*d*), (*e*), and (*g*) can be frequently neglected compared with reaction (*f*). The condition for such neglect is a sufficiently high value of the dimensionless parameter $\Phi = k'_t(k_t k''_t)^{-1/2}$, which depends solely on the elementary chain termination constants. This condition is always fulfilled, because the above constants for diffusion-controlled reactions are linked, in terms of order of magnitude, by the relations $k''_t \sim k'_t \sim (10^2-10^3)k_t$.

The theoretical expressions for the rate of polymerisation under the influence of iniferters,[55] i.e.

$$W = k_p M\sqrt{I/k_t^e}, \text{ where } k_t^e = k_t\Phi, \qquad (43)$$

have the same form as for traditional polymerisation. The only difference is the replacement of the usual termination rate constant k_t by its effective value k_t^e. The ratio of the latter to the former is equal to Φ and therefore even for the same rate of initiation I the use of iniferters retards the rate of polymerisation by more than an order of magnitude compared with the usual initiators.

The systems in which the rate constant k_d for the breakdown of the terminal labile bond in the molecule is independent of its length and is identical with the constant k'_d for the decomposition of the iniferter are simplest. For ideal systems, where the familiar Flory principle[21] holds for all the elementary reactions, the reduced rate of polymerisation

$$W/M = k_p\sqrt{k_d C^0/k_t^e}, \quad I = k_d C^0 \qquad (44)$$

is constant and proportional to the square root of the initial iniferter concentration C_I^0.

Together with ideal systems, where this condition holds,[41,47] a considerable number of monomer + iniferter pairs have been observed experimentally for which the rate of polymerisation varies from the very beginning of the process.[41,42,44] A typical form of the kinetic curve for such non-ideal systems is illustrated in Fig. 5. It shows that in the initial stage of the conversion, the rate of its change diminishes, starting from an initial value W_0, gradually attaining a stationary value W_S.

In order to account for this form of the kinetic curve, the hypothesis of the possible breakdown of the Flory principle in the polymerisation initiation reactions with participation of certain iniferters was put forward and justified experimentally.[55] For this purpose, the rate of decomposition of the terminal labile groups within narrow fractions of macroiniferters of different molecular weight, obtained in the course of the photopolymerisation of styrene in the presence of compound (V), was measured by the spin trapping method.[55–57] The results of this experiment, presented in Fig. 6, demonstrate a fairly sharp decrease in the reinitiation rate constant k_d with increase in the number of units l of the oligoiniferters up to a certain limiting value k_d for values of l exceeding ~100 units. After the attainment during the polymerisation process of P_N close to 100, the rate of polymerisation actually attains a constant value, in full agreement with Eqn. (43). The latter predicts also a proportionality between the initial (W_0) and stationary (W_S) rates of polymerisation and the square root of the concentration of iniferters. This conclusion was confirmed experimentally[55–57] in relation to the photopolymerisation of styrene in the presence of the iniferter (V) over a wide range of concentrations of the latter. Furthermore, it was found that the observed experimental ratio W_0/W_S is virtually constant in this range and equal to approximately three. This in fact agrees with the theoretical predictions, if one takes into account the dependence of the rate constants k_d for the decomposition of macroiniferters on their length illustrated in Fig. 6.

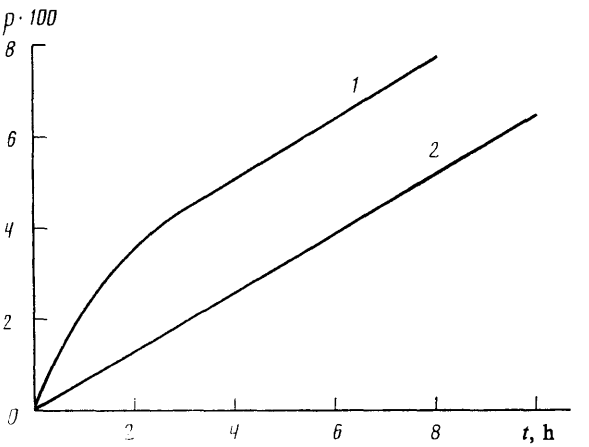


Figure 5. Kinetic curves for the photopolymerisation of styrene in solution in benzene in the presence of the iniferter (II) (curve *1*) and the macroiniferter (curve *2*) containing about 170 styrene units.[55–57]

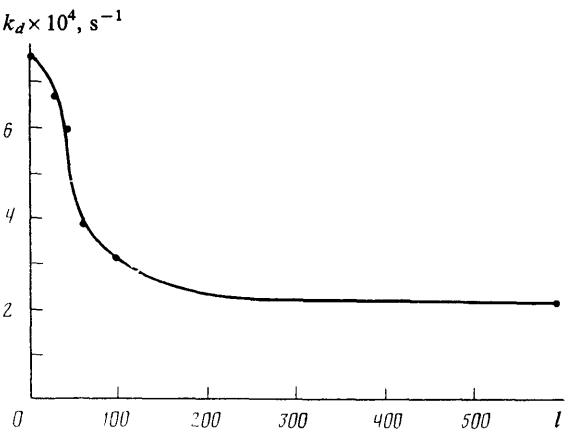


Figure 6. Dependence of the rate constant for the decomposition of the labile bond in the macroiniferter (oligostyrene with a terminal thiocarbamate group) molecule on the degree of polymerisation of the latter.[55–57]

Since this dependence in the given system is important only for macroiniferters whose length is less than 100 units, in the case of the initiation and polymerisation by higher-molecular-weight homologues

one may expect a constant rate of polymerisation W from the very beginning of the process. Furthermore, this value of W should agree with the stationary rate of polymerisation W_S carried out under the same conditions in the presence of the low-molecular-weight iniferter (V). Indeed, the experimental kinetic curve *2* in Fig. 5 fully confirms these theoretical conclusions.

The very fact that there is virtualy no chain termination via the interaction of polymeric radicals with one another during polymerisation in the presence of the iniferter leads to interesting conclusions concerning the kinetics of certain extremely important industrial processes. These include the polymerisation of vinyl monomers in bulk, which is of great interest in the manufacture of plastics and especially organic glasses. During such processes, a sharp increase in the rate of polymerisation is usually observed in the region of moderate conversions, which can exceed by several tens its initial value. This phenomenon, referred to as the "gel effect", is extremely undesirable in the planning of industrial manufacturing processes, because it induces overheating in the reaction system and the impairment of the operating parameters of the polymer.

The cause of the "gel effect" is the appreciable decrease in the rate constants k_t for reaction (*d*) and (*e*) in Scheme (42) associated with the significant retardation of the mutual diffusion of the macroradicals when the solution becomes concentrated as a result of the conversion of the monomer into the polymer. Since in the course of polymerisation with participation of an iniferter these chain termination reactions do not play a significant role, there is every reason to expect the absence of the "gel effect" in such processes. This theoretical conclusion was convincingly confirmed[58] in the bulk polymerisation of styrene and methylmethacrylate in the presence of *N,N,N',N'*-tetraethylthiuram disulphide as the iniferter.

In conclusion of this section, it is natural to formulate the quantitative conditions for the applicability of the iniferter mechanism of radical polymerisation decribed above. Here it is most important to answer the question whether or not a specific initiator will manifest the properties of an iniferter. This depends both on the occurrence of the reinitiation reaction and on the choice of the reaction pathway for the less reactive of the two primary radicals formed on decomposition of the initiator molecule.

This primary radical B has two possibilities of reacting—either with the monomer M or with the polymeric radical R. The predominance of one of these reactions depends on the relation between their probabilities $\mathscr{P}_a = k_{pB}\mathrm{M}$ and $\mathscr{P}_t = k'_o\mathrm{R}$. Evidently, if the activation reaction of the primary radical B predominates, the traditional radical polymerisation occurs. Otherwise, when $\mathscr{P}_a \ll \mathscr{P}_t$, whereupon the chain termination reaction becomes dominant for B, iniferter polymerisation takes place. The range of rates of polymerisation corresponding to this is wider the greater the ratio $k'_{pA}k'_{pB}$ of the rate constants for the addition of the monomer to the active (A) and inactive (B) primary radicals. Only for a sufficiently large difference between the reactivities can the following inequalities hold:

$$1 \ll \frac{W}{W^*} \ll \frac{k'_{pA}}{k'_{pB}}, \text{ where } W^* \frac{k'_{pB}k_p}{k'_t}\mathrm{M}^2. \qquad (45)$$

When these inequalities are valid, the iniferter polymerisation mechanism operates. The first inequality implies that the rate of polymerisation must be fairly high compared with the characteristic value W^* so that the primary radicals B do not have enough time to initiate the polymer chains. On the other hand, according to the second inequality, the rate W should be significantly smaller than the quantity $(k'_{pA}/k'_{pB})W^*$ to rule out the chain termination by the primary radicals A which leads to the formation of polymer molecules incapable of reinitiation.

3. The molecular weight distribution and its characteristics

In the iniferter mechanism of polymerisation, the macromolecules consist of several elementary chains. This makes it possible to employ the superposition principle formulated in Section II.3 for the calculation of the molecular weight of the polymer in ideal systems. The generating function

$$U(x, t) = [\mathrm{e}^{(x-1)\tau} - \mathrm{e}^{-\tau}]/[1 - \mathrm{e}^{-\tau}], \text{where } \tau = k_d t, \qquad (46)$$

found neglecting the chain transfer reactions, leads to the simple expressions

$$\mathrm{P}_N = \frac{\tau\langle\nu\rangle}{1 - \exp(-\tau)}, \quad K = \frac{[1 - \exp(-\tau)]}{\tau}\left[\tau + 2\frac{\langle\nu^2\rangle}{\langle\nu\rangle^2}\right] \qquad (47)$$

for the number-average degree of polymerisation and the polydispersity coefficient. An increase in the number of elementary chains in the macromolecule naturally promotes an increase in their molecular weight and a narrowing of the molecular weight distribution, which can be seen from Eqns. (47). However, the opposite effects are induced by a decrease in the course of the polymerisation of the length $\nu = \nu^0\mathrm{M}/\mathrm{M}^0$ of the kinetic chain from its initial value $\nu = \nu^0$ to $\nu = 0$ when the monomer concentration changes from M^0 to 0. When account is taken of this effect, Eqns. (47) assume the following form:

$$\mathrm{P}_N = \frac{\nu^0(1 - e^{-\beta\tau})}{\beta(1 - e^{-\tau})}, \ \beta = \frac{C^0}{\mathrm{M}^0}\nu^0, \ \nu^0 = \frac{k_p\mathrm{M}^0}{(k_t\Phi k_d C^0)^{1/2}}; \qquad (48)$$

$$K = (1 - e^{-\tau})[\beta \operatorname{cth}(\beta\tau/2) + 1]. \qquad (49)$$

The quantity P_N increases with time from $\mathrm{P}^0_N = \nu^0$ to $\mathrm{P}^*_N = \nu^0\beta^{-1}$, where the parameter β^{-1}, having the significance of the average number $\bar{m}$ of elementary chains in the macromolecule of the final polymer, can be fairly large in the iniferter polymerisation mechanism. In this case, the limiting value $K = 1 + \beta$ of the polydispersity coefficient [Eqn. (49)] corresponding to $\tau \to \infty$ differs little from unity, which indicates a fairly high degree of uniformity of the molecular weight distribution of the final polymerisation product. Eqns. (48) and (49) predict a monotonic time variation of the quantities P_N and K. As regards the molecular weight distribution function, an explicit expression can be quoted for it in two important cases. One of them refers to the region of initial conversions:

$$f_N(l, t) = (\tau/\nu^0)\exp[-\tau(z/\tau - 1)^2]\psi(z),$$
$$\psi(z) = \exp(-2z)\mathrm{I}_1(2z)/z, \quad z = (l\tau/\nu^0)^{1/2}, \qquad (50)$$

where I_1 is a modified first-order Bessel function of the first kind. The other describes the final polymerisation products:

$$f_N(l, \infty) = [\nu^0\Gamma(1/\beta)]^{-1}(l/\nu^0)^{1/(\beta-1)}\exp(-l/\nu^0), \qquad (51)$$

where Γ is the Euler gamma-function.

The inclusion in the consideration of reactions (*h*) and (*i*) of Scheme (42), which take into account the chain transfer to the iniferter, leads to only non-fundamental modifications of Eqns. (46)–(49). They all retain their form as functions of τ when the average length ν of the kinetic chain is replaced in them by the average length $\nu[1 + k_1C^0(k_t\Phi k_d C^0)^{-1/2}]^{-1}$ of the elementary chain.

In the more general model of ideal polymerisation, the labile bonds in the initial iniferter and in the polymer molecules differ kinetically. For a large difference $k'_d \gg k_d$ between the rate constants k'_d and k_d for their decomposition reactions, the polymerisation will actually occur in two stages. In the first comparatively short stage, all the molecules of the initial iniferter decompose and macromolecules, each of which consists of exactly one elementary chain, are formed. During the second, longer stage, these macroiniferter molecules initiate further polymerisation. Here it is significant that the molecular weight distribution of the products formed is initially broadened and then narrowed. Such non-monotonic variation of the polydispersity coefficients k is possible in systems where the rate constant k_d for the breakdown of the labile bond diminishes fairly sharply as a function of the length of the macroiniferter molecule containing it. This theoretical conclusion follows from the solution of the system of kinetic equations quoted[55] for an arbitrary $k_d(l)$ relation. The experimental $K(t)$ curves obtained for the polymerisation of styrene in the presence of the iniferter (V)[56] pass in certain cases through a maximum, confirming the theoretical conclusions.

One of the most characteristic features of polymerisation with participation of iniferters is the linear increase with the degree of conversion p of the number-average molecular weight of the products formed.[38,41–43,48,53–57] This relation $P_N = (M^0/I^0)p$ follows directly from the iniferter polymerisation mechanism itself in the range of conversions $p \gg p^* = k_p(I^0/k_t\Phi k'_d)^{1/2}$, where there is virtually no initial initiator in the reaction system. Since each initiator molecule initiated the polymer chain on decomposition, the concentration of such chains corresponding to $p \gg p^*$ is identical with I^0.[42,44–45,53–57] For fairly low conversions, comparable to p^*, the expression $P_N = (M^0/I^0)p$ is naturally invalid because in this range of conversions the number of polymer chains increases with conversion. A correct extrapolation of the variation of P_N to the point $p = 0$ yields $P_N = \nu^0 = k_pM(k_t\Phi k'_dC^0)^{-1/2}$, which reflects the fact that the macromolecules formed at the very beginning of polymerisation consist of only one elementary chain.

In conclusion of Section III, one may say that at present there is sufficient experimental justification of the main features of the iniferter polymerisation mechanism. Naturally, in individual specific processes there is a possibility of side reactions which are not represented in Scheme (42) and which must be taken into account in kinetic calculations for the polymerisation and the molecular weight distribution of its products. Allowance for these side reactions involves the specific features of a particular monomer–iniferter pair, each of which can differ in its non-fundamental characteristics. On the other hand, the most characteristic general features typical for the iniferter polymerisation mechanism are reflected by its simplest kinetic Scheme (42).

IV. Conclusion

Radical polymerisations in the presence of polyfunctional initiators and iniferters have a whole series of common features despite the fundamental differences between the mechanisms of the formation of polymer chains. We shall now list the main features of this kind which distinguish these processes from the usual polymerisation with participation of traditional initiators.

The most important feature is the continuous growth of the molecular weight of the polymer with conversion, which is described by a linear law for a fairly large average number of elementary chains in the macromolecule. Under these conditions, the initial initiator disappears in the very early stages of the process, after which the number of polymer chains remains unchanged and only their length increases.

The second common feature of the processes is that the mechanism of the formation of macromolecules during polymerisation promotes a decrease in the conversion-induced broadening of the molecular weight distribution associated with the exhaustion of the concentrations of the monomer and initiator during the process. For the same reason, one should expect an appreciable increase in the non-uniformity, as regards composition, of the products of joint polymerisation obtained at advanced conversions.

The third common feature of the two processes is the formation during them of macroinitiator molecules, which are capable, after liberation, of promoting further growth of the molecular weight under appropriate conditions on coming into fresh contact with the monomer. This property makes it possible to employ both types of non-traditional initiators for the synthesis of block-copolymers. Polyperoxides make it possible under these conditions to obtain macromolecules with a fairly large number of blocks, while iniferters are used to obtain diblock copolymers.

The principal disadvantages of polyfunctional initiators are the ineffectiveness of their use in the polymerisation of monomers of the type of methyl methacrylate, where the fraction of radicals destroyed via the disproportionation mechanism is fairly large. The polymerisation initiated by iniferters is free from this disadvantage. The use of iniferters makes it possible, in addition, to eliminate almost completely the undesirable "gel-effect", manifested in the bulk polymerisation reactions of certain monomers. Polyperoxides do not allow this.

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Translated from *Uspekhi Khimii* **60** 1368–1390 (1991) U.D.C. 541.64;541.128;541.68;691.175.51.8

Polyfunctional components in radical polymerisation and in the preparation of polymer compositions

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ABSTRACT. The possibilities in the use of polyfunctional components in polymerisation systems are surveyed and analysed in the present review. The kinetics and mechanisms of the chemical reactions of polyfunctional monomers, initiators, emulsifying agents, and modified reactive fillers in radical polymerisation are examined. The kinetics and mechanism of polymerisation in systems with polyfunctional emulsifying agents or modified fillers are considered from the standpoint of considering them as locally organised systems with a regulated distribution of components.

A classification of polyfunctional components based on the available data is proposed.

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VI. Classification of polyfunctional components of polymerisation systems 712

I. Introduction

The development of optimum procedures for the preparation of various polymers or polymer systems by radical polymerisation has been achieved over several decades on the basis of the theory of radical reactivity and the advances in technology. As a result, the view has been established in practice that the optimum components for the preparation of polymers ensuring the necessary molecular structure and properties of the product and a satisfactory reproducibility of the process are monofunctional components—monomers, initiators, regulators, emulsifying agents, etc. Indeed, in recipes for polymerisation systems using monofunctional components, the highest selectivity of the polymerisation process is achieved and possible side reactions, associated with polyfunctionality and introducing disturbances and defects into the structure of the macromolecules formed, are eliminated. These factors account for the fact that in the course of a long period efforts in the research into radical polymerisation processes and in the development of procedures for polymerisation systems were directed to the study of the reactivity of functional groups and the possibility of regulating it for monofunctional compounds—monomers, initiators, emulsifying agents, etc. By the beginning of the 1960's, the construction of an elegant theory of radical polymerisation, which has since become classical, ensuring the development of a technology for many large-scale processes involving the synthesis of polymers and polymer systems, was completed. This was the reason for the temporary loss of interest by investigators in radical polymerisation processes.

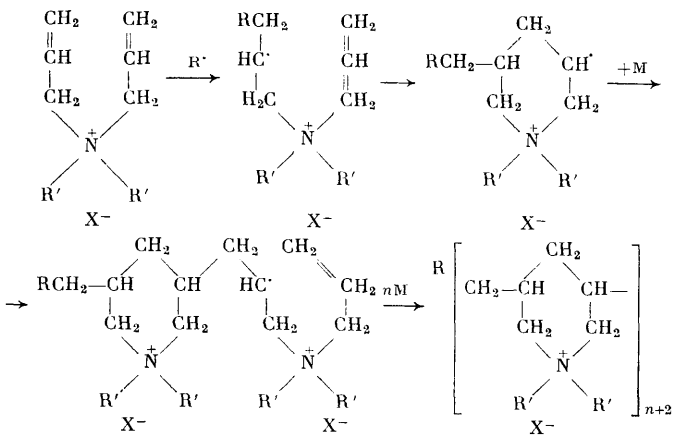
However, for some time there has been a renewed growth of interest in radical polymerisation processes. On the one hand, this has been reflected in the new scientific field of complex-radical polymerisation,[1–3] which suggested ways of controlling the elementary reactions in radical polymerisation via the formation of complexes by monomer molecules and the radicals. On the other hand, investigators have become interested in polymerisation systems involving the use of components (monomers, initiators, and emulsifying agents) of the polyfunctional type, capable of reacting via different functional groups.[4–7] Such polymerisation systems make it possible to reduce the number of components in procedures for polymerisation systems, for example, by combining the functions of the monomer and initiator in one molecule, to simplify the technology of the process, and to obtain reactive polymer systems with new chemical structures, capable, without special additives, of further chemical or structural changes. Such polymers can be used to obtain block-copolymers or graft polymers[4,5,7] in processes involving the liquid-phase formation of polymer articles,[8,9] for the creation of rubbers capable of self-induced structure formation,[10] etc.

Yet another important consideration has been developed very recently. Using polyfunctional components in polymerisation systems, it is possible to achieve under appropriate conditions a consecutive series of reactions via the appropriate functional groups and the formation of a pre-specified structure of the polymer matrix produced. This approach makes it possible to devise specific rules for the preparation of linear, comb or three-dimensional macromolecules with a particular branching density, reactive oligomers or polymers, and hence block-copolymers based on them. Thus, it is possible to devise procedures for regulating the structure of the macromolecular systems formed in the polymerisation process and to some extent also procedures for macromolecular design.

Numerous results of studies of the kinetics and mechanism of the polymerisation of systems with polyfunctional components have accumulated during the last 15 years. A survey of such data has become not only realistic but also desirable. In the present review, we attempt to consider the main advances in the use of polyfunctional components in polymerisation systems. Naturally, whilst endeavouring to achieve an objective analysis, the author is not always able to avoid a subjective view on the problem, which is reflected also in the treatment and selection of data. Nevertheless, the author hopes that the review will be of interest to a wide range of specialists in the field of the synthesis of polymers.

II. Polyfunctional monomers

Polyfunctional monomers include those whose molecules contain, apart form the polymerisable double bond, also another functional group (or other functional groups). Monomers with conjugated double bonds (butadiene, isoprene, etc.) can also be classified as polyfunctional monomers (PFM). Bearing in mind that information about such monomers is widely available in the literature on rubbers,[11] we shall not discuss the characteristic features of their reactions. As regards polyfunctional monomers with non-conjugated double bonds, the results of systematic studies on the intramolecular and intermolecular mechanisms of chain propagation in the polymerisation of non-conjugated dienes have been included in numerous other reviews and monographs[12,13] and were subsequently revised in a more recent publication.[14]



The cyclisation process in the polymerisation of various conjugated dienes can also proceed vigorously with formation of six-membered[13] and five-membered[14] rings or may not occur at all. The characteristic features of the polymerisation of alkene-alkyne polyfunctional monomers are determined by their structure. The polymerisation process usually involves a double bond with formation of reactive macromolecules with multiple bonds in the side chain which subsequently readily form a structured system.

In the last two decades, there has been a wide-scale growth of interest in monomers with peroxy-groups, which arose as a result of the studies by Yurzhenko and his school.[10,15–25] Monomers involving a combination of peroxy-groups of different structure in their molecules have been synthesised. This made it possible to regulate within certain limits the reactivity of the multiple bond and of the initiating peroxy-group.

In the first studies, the polymerisation of peroxides of the polyfunctional monomer type was achieved by simply heating them or by initiating the process by their own peroxy-groups. The polymerisation proceeded up to a conversion of 20–50%, after which the reaction mixture decomposed with formation of gaseous products without the formation of the polymer.

In copolymerisation with other monomers, a decrease in the rate of polymerisation and in the molecular weight of the copolymer formed with increase in the concentration of the peroxide monomer was observed, which made it possible to put forward the hypothesis of weak inhibiting effects of the peroxide monomer in the polymerisation process as a result of the degradative chain transfer to the peroxide monomer with formation of a less reactive radical.[17,18]

In self-initiation without the addition of another initiator, the polymerisation process is complicated by structure formation in the polymer, which precludes a reliable determination of the molecular weight and of the structure of the polymer formed. Because of this, the subsequent study of the polymerisation of peroxide monomers was carried out using another lower-temperature initiator and temperatures permitting the maximum retention of the peroxy-groups of the polyfunctional monomer in the unreacted state. The conditions for the preparation of virtually unbranched soluble copolymers of styrene with unsaturated esters of α-hydroxydialkyl peroxide containing peroxy-groups in the side chain were thus established.[19] Comb graft polymers can be readily obtained from such polymers.[20]

New procedures for the preparation of impact-resistant polystyrene plastics, (including ABS-plastics),[5,22,23] synthetic rubbers capable of sulphur-free vulcanisation, benzene- and oil-resistant cured rubbers, reactive oligomers, reactive latexes, and other polymer systems of practical importance have been proposed on the basis of polyfunctional monomer peroxides.[5,10,15,24,25]

The data presented above demonstrate the possibility of using polyfunctional monomers for the synthesis of branched and cross-linked polymers and copolymers and for the preparation of microheterogeneous polymer systems with a controllable microheterogeneity.

III. Polyfunctional initiators of radical polymerisation

Polymer systems based on polyfunctional components have been developed most vigorously in the last two decades using polyfunctional initiators.[4–7] Compounds (Table 1) whose molecules contain two or more groups capable of generating free radicals initiating the polymerisation process, or containing, apart from the initiating group, other functional groups capable of subsequent chemical reaction can be classified as polyfunctional initiators (PFI). Peroxides and azo-compounds of different structure have come to be most widely used as polymerisation initiators. Peroxides and azo-compounds with functional group substituents, for example, di-, oligo- and polyperoxides,[4,5,7,9] di- and poly-azo-compounds,[4,5,7,9] azoperoxides,[5,7,9] as well as peroxides or azo-compounds containing other reactive functional groups (hydroxy-, carboxy-, etc.,[4,7,9]) have been most widely used as polyfunctional initiators. Polyfunctional initiators of the last type do not differ, as regards the mechanism of their initiating action in polymerisation, from monofunctional initiating systems and are normally used in the preparation of reactive oligomers and polymers with functional end groups. They have been examined in detail in other reviews.[7,9]

Polyfunctional initiators of the type of di- and poly-peroxides have been studied systematically by Ivanchev and co-workers[4–6,9,26–30,36–39] and Tsvetkov and co-workers.[31–34]

In the study of the initiating capacity of diperoxides with structurally identical peroxy-groups separated by aliphatic bridges, it has been shown that the kinetics of the thermal decomposition of peroxy-groups can be characterised by a single set of parameters.[4,26] As shown in Fig. 1, the rate constants for the decomposition of diperoxides based on aliphatic dibasic acids depend on the length of the methylene bridge n between the peroxy-groups, the rate constant increasing with increase in n from 1 to 6 and subsequently remaining unchanged for $n \geqslant 6$.

Table 1. Polyfunctional components of polymerisation of systems.

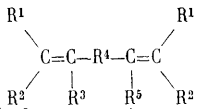
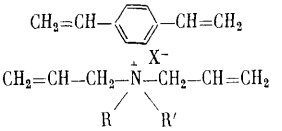
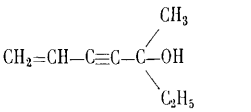
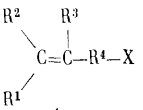
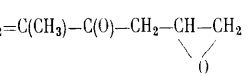
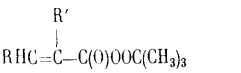
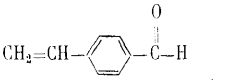
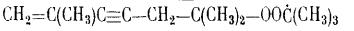
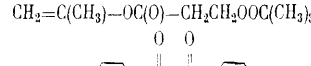
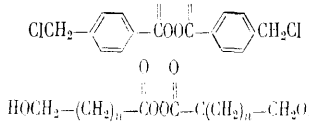
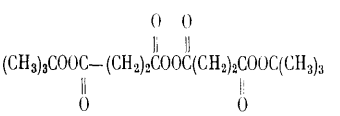
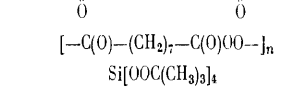
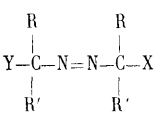
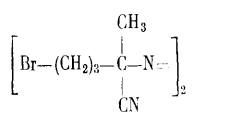
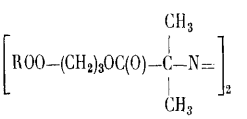
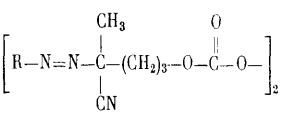
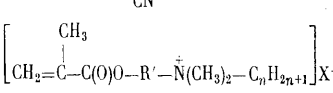
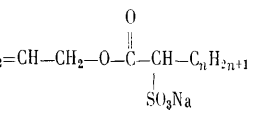
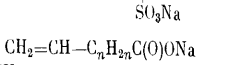
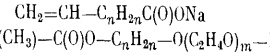
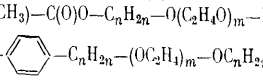
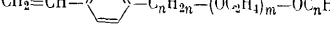
Class of compound	Chemical formula	Examples of compounds
Non-conjugated dienes	 R^1, R^2, R^3, R^5 = Alk or H; R^4 = Alk; X = halogen	
Alkene – alkyne systems	$CH_2=CR-C\equiv C-CRR^1R^2$	
Monomers containing other reactive groups	 $R^1R^2R^3$ = Alk or H; R^4 = Alk or Ar; X = functional group	   
Peroxides	$X'ROO-RX$ X, X' = functional groups	   
Azo-compounds	 R = Alk; R' = Alk or CN	 
EM-monomers		      

Table 1 (contd.).

Class of compound	Chemical formula	Examples of compounds
EM-initiators		$R(OCH_2CH_2)_nOC(O)-CH_2CH_2-C(O)OC(CH_3)_3$ $R(OCH_2CH_2)_nOC(O)-CH=CH-CH_2$ CH_2 C $C-R^2$ $R^1-C=O$ O O OOH $ROO-(CH_2CH_2O)_n-H$ $RC(O)OOC(O)CH_2CH_2C(O)(OCH_2CH_2)_nOC(O)-CH_2CH_2C(O)OOC(O)R$ $CH_3(CH_2)_6-C(OOH)-CH=CH-(CH_2)_7C(O)ONa$
Filler-monomers	E—R=R'	Si—$OCH_2CH=CH_2$ Si—O, Si—O, $CH-CH=CH_2$ Si—$CH_2OC(O)C(CH_3)=CH_2$, CH_3
Filler-initiators	E—ROOR'	OR, Si—CH—OOH, CH_3 CH_3CN, —Ca—$OC(O)-(CH_2)_2-C$, N, N, —Ca—$OC(O)-(CH_2)_2-C$, CH_3, CN Si—O, Si—O, $Si(CH_3)_2-CH=CH-COOCH_3$, CH_3, CH_3

The rate of polymerisation initiated by diperoxides varies in parallel with their k_{decomp}. A model has been proposed recently[35] which describes the rates of formation of various growing radicals and molecules in the polymerisation of styrene initiated by diperoxide initiators. The unimodal nature of the molecular weight distribution of the polymers formed, the slight increase in the molecular weight of the polymer with increase in the degree of conversion, and the inadequate fraction of polymers formed with terminal peroxide fragments lead to the conclusion that diperoxides with identical structures of peroxy-groups differ little as regards the mechanism of the initiating action from monoperoxides and are relatively ineffective in processes involving the formation of reactive polymers with peroxy-groups.[4,26]

It has been shown[31–34] that in the case of diacyl oligo- or polyperoxides the decomposition of peroxy-groups takes place statistically at rates which depend on the length of the bridge between the peroxy-groups and involve the insertion of polyperoxide fragments, and not individual peroxy-groups, into the macromolecule produced.

The degree of retention of the undecomposed peroxy-groups depends on the decomposition time and the process temperature. Systems of this type used as initiators make it possible to obtain reactive polymers and block-copolymers, but work with them entails a series of experimental difficulties because of the dangerous properties of polyperoxides.

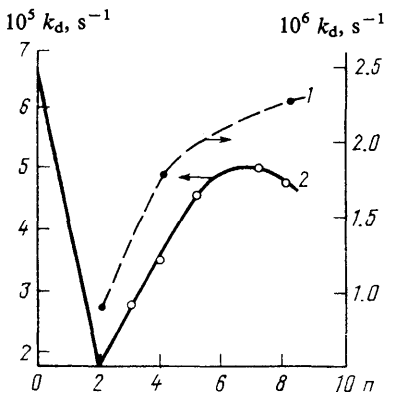


Figure 1. Dependence of the decomposition rate constant k_d on the length of the methylene bridge n between the peroxy-groups of peresters (1) and diacyl peroxides (2) based on unsubstituted aliphatic acids.

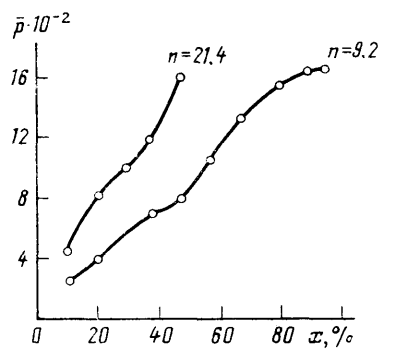


Figure 2. Dependence of the average degree of polymerisation $\bar{p}$ of polystyrene on the degree of conversion x for different "functionalities" of the initiator $[OOC(CH_2)_5COOCHBr(CH_2)_4C(=O)-]_n$ (initiator concentration 0.025 M, temperature 80 °C).

In order to eliminate these difficulties, bifunctional[4,27,36] and oligomeric[4,28,30,38] peroxides with peroxy-groups having different thermal stabilities, trifunctional peroxides having the bis-structure,[4,29,37] and azoperoxides[7,9,39–41] have been synthesised and investigated in polymerisation processes. It was shown that, depending on the polymerisation process temperature, new polyfunctional initiators make it possible to obtain polymers containing peroxy-groups in the polymer macrochain, or as end groups (bifunctional and trifunctional systems), or within the macrochain (polyfunctional systems). The rate of polymerisation is determined by the kinetic parameters of the decomposition of the peroxy-groups, whereas the molecular weight of the polymer formed depends on the degree of conversion and increases with polymerisation time. As shown in Fig. 2, the average degree of polymerisation of the polystyrene formed also depends on the "functionality" of the initiator and increases appreciably with the degree of conversion. Differential molecular weight distribution curves likewise vary sharply with the degree of conversion (Fig. 3) and the molecular weight distribution remains fairly narrow at advanced stages of the reaction.

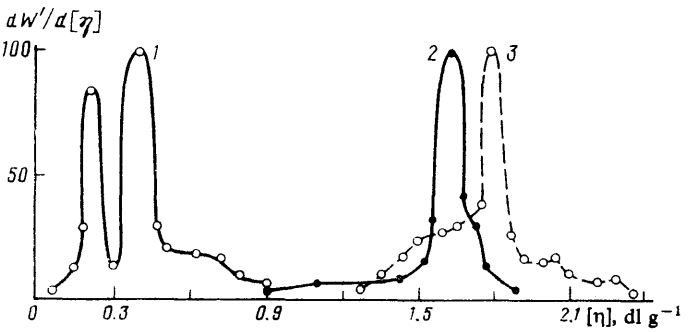


Figure 3. Differential molecular weight distribution curves for polystyrene obtained in polymerisation initiated by the oligoperoxide $[C(O)(CH_2)_7C(O)OOC(O)CHBr(CH_2)_8C(O)OO]_{18}$. Initiator concentration 0.0125 M; degree of conversion 6% (curve *1*) and 100% (curves *2* and *3*); polymerisation temperature 60 °C (curves *1* and *3*) and 60 and 80 °C under two-stage polymerisation conditions (curve *2*).

All these data enabled us to put forward a new polymerisation-polyrecombination mechanism of the formation of macromolecules[4] for radical polymerisation initiated by monofunctional initiators. This mechanism reduces to the following elementary reactions:

(1) initiation:

$$PFI \xrightarrow{k_{decomp}} 2R^{\cdot}; \quad R^{\cdot} + M \xrightarrow{k} RM^{\cdot};$$

(2) chain propagation:

$$RM^{\cdot} \xrightarrow[k_p]{nM} RM^{\cdot}_{n+1};$$

(3) chain termination:

$$RM^{\cdot}_{n+1} + RM^{\cdot}_{m} \begin{cases} \xrightarrow{\text{recombination}} \Pi_a \\ \xrightarrow{\text{disproportionation}} \Pi_{1a} + \Pi_{2a} \end{cases};$$

(4) repeated initiation by the initiating groups which have entered the macromolecule (reinitiation):

$$\Pi_a \xrightarrow{k_{decomp}} 2R_p^{\cdot} \xrightarrow{M} R_pM^{\cdot};$$

chain propagation:

$$R_pM^{\cdot} \xrightarrow[k_p]{nM} R_pM_{n+1}^{\cdot} \quad ;$$

chain termination:

$$R_pM_{n+1}^{\cdot} + R_pM_m^{\cdot} \xrightarrow{k_t} \Pi'_a(\Pi'_{1a} + \Pi'_{2a}),$$

$$\Pi'_a \xrightarrow{k_{decomp}} 2R_{p_2}^{\cdot}, \text{ etc.}$$

In the general case, all the elementary reactions should naturally be taken into account in the above scheme including reactions involving chain transfer to the monomer, the polymer, etc., but the reinitiation reactions or reactions involving the repeated formation of initiating radicals of the macromolecules formed, which depend on the functionality of the polyfunctional intiator employed, are decisive and fundamental.

The proposed mechanism of the formation of macromolecules makes it possible to explain the observed kinetics of the initiated polymerisation and the nature of the variation of the molecular weight and the molecular weight distribution of the polymer formed. It is of interest to note that, in the initiation of polymerisation by polyfunctional initiators, the inverse relationship, which follows from the main equation of radical polymerisation, between the rate of polymerisation and the molecular weight of the polymer formed as a function of the increasing initiator concentration may not hold because of the specific features of the mechanism of the formation of macromolecules.

Thus in industrial practice, the optimum process conditions and rate of initiation, ensuring the necessary molecular weight and the appropriate operating properties of the polymer, are selected in the preparation of the principal assortment of polymers. These requirements significantly restrict the possibilities of increasing the productivity of the reactor by increasing the rate of polymerisation as a result of increasing the concentration of the initiator. For polyfunctional initiators, this limitation is manifested to a much lesser extent because if the polyrecombination-polymerisation mechanism of the formation of macromolecules and the significant increase of the molecular weight with increasing degree of conversion. For polyfunctional initiators, it is possible to carry out a polymerisation with formation of a conditioned polymer having a narrow molecular weight distribution even at variable process temperatures.[4,5]

We are now able to predict the average molecular weight and the molecular weight distribution of the polymers formed when polymerisation is initiated by a polyfunctional initiator. Thus equations for the variation of the molecular weight and hence of the molecular weight distribution as a function of the degree of conversion of styrene were derived[42] in a study of the polymerisation of styrene initiated by various polyfunctional initiators. The calculation was performed on the assumption that the peroxy-groups decompose independently of one another, that the decomposition rate constant does not vary, that the radicals are formed effectively in the decomposition reaction, and that the rate of initiation is proportional to the overall concentration of peroxy-groups regardless of the nature of their distribution. The structure of the macromolecules formed during polymerisation constitutes a number of interconnected monomer units separated by peroxide clusters (Fig. 4).

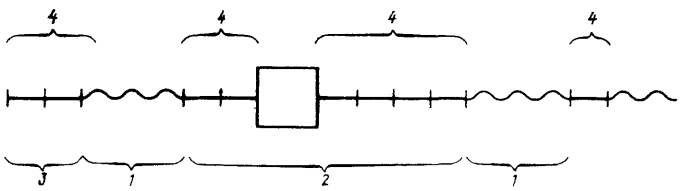


Figure 4. Schematic illustration of the structure of the macromolecules of the polymers formed in polymerisation initiated by a polyfunctional peroxide: *1*, elementary polymer chain; *2*, and *3*, closed and semi-open clusters; *4*, peroxide blocks.

Assuming that the contribution of the peroxide clusters to the molecular weight may be neglected because of their small size compared with the sequences of monomer units, the molecular weight distribution can be regarded as a superposition of the distributions of random quantities. As a result, we obtain the following equation for the dependence of the number-average molecular weights on the process time:

$$\frac{\overline{M}_n}{\overline{M}_n'} = \frac{\lambda + 1}{\lambda + 1 - \rho}; \quad \rho = \frac{1 - \sum_{j=1}^{\infty} \alpha_j (1 + \theta)^j}{\theta \sum_{j=1}^{\infty} j\alpha_j}, \qquad (1)$$

where $\overline{M}_n'$ is the number-average molecular weight of the polymer obtained using a simple monofunctional initiator under the same conditions and at the same concentration of $-O-O-$ groups, λ the probability of termination as a result of disproportionation, α_j the fraction of initiator molecules containing j peroxy-groups, and θ the fraction of the effectively decomposed $-O-O-$ groups: $\theta = f(1-e)^{-k_{decomp}t}$ (f is the initiation efficiency).

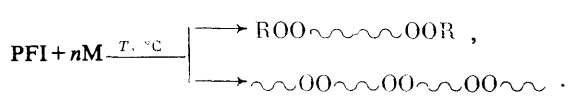
Putting Eqns. (1) in the form

$$\overline{M}_{n\infty} = \overline{M}_n \frac{\lambda + 1}{\lambda + 1 - \rho_\infty}; \quad \rho_\infty = \frac{\left[1 - \sum \alpha_j (1 - f)^j\right]}{\theta f \sum j\alpha_j}, \qquad (2)$$

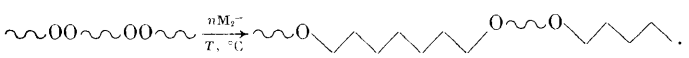
we find that the molecular weight increases continuously from $\overline{M}_n'$ to a limiting value $\overline{M}_{n\infty}$, which depends on the functionality of the peroxide and the initiation efficiency. The experimental confirmation of the validity of the proposed equations is demonstrated in Fig. 5. Somewhat later we carried out a similar calculation by solving differential material balance equations.[43]

The incorporation of the initiating groups into the composition of macromolecules in polymerisation initiated by polyfunctional initiators gives rise to effective possibilities for the preparation of block-copolymers. The essential feature of the mechanism of the formation of block-copolymers reduces to a two-stage process.

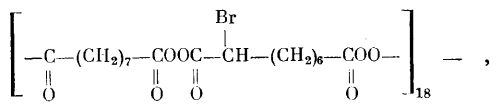
The first stage is the polymerisation of the first monomer using a monofunctional initiator under conditions ensuring the formation of polymer molecules with initiating groups incorporated into the macrochains, for example:



The second stage reduces to the polymerisation of the second monomer M_2 initiated by the "active" polymer (macroinitiator) obtained in the first stage.



styrene (polymerisation in block at 60 °C) using a polyfunctional initiator—oligoazelaoyldiperoxy-α-bromoazelaoyl peroxide having the general structure



a study was made of the kinetics of the decomposition of peroxy-groups by the method of inhibitors regulating simultaneously the variation of the average degree of polymerisation in the course of the decomposition of peroxy-groups. As shown in Figs. 6 and 7, the decomposition of the peroxy-groups in the macroinitiator produced is a first-order reaction; there is a simultaneous decrease in the degree of polymerisation of the macroinitiator, which confirms the intermolecular statistical distribution of the initiating groups in the macroinitiator.

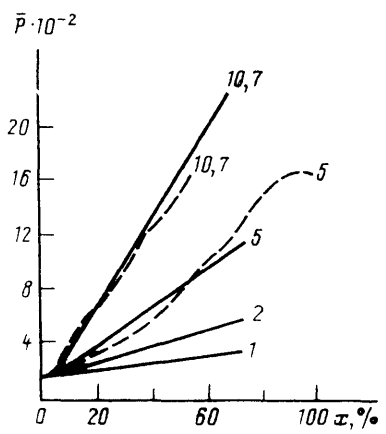


Figure 5. Dependence of the average degree of polymerisation of styrene $\bar{p}$ initiated by the oligoperoxide $[C(O)(CH_2)_7.C(O)OOC(O)CHBr(CH_2)_6C(O)OO-]_n$ for different values of n on the degree of conversion x at 80 °C and an initiator concentration of 0.025 M; continuous lines—calculated theoretically; dashed lines—determined experimentally. The numerals opposite the curves correspond to the numbers of peroxy-groups (n) in the peroxide.

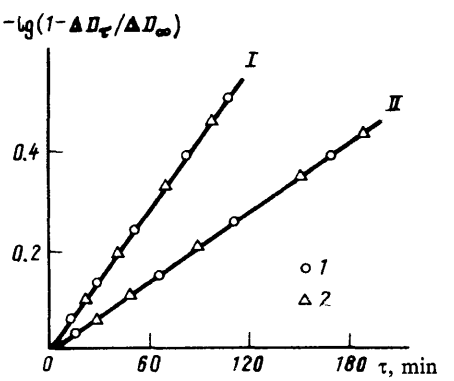


Figure 6. Semilogarithmic plots of the decomposition curves for the peroxy-groups in "active" polystyrene obtained in the presence of the oligoperoxide $[C(O)(CH_2)_7C(O)OOC(O)CHBr(CH_2)_6.C(O)OO-]_{18}$ at 80 °C (I) and 75 °C (II); $\Delta D\tau$—the change in the optical density of the inhibitor (iodine) solution during the decomposition of the initiator during a period τ; ΔD_∞—ditto for the complete decomposition of the initiator.

The dependence of the functionality of the polyfunctional initiator on the number of peroxy-groups in the macroinitiator is fairly simple.[4,5] For bifunctional initiators, there is a possibility of obtaining macromolecules which have on average one peroxy-group, while trifunctional initiators can give rise to macromolecules with two and more initiating groups. Accordingly, the second stage of the block-copolymerisation can give rise to block-copolymers of different structure—from diblock polymers of the type A–B (bifunctional initiators) to multiblock polymers of the type A–B–A–B.

The incorporation of initiating groups into the molecular chain of the macroinitiator formed when a polyfunctional initiator is used has been demonstrated experimentally.[44] For the synthesised and reprecipitated macroinitiator, obtained in the polymerisation of

Naturally, both the distribution of macromolecules with respect to molecular weight and the distribution with respect to the number of initiating functional groups are statistical. The block-copolymer is therefore non-uniform as regards the alternation of blocks.

The structure of the polyfunctional initiator, i.e. the presence in the structure of identical initiating functional groups or such groups differing in reactivity or thermal stability, is important in the synthesis of "active" polymers in the first stage. When polyfunctional initiators with initiating groups having identical structures are used, additional complications arise in the formation of macroinitiators, namely the necessity to restrict the process in time (and hence as regards the degree of conversion) in order to retain at least some of the initiating groups in the macroinitiator.

Polyfunctional initiators with initiating groups having different thermal stabilities, especially when these groups alternate in the molecule, are more convenient for the synthesis of the macroinitiator. The choice of temperature conditions in conformity with the thermal decomposition constant for the more reactive initiating group makes it possible to achieve the first stage of the polymerisation up to high degrees of conversion and to obtain a macroinitiator which is comparatively uniform as regard composition and molecular weight.

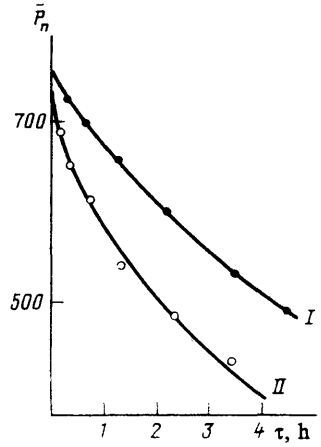


Figure 7. Variation of the degree of polymerisation of "active" (containing peroxy-groups in the macrochain) polystyrene in the thermal decomposition of peroxy-groups in solution in chlorobenzene in the presence of iodine at 70 °C (I) and 80 °C (II).

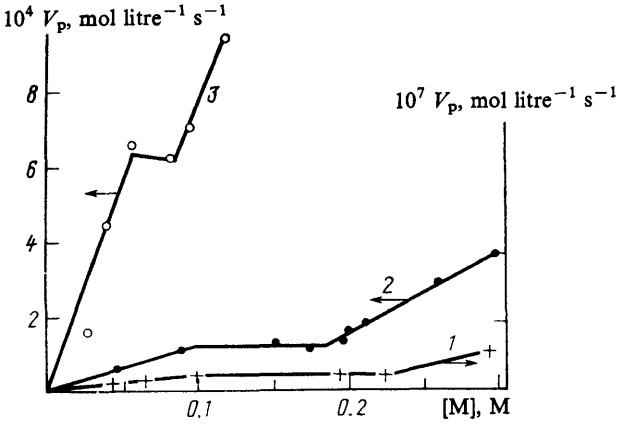


Figure 8. Dependence of the initial rate of polymerisation of polyfunctional emulsifier salts of methacryloylethylammonium (curves *2* and *3*) and allyl ammonium (curve *2*) at 70 °C on the monomer concentration in water:

(*1*) $[CH_2{=}CH{-}CH_2\overset{+}{N}(CH_3)_2CH_2COOC_{12}H_{25}]Br^-$;
(*2*) $[CH_2{=}C(CH_3){-}COOC_2H_4\overset{+}{N}(CH_3)_2CH_2COOC_{12}H_{25}]Br^-$;
(*3*) $[CH_2{=}C(CH_3){-}COOC_2H_4\overset{+}{N}(CH_3)_2CH_2COOC_{16}H_{25}]Br^-$.

The block-copolymers formed using a polyfunctional initiator are non-uniform both in molecular weight (molecular inhomogeneity) and in composition (composition inhomogeneity).

The synthesis of block-copolymers using polyfunctional initiators has been described in greater detail in a number of communications,[44–52] while other reports[49–52] give a more detailed account of polyfunctional azo-initiators or azoperoxides.

A calculation of the composition and microstructure of the block-copolymers formed using a polyfunctional initiator with two types of initiating groups differing in thermal stability, taking into account the molecular weight distribution of the macroinitiator formed in the first polymerisation stage, has been proposed.[46] The adequacy of the relations obtained has been tested experimentally.

The above brief analysis shows that the use of polyfunctional initiators of polymerisation makes it possible to improve significantly the possibilities available to us in the synthesis of polymers as a result of the increase in the amount of polymers recovered from a unit volume of the reactor and the preparation of reactive oligomers, polymers, and block-copolymers of different composition based on them.

IV. Polyfunctional surfactants

Investigators have recently clearly manifested their interest in two types of polyfunctional surfactants—surface-active monomers (SAM), which are compounds exhibiting the properties of surfactants and simultaneously retaining their capacity for polymerisation or copolymerisation, and surface-active initiators (emulsifier-initiators) (SAI), which combine the properties of a surfactant with ability to generate free radicals in a certain temperature range (Table 1).

Surface-active monomers have been known for a comparatively long time.[53] In the first studies devoted to such monomers, attention was concentrated on the study of their copolymerising capacity without a profound analysis of the kinetic behaviour of these compounds in polymerisation systems. During the last two decades, there has been a growth of interest in their investigation and they have become the subject of a review.[54]

The characteristics of the molecular structure of surface-active monomers and their ability to form associated species (micelles, lamellae, etc.) make it possible to predict their influence on the polymerisation (or copolymerisation) process. For a well founded explanation of the behaviour of such monomers in polymerisation systems, the polymerisation kinetics were therefore compared with the colloidal-chemical characteristics of solutions of surface-active monomers and the polymers formed from them.

Different dependences of the initial rate of polymerisation on the concentration of the surface-active monomer in water were observed for vinylpyridinium salts differing in the length of the aliphatic chain. For short-chain surface-active monomers, a linear growth of the rate of polymerisation with increase in the monomer concentration is observed, whereas in the case of long-chain surface-active monomers a break is observed at a certain concentration with a change in the slope of the straight line in the direction of an increase in the rate.[54] The increase in the rate of polymerisation is accompanied by the increase in the ratio of the propagation rate constant to the square root of the chain termination rate constant and by an increase in the rate of initiation.[55]

In the study of aqueous dispersions of surface-active monomer salts of methacryloylethylammonium and allylammonium, an even more complex dependence of the initial rate of polymerisation on the surface-active monomer concentration was observed. As shown in Fig. 8, in the region corresponding to the existence of micellar formations there are three sections on the curve relating the rate of polymerisation to the monomer concentration.[56] The first, initial section is characterised by a linear growth of the rate, the second by a constant rate, and the third by a renewed growth of the rate of polymerisation. The three linear sections in the variation of the rate of polymerisation were attributed by the authors to structural changes in the monomer formations within certain concentration ranges (spherical micelles, anisotropic micelles, multilayer lamellae).

In drawing a general conclusion concerning the outcome of the studies in this field,[53–58] one may note the following principal features. The polymerisation of surface-active monomers in aqueous micellar dispersions exhibits a series of differences from homogeneous polymerisation in solution, associated primarily with structure formation processes involving the molecules of the surface-active monomer and influencing the polymerisation kinetics and the microstructure of the polymer formed.

The nature of the kinetics of the polymerisation of surface-active monomers may vary as a function of the variation of the constants for the elementary reactions or of the reaction order with respect to the monomer and the initiator. The copolymerisation of surface-active monomers with other monomers takes place in those cases where the reactivity of the surface-active monomer is close to or greater than the reactivity of the comonomer.

Surface-active monomers can be used to prepare latexes not containing the free emulsifier in the aqueous phase, especially stable monodisperse latexes, ion-exchange resins, polymeric carriers for medicinal and biological preparations, etc. Surface-active monomers used to obtain thin molecular polymer layers are of special interest.

The effects observed in polymerisation systems of another type, comprising surface-active initiators—compounds in which surface-active properties and initiating capacity are combined—are extremely interesting. The location of the initiating centres in the region of adsorption layers or of the interface in heterogeneous polymerisation systems leads to extremely interesting kinetic effects associated with the change in the rates of elementary polymerisation reactions, in the first place initiation and chain termination reactions. We demonstrated experimentally the change in the rate of decomposition of a peroxide initiator located in the surface region of latex particles.[60]

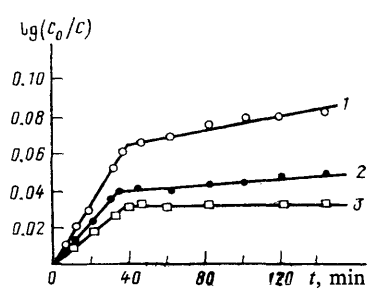


Figure 9. Semilogarithmic forms of the kinetic curves for the decomposition of the peroxy-groups of the polymeric initiator in the n-butyl acrylate—permonomer copolymer latex at 333 K. Diameter of the latex particles (nm): *1*, 50; *2*, 96; *3*, 160.

Fig. 9 presents the logarithmic forms of the curves for the decomposition of peroxy-groups located in the surface region of polymer-monomer species as a result of a special procedure for the metered introduction of the peroxide monomer in seeded emulsion copolymerisation in the system butyl acrylate–methacrylic ester of t-butyl α-hydroxyethyl peroxide.[59–61] Fig. 9 shows that the rate of decomposition of the peroxy-groups in the surface region is appreciably higher than in the bulk of the particle. A decrease in the rate constant leads to an alteration of the ratio of the peroxy-groups in the surface region of the particles. If kinetic relations are plotted taking into account the initial concentration of the peroxide, corresponding to its amount in the surface region of latex particles, then all the curves have the same slope regardless of the dispersity of the particles.

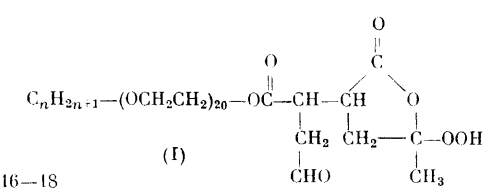
In the case of surface-active initiators, the region corresponding to the formation of free radicals is located either in the micelles or in the surface layers of latex particles depending on the characteristics of the structure of the surface-active initiator. This factor makes it possible to follow the influence of adsorption layers on the reactivity of the peroxy-groups and to investigate the characteristic features of the initiation reaction. The data presented in Table 2 make it possible to demonstrate the influence of the characteristics of the absorption layer on the rate constant for the decomposition of the surface-active initiator k_{decomp}.

Table 2. Parameters of the thermal decomposition of surface-active peroxides (SAI) in aqueous solutions.

SAI*	T, K	pH	$10^5 k_{decomp}$, s^{-1}	E, kJ mol^{-1}
(I)	333	5	1.3	59.5
(I)	363	5	7.0	
(I) with added Alkamon OS-2	333	7	3.3	63.5
	363	7	23.5	
(I) with added E-30	333	7	3.3	–
(I) with added SDS	333	7	4.5	–
(II)	363	5	3.9	–
(II) with added Alkamon OS-2	363	7	9.0	–
(III) with added Alkamon OS-2	363	5	0.9	–

*Alkamon OS-2 = $[C_{16-18}H_{32-37}(OCH_2CH_2)_2CH_2\underset{\displaystyle CH_3}{\underset{|}{N}}(C_2H_5)_2]^+ . C_6H_5SO_3^-$; E-30 = $C_{15}H_{31}SO_3Na$; SDS = sodium dodecyl sulphate.

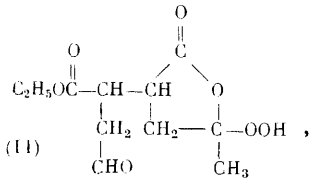
Evidently k_{decomp} for micelle-forming surface-active initiators (I), having the same structure of the peroxy-group, i. e.



(I)

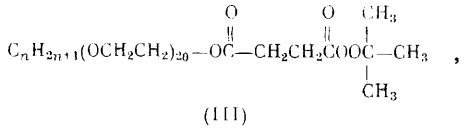
n = 16–18

is initially higher than for the non-micelle-forming surface-active initiators (II):



(II)

It is of interest to note that, for the perester analogue (III), i.e.



(III)

$n = 16-18$

k_{decomp} does not differ from the values for the usual peresters in hydrocarbon media. This is due to the fact that a special structure of the micelles, in which the hydrophobic fragment with the peroxy-group is drawn into the hydrocarbon nucleus of the micelle, is characteristic of compound (III).

The data presented emphasise the significant role not only of the structure but also of the location of the peroxy-group in the hydrophilic region of the micelle on the decomposition rate constants k_{decomp}.

The efficiencies of the initiation of emulsion polmerisation using surface-active initiators proved to be low (0.10–0.03).[60,61] This is probably due to the difficulties arising in the interaction of the primary radicals, fixed in the adsorption layer, with the monomer in the hydrocarbon nucleus of the micelle. The high rate of destruction of the primary radicals owing to their local concentration can be abolished with decrease in the concentration of the surface-active initiator. The observed increase in the initiation efficiency on reduction of the concentration of the surface-active initiator is associated with this factor.

The change in the initiation efficiency with decrease in the concentration of the surface-active initiator in the adsorption layer makes it possible to explain the change in the emulsion polymerisation reaction order with respeect to the initiator and the emulsifier. These phenomena are caused by the change in the average number of radicals in the polymer-monomer particles.

Experiments carried out[61] in order to investigate the influence of the surface-active initiator on the chain propagation reaction lead to the conclusion that the chain propagation reaction parameters in emulsion polymerisation are independent of the characteristics of the adsorption layer and the type of initiating group. Calculation showed that in this case the chain termination rate constants decrease sharply (by 2–4 orders of magnitude) compared with those for homogeneous systems and depend on the type of polymerisation system, the volume of the polymer-monomer particles, and the fixation of the growing radicals in the surface region. This is associated with the increase to some extent of the translational and possibly the conformational entropy of the macroradicals (depending on the structure of the surface-active initiator). These data permit the conclusion that in such systems the initiation reaction influences the chain termination steps and hence the chain termination constant. Hence the possibility arises of regulating with the aid of the surface-active initiators the chain termination reaction in emulsion polymerisation and of obtaining thereby ultra-high-molecular-weight polymers (with molecular weights up to 10^7 and above).

Polyfunctional initiators can be used successfully in polymerisation systems in the preparation of ultra-high-molecular-weight polymers, highly stable polymer dispersions, polymer dispersions with a narrow size distribution of particles, etc.[59,60]

Although the history of the research into polyfunctional surfactants has so far been short, the possibilities in their use to obtain stable latexes with a specified particle size, for the creation of microheterogeneous polymer systems with a controllable size of the region of microheterogeneity, or for the creation of polymeric molecular layers are unique. It is difficult to overestimate their importance. They will undoubtedly develop in the near future.

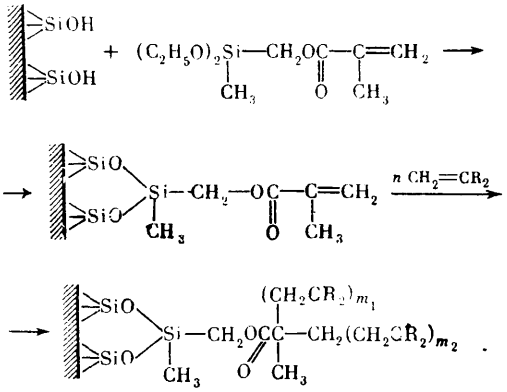
V. Polyfunctional active fillers

Filled polymer compositions have been finding in recent years increasingly wider applications in a wide variety of fields in engineering and the National Economy. The introduction of various solid disperse or fibrous fillers into the polymer matrix makes it possible not only to economise on the polymer (which is important in the case of scarce polymers) but also to improve greatly the physicomechanical and operating properties of the polymer compositions obtained.[62–67]

One of the main factors determining the strengthening effect of fillers in polymer compositions is the polymer–filler interfacial interaction, which depends on the nature of the polymer and of the filler surface.[64–67] The partial or complete binding of the polymer matrix to the surface of inorganic fillers makes it possible to vary widely the physicomechanical, rheological, thermal, electrical, and other properties of filled polymer compositions. As shown comparatively recently,[65–67] the occurrence of such interaction may be predicted beforehand in the preparation of filled polymer compositions by the method of polymerisation filling. The physical significance of polymerisation filling reduces to carrying out the polymerisation (or copolymerisation) in a heterogeneous system containing a filler subjected to the preliminary surface modification by the chemical binding of compounds capable of interacting with the polymerisable monomer or the growing macroradicals. Such fillers, which are capable of reacting via their surface functional groups with the polymerising monomer, can be classified as polyfunctional fillers. Table 1 presents examples of polyfunctional filler-initiators and polyfunctional filler-comonomers, which, in conformity with the structure of the compounds grafted to the surface, can either initiate polymerisation or can function as comonomers. The characteristics of the behaviour of polyfunctional fillers in polymerisation reactions are described in detail in a recently published review.[65,67] Here we shall deal only with the most important features.

The fixation of groups capable of polymerising on the surface of the filler makes it possible to obtain a polymer grafted to the surface as a result of the copolymerisation reaction. The fixation of such compounds on the surface can be achieved via the formation of strong chemical bonds, for example, by the interaction of the hydroxy-groups of aerosil or silica gel with functional carboxy- and halo-groups. Thus the possibility of achieving the copolymerisation of unsaturated ethers or acetals (obtained by the reaction of silanol groups on the silica gel surface with allyl alcohol or acrolein)

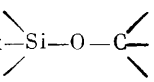
with butadiene has been described.[68] Alkoxy- or chloro-silanes, deposited on the surfaces, subjected to a preliminary treatment with an inorganic acid, of silica gel, aerosils, quartz, glass, etc. are widely used for the preparation of polyfunctional fillers.[69,71] The modification and grafting scheme is as follows [in relation to diethoxy(methacryloyloxymethyl)methylsilane]:

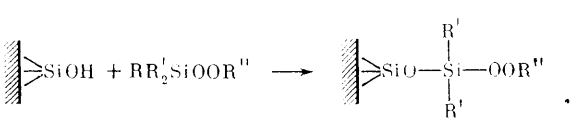


The density and hence the concentration of the monomeric groups bound to the surface can be regulated by varying the specific surface of the disperse filler and the conditions of the treatment of the surface.[67] The usual initiators are as a rule employed to initiate the polymerisation. During the polymerisation, a polymer not grafted to the surface is inevitably formed together with the grafted copolymer. The ratio of the grafted and non-grafted polymers depends on the degree of reaction, the content and surface area of the modified filler, and also the initiation procedure.[65,67]

It is possible to combine the stages involving the modification of the filler surface with the stage involving the copolymerisation and formation of the grafted copolymer.[73] The order in which the reactions between the modifier-copolymer and the filler surface and the copolymerisation reaction take place depends on the relative reactivities of the copolymerising groups and on the reactivity of the functional group which reacts with the surface silanol groups. However, when the modification and polymerisation stages are combined, it is not possible to avoid the excess consumption of the polyfunctional monomer, which is as a rule more scarce.

Another aspect of the chemical modification of the filler surface is the fixation on it of compouds with initating groups. For example, Dekking[74] achieved for the first time the synthesis of a monomer grafted to kaolin (or bentonite) via the emulsion polymerisation of vinyl monomers initiated by 2,2′-azobisisobutyramidine hydrochloride bound to the filler surface. Initiating systems for the surface-initiated polymerisation of vinyl monomers have been described. One of such systems consists of particles of calcium carbonate modified with 4-azobis-4-cyanopentanoic acid.[75–77]

Peroxidised fillers based on silicon-containing peroxides and not containing the hydrolytically weak  bonds are of great interest:[67,78]



where R = Cl, OR′, or NH_2 and R′ and R″ = alkyl. A convenient method for obtaining surface-peroxidised mineral fillers from modified vinyl-containing fillers by ozonisation has been proposed.[79,80] It must be emphasised that the use of peroxidised fillers with groups fixed to their surfaces makes it possible under certain conditions to synthesise monomers grafted to the filler surface without an admixture of non-grafted polymers. It has been shown[81] that, when an oxidation-reduction initiating system grafted to the surface of the hydroperoxide–iron stearate–benzoin system is used, it is possible to achieve the initiation of polymerisation exclusively on radicals grafted to the filler surface.

The kinetics of polymerisation with participation of polyfunctional fillers are associated, firstly, with the microheterogeneous nature of the polymerisation system and, secondly, with certain consequences of the fixed position of the monomeric or initiating group on the polyfunctional filler. The fixation of these groups on a solid surface leads to the restriction of the mobility of the comonomer groups or the primary initiating radicals and simultaneously to the concentration-dependent location of these groups on the surface. The set of these factors (taking into account the influence of the surface on the reactivity) leads to either the acceleration or retardation of the decomposition of the initiating group.[67] A common feature is the decrease of the initiating efficiency when polyfunctional filler-initiators are employed[67,75,78] and the dependence of the efficiency of the initiation of graft polymerisation on the concentration of the monomer in the surface region.

The fixation of the comonomers on the surface of silicon-containing fillers leads to a significant decrease in its reactivity relative to free radicals. The decrease depends on the structure of the monomer and on the nature of the surface.[82,83] An increase in the lifetime and a decrease in the probability of interaction with one another are characteristic of growing radicals fixed on the surface.[67] It has been noted that in this case the gel effect is manifested at earlier reaction stages than in the usual systems.[67,84] The increase in the molecular weight of the polymers formed as a result of the decrease in k_0 has been demonstrated.[76,81,82]

The prospects for the employment of polyfunctional fillers in the preparation of new polymeric composite materials are associated with the possibility of achieving high degrees of filling without disturbing the uniformity of the structure of the composition and with retention of high strength parameters.[85] An increased rigidity and thermal stability are characteristic of such systems. They are also distinguished from other systems in terms of their thermomechanical and rheological behaviour.[85,86]

The possibility of using polymers grafted to a disperse inorganic phase as sorbents for chromatography has been demonstrated recently.[87,88]

The polyfunctional components used to obtain polymer compositions were not touched upon to any extent in the preceding sections. The extensive possibilities for the use of polyfunctional fillers in the preparation of filled polymer compositions were examined in fair detail in previous publications. The prospects for the use of such fillers in polyolefin compositions capable of being cross-linked have also been examined in fair detail.[89,90]

In the general case, one should note that reactive oligomers and polymers readily obtained with the aid of polyfunctional components of polymerisation systems are exceptionally convenient for the formation of polymer compositions of a wide variety of types.

By varying the ratio of the components in the recipe, it is possible to vary within wide limits the structure and microheterogeneity of such compositions and hence their operating characteristics.

VI. Classification of polyfunctional components of polymerisation systems

The above analysis of studies concerning the possibility of using polyfunctional components in polymerisation systems makes it possible to undertake a new attempt at a classification of such components.

From the standpoint of polyfunctionality, the components of polymerisation systems can be most conveniently classified as a function of the nature and number of the reactive functional groups in the molecule taking into account the main purpose of the component. Accordingly, we can distinguish (1) polyfunctional monomers (PFM), (2) polyfunctional initiators (PFI), (3) polyfunctional surfactants or polyfunctional emulsifiers (PFE), (4) polyfunctional fillers (PFF), and (5) polyfunctional modifiers, etc.

The principal purpose of the components is determined by the nature of the reactive group which reacts under the given conditions (monomeric, initiating, etc.) and determines the course of the main reaction in the given process. Depending on the reaction conditions (temperature, medium, additives) the interaction in the polyfunctional component can proceed via different functional groups. Thus, depending on the polymerisation conditions, there is a possibility of the transformation of the functional groups of the polyfunctional component, for example, from a monomer to an initiator, and conversely. Naturally, the proposed classification may be expanded and transformed as new data are accumulated.

In conclusion of the consideration of polyfunctional components of polymerisation systems, we must emphasise the exceptionally dynamic nature of the development of this field of polymer chemistry. The approaches to the preparation of reactive polymers and the introduction of functional groups into the polymer matrix for a wide variety of purposes have been vigorously discussed at conferences in recent years. The data presented in this review will help to some extent to arrange systematically the available approaches in this field.

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Translated from *Uspekhi Khimii* 60 (7) 1406–1418 (1991) U.D.C. 541.64; 547.31

Polymerisation and characterisation of nitrile-terminated diacetylene materials

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ABSTRACT. A family of nitrile-terminated diacetylene materials were synthesised. Samples were prepared in various forms and polymerisation was performed photochemically and thermally. The resulting materials exhibited low molecular weights and were obtained in low yields. Although the diacetylene group had oligomerised, no evidence was found in support of $-C\equiv N$-chain formation. Thermochromism was exhibited by the irradiated 8-nitrile sample and a molecular interpretation of this chromic transition was discussed. Diffraction data implied that strong intermolecular interactions were present between adjacent nitrile groups in the low temperature phase. It is suggested that stresses are built up during polymerisation which cause the low degree of polymerisation and yield.

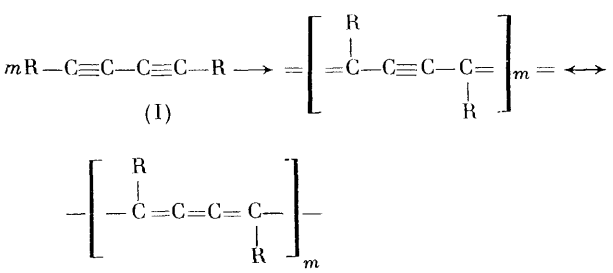
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I. Introduction

The polymerisation of diacetylenes has attracted a great deal of interest which was initially due to the unique nature of this solid state polymerisation reaction.[1–5] Initiation can be carried out simply by exposing crystals of the diacetylene monomer to high energy radiation (UV, gamma, X-ray) or by annealing the crystals at temperatures below their melting points. The resulting polymers are highly crystalline since there is relatively little movement of the molecules during polymerisation. As a result, fully extended conjugated backbones are formed which give rise to their deeply coloured appearance.



In recent years, polydiacetylenes have been reported to exhibit unique properties in fields such as non-linear optics, ferromagnetism, thermochromism/solvatochromism and electrical conductivity.[6–11] The polymerisation of acetylenes has also been the focus of much interest recently. Most of this interest has been a result of the relatively high electrical conductivity of this organic material when oxidised or reduced.[12–14]

Our previous work has concentrated on the polymers of a family of diacetylene materials of the form: $HC\equiv C(CH_2)_nC\equiv C-C\equiv \equiv(CH_2)_nC\equiv CH$. The polymers obtained from this class of diacetylene monomers are interesting not only from the viewpoint of polymer physics and crystallography, but, in addition, they have been observed to exhibit several properties unique for the crystalline solid state such as electrical and optical conductivity.[15–17]

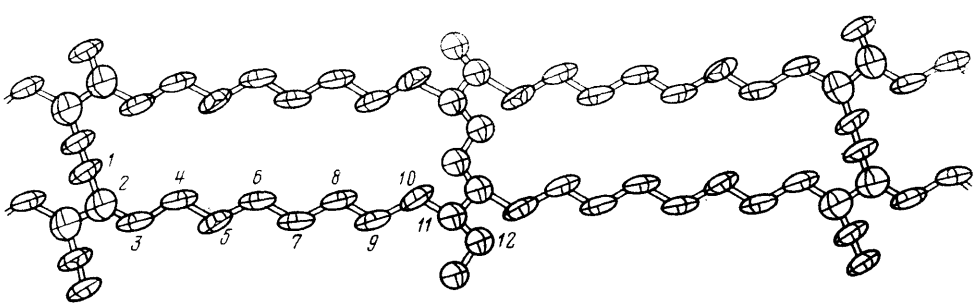
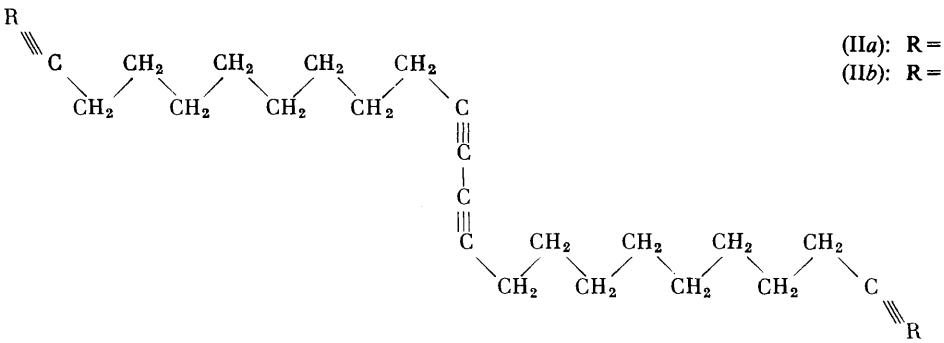


Figure 1. The *ac* section of the polymerised 1,11-dodecadiyne dimer. *1,2*, carbons in the PDA backbone; *11,12*, carbons in the PA backbone; *3–10*, methylene carbons.



(II*a*): R = CH,
(II*b*): R = N.

Figure 2. Nitrile terminated analogue of the 1,11-dodecadiyne dimer.

In addition to possessing a polydiacetylene backbone, the crystalline polymerised dimer of 1,11 dodecadiyne (II*a*) has been shown to have its adjacent acetylene groups polymerised in a head-to-head fashion. The resulting structure is composed of sheets of two dimensional networks of polyacetylene (PA) and polydiacetylene (PDA) backbones interconnected by eight methylene groups (Fig. 1).[18] Adjacent sheets are shifted one-half of a unit cell dimension along the "*a*" direction relative to one another. This results in a three-dimensional structure where polyacetylene chains are "sandwiched" between two polydiacetylene chains and *vice versa*. One possible explanation of its high room temperature conductivity of ca. 10^{-3} Ω^{-1} cm^{-1} utilised partial charge calculations in addition to π-electron overlap to propose a "self-doping" mechanism between sheets.[16]

One problem that persisted in working with this family of symmetric dimers (II*a*) is a result of the fact that they are aliphatic and contain no polar functional groups. Therefore, they are difficult to crystallise prior to solid state polymerisation. Due to this difficulty, a multistep synthetic route was developed with the intention that chemically pure species crystallise easier than the oligomeric mixtures which had been obtained previously using a controlled condensation reaction.[17] While the crystallisability of this diacetylene product was slightly increased, large macroscopic single crystals could not be obtained for other measurements.

We are presently considering a system analogous to the acetylene terminated dimers where the end groups have been replaced by nitrile groups (Fig. 2, II*b*). The added polarity of this functional group compared to substituted acetylene should aid the attempt to obtain large crystals of this polymerisable monomer. As an analogue to the acetylene terminated dimer, we can expect the diacetylene linkage to polymerise by the previously mentioned 1,4-addition reaction since the chemical distinction between the two materials is far removed from the diacetylene group.

The cyano group has been polymerised by cationic, anionic, radical and coordination catalysts.[19–23] Recent interest in these polymers has also focussed on their use as potential electrically conductive materials. However, the measured conductivities from various nitrile polymers were not as high as were anticipated ($10^{-8}-10^{-6}$ Ω^{-1} cm^{-1}). This is at least partially a result of the low crystallinity of the samples which is caused by the extra degrees of freedom allowed by the polymerisation conditions (solution or bulk liquid).

The radiation chemistry of the nitrile group has also been studied and is comparable to the acetylene group in that the main reaction is addition to the triple bond. The majority of work in this area has been performed on acetonitrile in both the solid and liquid phases. Although the degree of polymerisation is lower in nitrile compounds than in the acetylene compounds, the main product is a solid polymer. Ultraviolet and infrared spectroscopies are consistent with a conjugated $-C=N-$ chain.[24,25]

Perhaps the most interesting example of nitrile polymerisation is the one which occurs as polyacrylonitrile (PAN) is heated to 250–350 °C. The reaction of these nitrile groups in PAN and its copolymers was originally studied in order to understand the thermal discolouration of these polymers. The resulting material is sometimes referred to as "black Orlon" and typically exhibits 5–10 consecutively reacted nitrile groups.[26]

The colouration process has been studied using a variety of characterisation techniques. Thermal analysis has shown that an exothermic reaction occurs at about 250–350 °C.[27,28] Simultaneous gravimetric analysis indicates that a 10% loss in weight occurs at 270 °C, while spectral analysis of the products evolved showed that HCN and NH_3 are the major constituents. Hydrogen is suggested to be evolved at higher temperatures (450–700 °C). A series of papers by Coleman, et al.[29–31] utilises the advantages of FTIR spectroscopy to monitor the thermally induced reaction. It was found that the intensity of the nitrile absorbance steadily decreased as a function of degradation time. During the same period, numerous bands appeared which could be assigned to functional groups consistent with the proposed mechanism discussed in Ref. 21.

The conductivity of vacuum pyrolysed PAN has been studied by Lerner.[32] Using FTIR as a probe, it was reported that the pyrolysed PAN did not absorb iodine until the length of the cyclised segments exceeded a threshold value of 18 units. When the cyclicity exceeded this value, iodine could be absorbed by the polymer at room temperature to the extent of almost two iodine atoms per cyclised ring. The highest conductivity obtained was 10^{-2} Ω^{-1} cm^{-1}. Variable temperature studies yielded an activation energy of 0.59 eV and the room temperature mobility was calculated to be on the order of 10^{-5} cm^2/V sec. This is of the same order of magnitude as the mobilities of other polymeric conductors such as lightly doped polyacetylene.[33,34] Conduction in the iodine-doped pyrolysed PAN was suggested to be due to a hopping mechanism.

It was therefore decided to investigate the polymerisation and properties of the diacetylene-nitrile materials. This decision was made on the basis of the polarity and the polymerisability of the nitrile group, the electrical properties of the resulting nitrile polymers and the assumption of non-interaction between the nitrile and diacetylene groups. Since these materials are not commercially available, a synthetic route was devised to obtain the diacetylene nitrile analogues.

II. Experimental

In order to perform a more complete study, it was desired to obtain all members of the diacetylene-nitrile family with the number of methylene groups varying between 0 and 8. Materials with fewer than 2 methylene groups had to be prepared differently due to their reactivity. The synthetic pathways used here are illustrated in Fig. 3. Further synthetic details can be found elsewhere.[35] The convention used for nomenclature here and throughout takes the form of "*n*-nitrile dimer", where "*n*" represents the number of methylene groups present between the diacetylene and nitrile groups.

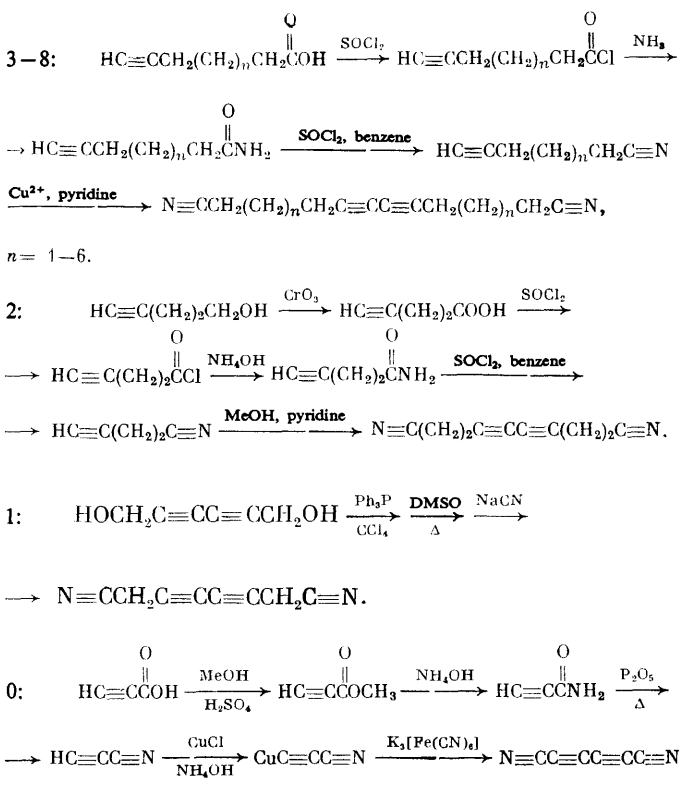


Figure 3. Synthetic pathways used in the preparation of the 0-through 8-nitrile diacetylene materials.

3-Through 8-nitrile synthesis:

A sample of acetylenic acid was reacted to form its amide using the method of Bishop.[36] The dehydrolysis of the amide to form the nitrile was accomplished using the method described by Krynitsky and Carhart.[37] Yields were typically on the order of 80%. The acetylenic nitrile was oxidatively coupled using a modified Glaser reaction[38] to give the desired product. All products were purified using column chromatography.

2-Nitrile synthesis:

The oxidation of 4-pentyn-1-ol to form 4-pentynoic acid was performed following the method of Heilbron, et al.[39] The acid could then be converted to the desired product as described above.

1-Nitrile synthesis:

The diacetylenic diol, 2,4-hexadiyn-1,6-diol, could be directly converted to the desired nitrile compound using the procedure described by Brett, et al.[40] to replace the hydroxyl groups with nitriles.

O-Nitrile synthesis:

Cyanoacetylene could not be obtained through commercial sources and was therefore prepared using the method of Moureu and Bongrand.[41] The coupling of the cyanoacetylene was accomplished using a cuprous derivative intermediate as described by Brockman.[42]

III. Polymerisation of nitrile diacetylenes

Sample preparation. Numerous experiments were performed on all of the synthesised nitrile materials in an attempt to polymerise both the diacetylene and nitrile functional groups. Three methods were employed to prepare samples for the solid state polymerisation experiments. The samples thus prepared were in the form of macroscopic crystals, thin microscopic polycrystalline films and thick microscopic polycrystalline films.

Chromic studies were performed on a Perkin-Elmer Lambda Nine UV/Visible/NIR spectrometer. The thermal characterisation was carried out using a Perkin-Elmer DSC-7 differential scanning calorimeter equipped with a workstation. X-Ray diffraction was measured using a Philips Diffractometer (Model APD 3520) with nickel filtered CuK_α radiation.

Ultraviolet polymerisation. Ultraviolet (UV) irradiation was performed at an intensity of 1600 μW/cm^2 at a wavelength of 254 nm. Ultra High Purity (UHP) argon was used as a purge gas in order to provide an inert atmosphere during irradiation. Samples were intentionally kept thin in order to minimise the surface absorption of UV light by the coloured reaction products. Exposure times of 5, 10, 20 and 45 minutes were used.

Gamma polymerisation. Gamma irradiation was carried out using a Gammacell 220 ^{60}Co source. The intensity of the source at the sample position has been calculated to be 48.2 krad/hour. The samples were flushed with UHP argon and sealed in glass containers before placing them into the source. The sample temperature could be controlled either internally or externally.

Thermal polymerisation. Polymerisation attempts at elevated temperatures were performed using a vacuum oven. Before heating, the oven was repeatedly purged with UHP argon and evacuated. Temperatures of 225, 250 and 300 °C and treatment times of 5, 15, and 30 hours were utilised.

IV. Results and discussion

The 0-nitrile dimer was found to be unstable during the course of these experiments and, therefore, no meaningful data could be obtained regarding its polymerisability.

It is known from numerous studies on other compounds that both polydiacetylenes and poly(nitriles) are highly coloured due to the conjugation present in the polymer backbone. It was, therefore, immediately noted that the absence of a coloured product from the various treatments in the case of the 1-, 2-, 3- and 4-nitrile materials probably inferred that no polymerisation had occurred. In addition, the physical appearance of the original diacetylene compounds and their experimental products were identical. This conclusion was substantiated by the infrared spectra of the monomer and irradiated samples which were identical throughout the scanned region ($3600-450$ cm^{-1}). A possible explanation for this observation will be discussed later.

A synopsis of the polymerisation attempts on the remaining crystalline diacetylene-nitrile materials (with $n > 4$) and the general results are listed in Table 1. Overall, the various methods employed were unsuccessful in producing a material with fully polymerised diacetylene and nitrile groups.

Table 1. Synopsis of polymerisation attempts and the general observations.

Treatment	Appearance	Physical characterisation	Spectroscopy
UV	blue → orange (R.T.)	melts, soluble	No C=N–
Gamma	blue → orange (R.T.)	melts, soluble	No C=N–
UV/gamma	blue → orange (R.T.)	melts, soluble	No C=N–
Heat	melts/evaporates	—	—
UV/gamma/heat	blue → orange → black	insoluble, not crystalline	No C≡N, –C=N–
n-Butyllithium	viscous yellow liquid	insoluble in benzene	No C≡N

The ultraviolet treatment of the crystalline nitrile dimers at subambient temperatures resulted in materials which are blue in reflected light. When these products were allowed to warm to room temperature, they underwent a transition from blue to reddish-orange in colour. In addition, the crystal habit was destroyed and the resulting material exhibited an appearance which could best be described as severely fragmented, pieces of orange film which precipitated from the crystallisation solution or the bulk melted dimer depending on which sample preparation was used. The coloured product was isolated in low yield (2–3%) and was found to be soluble in a variety of common solvents (e.g. acetone, methylene chloride, carbon tetrachloride and tetrahydrofuran). Infrared samples were prepared by solution casting a film onto a KBr plate. The resulting spectra gave no indication of polymerisation through the C≡N bond. This was determined by the intensity ratio of the C≡N stretching band (2240 cm^{-1}) relative to that of the aliphatic C–H stretching bands which remained constant throughout the radiation treatment. In addition, no absorbances which could be attributed to a poly(nitrile) chain were found (e.g. conjugated –C=N– bonds at 1570 cm^{-1}, C=N linkages at 1640–1610 cm^{-1} or C–N bonds at 1220 and 1145 cm^{-1}).[28,43]

Since the coloured product was soluble in tetrahydrofuran (THF), gel permeation chromatography could easily be used to follow the conversion of the diacetylene-nitrile dimers. The elution volume/molecular weight relationship was calibrated with monodisperse polystyrene standards using THF as a solvent. The maximum extent of polymerisation was not large. Using the 8-nitrile dimer as an example, the approximate maximum degree of polymerisation was calculated to be ca. 12 assuming that the calibration of the GPC data is valid in this low molecular weight range.

The results of experiments performed using gamma radiation for initiation were very similar in many respects. A blue sample at subambient temperatures transformed into the orange form after warming to room temperature. Infrared spectroscopy suggested that the C≡N groups did not appreciably react using this technique. Solubility and maximum molecular weight data were also in agreement with UV results. It was interesting to note that the yield of coloured product, although low in all cases, was approximately equal for the UV and gamma treatments in samples prepared in similar manners. That is Yield (crystals, UV) ≈ Yield (crystals, gamma) or Yield (thin film, UV) ≈ Yield (thin film, gamma). However, the yields using thin films were larger than those using thick films or crystals. Since the major difference between these samples lies in the surface area/volume ratio, which is largest for these thin samples, it would appear to be a surface related phenomenon. Certainly, it cannot be related to a surface absorption effect since the penetrating power of gamma radiation is much higher in this case than UV. But the observation does appear to be related to the relative surface area and this will be discussed later in more detail.

Several other solid state polymerisation techniques were utilised in an attempt to polymerise the nitrile group and increase the molecular weight and yields. A combination of UV treatment followed by gamma irradiation at low temperature was not found to be statistically different from either of the two separate treatments. Although expected, heat treatment of the nitrile dimers under vacuum similar to that used in the cyclisation of polyacrylonitrile resulted in the material melting and finally evaporating. A combination of UV irradiation followed by gamma irradiation, which was then followed by heat treatment, gave rise to a black-coloured product. X-Ray diffraction suggested that the material was not crystalline. Since the product was not soluble, infrared samples were prepared using a KBr pellet. Analysis of the spectra gave no indication that –C=N– bonds formed even though the C≡N band at 2240 cm^{-1} was absent. The presence of broad bands centred around 1636 cm^{-1} suggested that a dehydrocyanation reaction[26] may have occurred to form C=C linkages. Crosslinking may then randomly occur through these groups by the radical species which can form at elevated temperatures.

1. Thermochromism

The ability of a material to exhibit a shift in the UV/visible absorbance maximum with a change in temperature is referred to as thermochromism. A large number of polydiacetylenes have been shown to exhibit these effects. Initially, these chromic changes in polydiacetylenes were thought to be a manifestation of an electronic transition along the polymer backbone.[44] This can be visualised as a change in the bonding arrangement from the acetylenic to the butatrienic mesomer. More recently, experimental evidence suggests that the chromic transition in crystallisable samples is brought about conformationally by a transition which causes a decrease in the effective conjugation length of the polydiacetylene backbone.[45–47] This reduction in conjugation can be induced in the polydiacetylene backbone by either a crystal–crystal transformation[48] or by disordering the flexible side groups, if present.[49] It should be noted that the order–disorder transition can be caused not only by thermally randomising the side groups, but also by other methods which increase the entropy or disorder of these groups. An example of this can be found in situations where the polydiacetylene chains are soluble. When the solvating power of the solvent is reduced in these cases by the addition of a miscible non-solvent, intramolecular forces predominate over the intermolecular (solvating) ones and the conformation of the extended polydiacetylene backbone is regained. With the increase in effective conjugation length, a bathochromic (red) shift is observed in the visible absorbance maximum. This reversible, solvent-induced change of conformation in polydiacetylenes is commonly referred to as the coil-to-rod transition,[50] which emphasises the nature of the polydiacetylene chain in solution. The ease of reversibility of this transition has been attributed to the presence of functional groups which are capable of intrachain interactions (e.g. urethanes, esters, etc.). Although a sizable amount of work was performed in this area, a controversy still exists as to whether the chromic transition is a result of an isolated chain event[51–54] or an aggregation event.[55,56]

Polydiacetylenes have also been observed to undergo irreversible chromic transitions.[57] A number of these irreversible changes can occur during polymerisation. It is well established that the solid state polymerisation of diacetylenes requires a simultaneous rotation and translation of the diacetylene rod.[58] The movement of this set of atoms in each of the reacted monomeric units leads to the production of large stresses within the crystalline material for some diacetylene compounds. At some point, these stresses are relieved in the form of a crystallographic phase change and/or an order–disorder transition.[47] Disorder in the side groups can induce a conformational change in the polydiacetylene backbone as discussed above. This has the effect of reducing the coordinated conjugation length and a chromic shift is observed.

In the present study, the family of diacetylene-nitrile materials which could be polymerised all exhibited similar thermochromic characteristics. Since most of the data could easily be obtained using the 8-nitrile dimer, those data will be discussed throughout this section. Generalisation to the other materials may be implied except where noted.

As was mentioned previously, the nitrile materials which polymerised at subambient temperatures in the solid state all exhibited a blue colour in reflected light. When allowed to warm to room temperature, the result was a breakup of the crystal habit and the material became reddish-orange in colour. This product was isolated and a film was solution-cast onto a clean quartz plate. A UV/Visible spectrum of the resulting reddish-orange 8-nitrile material exhibited its lowest energy optical transition at 528 nm (18 900 cm^{-1}).

Since the blue phase is stable only at subambient temperatures, an isothermal spectrum could not be obtained for it, due to the lack of a sample cooling device. However, several qualitative spectra were obtained on the blue phase using quick scans over a short range. A piece-by-piece comparison of the spectra, which were cumulatively taken over the range of 300 nm to 700 nm, indicated that the lowest energy optical transition for the blue phase occurs at about 628 nm (15 900 cm^{-1}). These values are in good agreement with those reported for most polydiacetylene crystals or films which exhibit the chromic transition.[59–62]

Numerous recent studies have shown that the optical transition is accompanied by a loss of planarity in the polymer backbone.[45,59,63] A variety of experimental techniques have been used in these studies. For example, infrared spectroscopy has been used to monitor the disruption of hydrogen bonding in the side groups and the formation of "free" N–H in the polydiacetylene, poly-3BCMU (R = $(CH_2)_3OCONHCH_2COOC_4H_9$). Furthermore, ^{13}C NMR chemical shift and relaxation time data has been used to explain the post-transition changes as resulting from a decrease in the delocalisation of π-electrons and thus a decrease in the conjugation length.[63]

Studies performed on an optical microscope equipped with a hot stage in conjunction with DSC measurements have shown that the blue-red transition temperature correlates with the melting temperature of the original dimer. It appears that the melted dimer may act as a solvent for the polymer side groups. As will be discussed later, a large amount of stress is incurred on polymerisation. Once this stress is relieved by disordering the side chains, which in turn decreases the conjugation length of the polydiacetylene backbone, the order present in the original unpolymerised material cannot be recovered. As a result of the unrecoverable conjugation length, the transition from red back to blue does not occur.

It should be noted that another chromic transition, from reddish-orange to yellow, can be observed in these materials. This has been accomplished both in the solid state (thermochromism) and in solution (solvatochromism). Furthermore, it appears to be reversible unlike the previously discussed transition. A similar transition has been observed in other polydiacetylenes such as poly-3BCMU, poly-4BCMU and the polymerised dimers of α,ω-alkadiynes.[59,62,64,65] It had been suggested that the low temperature transition (blue–red) was due to the melting of the side groups whereas the high temperature transition (red–yellow) was a result of the polydiacetylene backbone becoming disordered.[61]

2. Structure work

In an attempt to understand at the molecular level why the yields and molecular weights of the products were so low, X-ray structure analyses of the unpolymerised dimer, the blue phase of the polymer in solid solution with the monomer and the reddish-orange phase of the polymer were sought for the 8-nitrile material.

Both the unpolymerised dimer and the partially polymerised blue phase undergo a transition if allowed to warm to room temperature. Various attempts at subambient-temperature single crystal work were unsuccessful, therefore, polycrystalline diffractometer data at subambient temperatures was taken instead. The reddish-orange phase was obtained from the blue phase by allowing the sample to warm to room temperature. This polymeric phase transition was accompanied by the melting of the dimer which constituted the

larger fraction of the sample. Note that all the samples include a rather large percentage of unpolymerised dimer. The results are shown in Fig. 4. All three spectra were taken on approximately equal amounts of material and the scales for each run are identical.

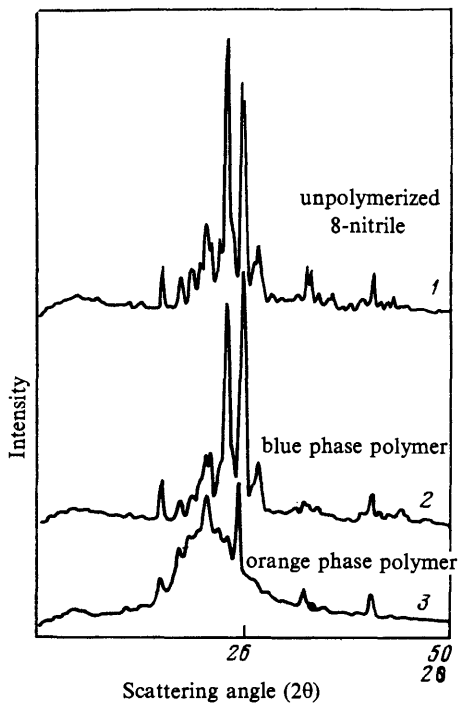


Figure 4. X-Ray diffractograms illustrating the crystallographic changes which accompany the polymerisation and the blue to reddish-orange transition in the 8-nitrile material.

A number of crystalline peaks can be observed in the top two diffractograms. Upon closer examination, it can be noted that peak positions and intensities are nearly identical for the unpolymerised dimer and the blue phase. There is a slight shifting of some of the peaks in the polymerised sample to larger scattering angles suggesting some contraction in the unit cell upon exposure to radiation. This would be expected in the solid state polymerisation of unsaturated compounds. In comparison to the other two diffractograms, the orange sample displayed a broad amorphous peak with some fine structure still present. The amorphous contribution is largely due to the melted dimer which is present in the sample. The observed crystalline peaks are located approximately at the same scattering angle as those seen in the blue phase. Some shifting to larger *d*-spacings is noted and can be attributed to a release of structural constraints which will be discussed later.

d-Spacings of the unreacted 8-nitrile dimer were measured and a unit cell which fits the data was determined by the method of least squares (see Table 2).

X-Ray density calculations performed on the unit cell indicated that there were two molecules per unit cell. A ball and stick model of the molecule was constructed using standard bond lengths, bond angles and dihedral angles. One molecule was placed at each corner of the unit cell and was centred at the midpoint of the diacetylene rod. The other molecule could be placed at (0, ½, ½), (½, ½, 0) or (½,½,½) in fractional coordinates. There are not enough data at the present time to determine which position is correct. The dimensions of the unit cell imply that there is some interdigitation of the nitrile groups on adjacent molecules. This interdigitation could be in either the *c* direction or the *b* direction (see Fig. 5).

Table 2. Unit cell data for the 8-nitrile material.

a=26.03 Å,	α=90.0°	
b=8.10 Å,	β=92.8°	Volume = 1122.4 Å^3
c=5.33 Å,	γ=90.0°.	Density = 0.960 g/cm^3

Considering the former case, the strong polar interactions of the adjacent nitrile groups obviously stabilise this structure. In addition, the intermolecular distance and orientation of the diacetylene rods in the polymerisation direction meet the requirements for diacetylene polymerisation as described by Baughman.[58] The other possibility for interdigitation would also have the polar interactions to stabilise the structure, but in order for these groups to be positioned as shown, the angle that the diacetylene rod makes with the *c*-axis must be larger than in the previous case. A qualitative calculation of this angle (ca. 57°) suggests that the diacetylene molecule will not polymerise according to Baughman's criteria.[58] From the experimental observations on the 8-nitrile material, it can be concluded that the diacetylene group does react and therefore the former model is more probable.

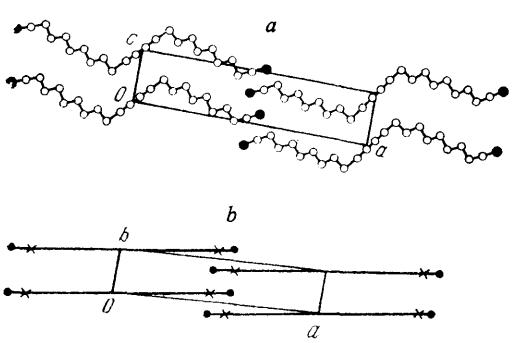


Figure 5. Projections of the 8-nitrile material illustrating nitrile interdigitation in the (*a*) *c*-direction and (*b*) *b*-direction. Hydrogens have been omitted for clarity, ● = nitrogen.

The reason as to why the diacetylene compound does not polymerise to a large degree can now be addressed. From a comparison of the crystal size and the rate of crystallisation for the

nitrile dimers and their acetylene terminated analogues, it is apparent that the polar nitrile groups interact strongly with each other. The interaction is strong enough such that one may consider the interdigitated nitriles to act as non-covalent "tie-points". Once the polymerisation of the diacetylene group is initiated, the rotation and translation which accompanies the diacetylene polymerisation is restricted at a certain point. This is a result of stresses which are built up with the addition of each molecule to the growing chain (lattice mismatch between dimer and polymer). Energetically, one may consider that the decrease in free energy associated with the polymerisation of the diacetylene group (with its required movement) is not great enough to overcome the intermolecular attraction of adjacent nitrile groups. This explains why the yield and the molecular weights of the reaction products are so low. Since the diacetylene polymerisation is considered to be topochemical, initiation occurs homogeneously throughout the crystalline lattice.[66] Thus, one would expect relatively similar yields for samples of the same mass even though the surface area may be different. The observation that this does not occur suggests that the polymerisation stress may be relieved at the crystal edges or faces by relaxation of the polymer.

The blue-to-red colour change exhibited by the polymer can be explained as a crystal–crystal transition or as an order/disorder transition. From the polymer yield calculations, the blue polymer phase can be considered to be dissolved in a crystalline matrix of dimer. As the temperature is increased, the dimer melts and can solvate the polymer side groups in the conventional sense. The disorder induced in these side groups can be covalently transmitted to the polydiacetylene backbone which is then manifested by a change in colour. However, the presence of crystalline peaks in the diffractograms of the orange phase implies that order is still present in this phase. This observation would favour the suggestion that the polymer itself undergoes a crystalline phase change once the structural constraints of the monomer are released as the monomer melts. Crystallographic phase changes which cause a chromic transformation have been observed in other polydiacetylene materials.[48,67] Finally, one must consider the possibility that a combination of these effects may account for the observed results. There are not enough data at the present time to determine which of these explanations governs the chromic transition.

At this point, some explanation must be given as to why the 8-nitrile material was chosen for most of the experimental work and discussion. Quite simply, this material exhibited the highest yields and molecular weight of all the nitrile dimers which were prepared. In consideration of the cyclisation reaction in polyacrylonitrile, it was initially believed that the nitrile groups in the irradiated 8-nitrile material would not polymerise because the long methylene chains were too flexible. As a result, adjacent nitrile groups could not be brought together into position to react. It was believed that after polymerising the diacetylene groups in nitrile dimers with fewer methylenes ($n < 8$), the nitrile group could be subsequently polymerised thermally if not photochemically. However, the number of nitrile groups per unit volume increases as the number of methylene groups decreases and the strong electrostatic interactions of the C≡N groups prevent the diacetylene polymerisation from occurring at all at a certain point.

3. Further work

Other attempts at obtaining a material which possessed both conjugated polydiacetylene and polynitrile chains were investigated. One of these involved varying the crystallisation procedure since there is a possibility that the diacetylene materials may exhibit polymorphism with one of the phases being more reactive than the others.[68,69] Crystallisations in various solvents and at different rates were performed. However, the results indicate that no different phases were achieved.

A number of procedures which may result in the simultaneous crystallisation and polymerisation of the materials were also attempted. Diacetylene materials which are analogous to those used in the present study have been reported to simultaneously crystallise and polymerise from solution upon exposure to gamma radiation.[70,71] This procedure was attempted using the nitrile materials but no polymer was observed before radiation damage took place.

Nitrile groups have been polymerised electrochemically from solution as was demonstrated by Tourillon, et al.[72] using acetonitrile. They have also been polymerised from pendant groups on polyacrylonitrile which had been deposited on the electrode.[43] It is known that polar species such as the C≡N group are oriented by an electric field and this may aid in the polymerisation process. However, the various electrochemical and chemical methods which were performed gave no evidence of the desired effect.

The authors would like to acknowledge the support of the Office of Naval Research (grant number N00014-83K-0246).

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Translated from *Uspekhi Khimii* **60** 1419–1448 (1991) U.D.C. 541.64;678.674:542.953.678.675

Progress and problems in activated polycondensation

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ABSTRACT. New polycondensation methods for the synthesis of polymers based on non-traditional ways of activating monomers are classified. For the sake of convenience and as a contrast to traditional low-temperature polycondensation, it has been proposed to combine the new methods under the general title of "activated polycondensation". It is shown that the most versatile method in terms of synthesis is that based on the activation of the "leaving" part of the biselectrophile—the "activated amide and ester method". The considerable future potential of the latter is demonstrated. Questions relating to the synthesis, structure, and reactivity of different classes of activated diesters are examined. The possibility of synthesising various heterochain polymers by reaction of activated diesters with di- and poly-functional nucleophiles is demonstrated. The advantages of this method for the synthesis of polymers are established.

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I. Introduction

It is widely known that two methods are principally used to synthesise large chains of macromolecules—polymerisation and polycondensation.

Each of these methods has its distinct features. Without analysing them in detail, we shall merely note that in terms of synthesis the polycondensation method has advantages which are reflected in particular by the fact that it can be used to obtain a higher proportion of novel polymers.[1]

In turn, it is usual to subdivide polycondensation processes into two types—high-temperature and low-temperature.

With high-temperature polycondensation[2] (carried out at 200–300 °C in a molten state or in a high-boiling organic solvent) it is possible to use monomers (mainly biselectrophiles) with low reactivity either in an "inactive" state or as their low-activity derivatives (for example, dicarboxylic acids and their alkyl esters for the synthesis of polyamides, polyesters, etc.). High-temperature polycondensation, however, occurs in many cases at a low rate and is accompanied by numerous side reactions which lead to decomposition of the functional groups (and hence to disruption of their equimolarity) as well as to the formation of anomalous chain units ("unit heterogeneity").[3] In a number of cases such as when aromatic diamines are used, high-molecular-weight polyamides are not formed at all.[4]

In such cases low-temperature polycondensation methods (most frequently carried out over a temperature range from –30 to +50 °C in an organic solvent or by phase transfer) are more effective. These are based on the use of activated monomers—acid dichlorides, cyclic dianhydrides, bischloroformates, diisocyanates, and others.[5–8]

These methods have contributed to the further development of macromolecular chemistry and to the solution of many practical problems, but they are characterised by a number of disadvantages, the main ones being:

1) numerous side reactions (namely, the "multi-channelling" of the process),[3,5–8] leading to a restriction in chain growth and also to "unit heterogeneity";[3]

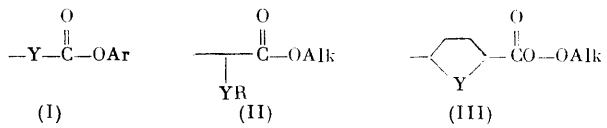
2) the need to synthesise individual activated monomers (acid dichloride, dichloroformate, or diisocyanate) that are not possible to obtain in a number of specific cases;

3) limited synthetic opportunities, for example, in the development of novel macromolecular systems, particularly of functional polymers.

These factors have in many respects determined during the last 10–15 years the development of new polycondensation methods of polymer synthesis based on nontraditional ways of activating monomers, the so-called "activated polycondensation".

Five main variants of activated polycondensation can be distinguished in relation to the method of activating the monomers.

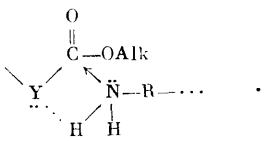
1) "Activated alkyl esters" method. This may also be called the "skeletal activation" method, and it is based on the introduction of heteroatoms (O, S, N) into the skeleton of a dicarboxylic acid at the α- or β-position relative to the carbonyl group of the ester;[9–21] the heteroatom can form part of the main molecular chain [compound (I)], of side groups (II), or a heterocycle (III).



(I) (II) (III)

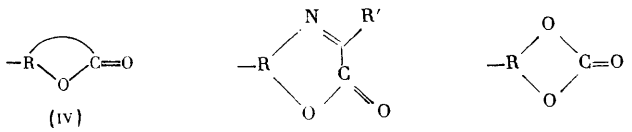
Y = O, S, NR_2, where R = H or a univalent radical.

The reactivity of alkyl diesters of the type (I)–(III) increases approximately by a factor of 10^1-10^4 compared to the unsubstituted analogues,[22] and they react with aliphatic diamines under quite mild conditions. The acceleration in these cases is mainly achieved through the so-called "anchor effect":



The inductive effect of heteroatom Y may also play a decisive role, particularly if it is situated at the α-position.

2) "Active rings" method. Many bifunctional monomers which contain different heterocycles—lactones (IV),[23–27] azalactones (V),[28–40] cyclic carbonates (VI),[41–44] and others—as functional groups exhibit a higher activity than their linear analogues as a result of intramolecular electronic effects or ring strain, and they react with nucleophiles (mainly with highly basic aliphatic diamines) under mild conditions to give high-molecular-weight polyamides, including those with different functional groups.



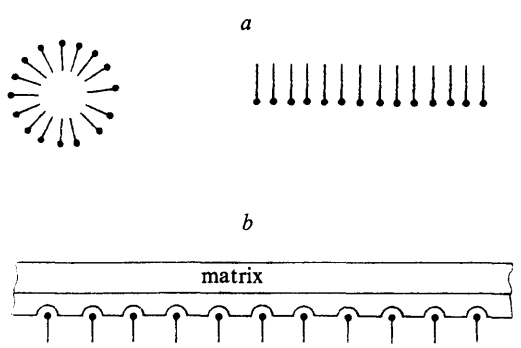
(IV) (V) (VI)

3) "Direct polycondensation" method (or "activation *in situ*"). The reaction between dicarboxylic acids or carbon dioxide and bisnucleophiles (mainly aromatic amines and bisphenols) occurs under mild conditions in the presence of various condensation agents (B).

$$n\text{HOOCRCOOH} + n\text{HY} - \text{Ar} - \text{YH} \xrightarrow{B} -(-\text{CORCOYArY}-)_n-,$$

Y = NH, O.

This modification of polycondensation as well as the condensation agents used have been reviewed by Katsarava.[45]



where | – is a molecule of monomer

Figure 1. Polycondensation of "organised molecular masses". Possible molecular orientation: *a*, in micellar and liquid-crystalline forms; *b*, in matrix forms.

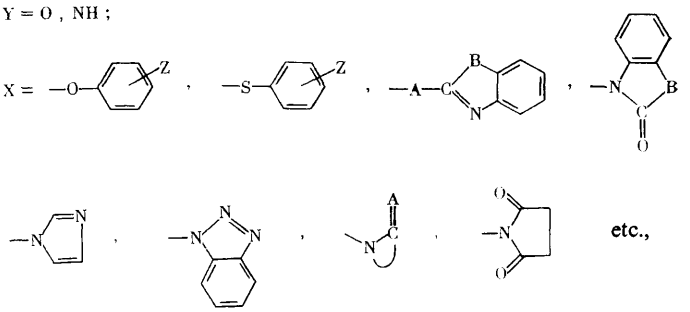
4) "Organised molecular masses" method. It has been shown that a considerable acceleration of the reaction that forms the basis of many polycondensation processes can be achieved by the formation of organised molecular masses (according to Oakenfull[46] this acceleration in a number of cases reaches a factor of 10^6, which corresponds to the level of enzyme processes) of a micellar or liquid-crystalline phase[45–47] (Fig. 1*a*) or by the introduction of various matrices, more often those that are polymeric in nature, into the reaction medium[58–67] (Fig. 1*b*).

In these systems the acceleration is achieved either through the favourable relative configuration of the monomers in space or through the increase in their local concentration. We should note that the formation of organised molecular masses not only accelerates the reaction but also alters its course. For example, when α-amino acid derivatives are used, high-molecular-weight polypeptides are formed instead of cyclic diketopiperazines.[47–49] A change in the course of the reaction was also detected in the polycondensation of urea with formaldehyde in the presence of a polyacidic matrix.[68,69]

5) "Activated esters and amides" method. In contrast to the "activated alkyl esters" method, this method is based on activation of the leaving groups, i.e. that part of the monomer which is eliminated as a low-molecular-weight by-product of polycondensation.

$$n\text{XOC—R—COX} + n\text{HY—R'—YH} \xrightarrow[-2n\text{HX}]{} \longrightarrow -[-\text{CO—R—CO—Y—R'—Y}-]_n-,$$

Y = O, NH;



(A, B = O, S); Z = electron-withdrawing substituent.

Attempts to use activated dicarboxylic acid derivatives other than acid chlorides in polycondensation (polyamidation) were made as early as the 1950s. Thus, for example, mixed anhydrides of dicarboxylic acids and diesters of orthophosphoric acid[70] or monoesters of carbonic acid[71] as well as dinitrodiamides[72] and diimidazole derivatives of dicarboxylic acids ("activated amides")[73] have been used. However, the majority of these compounds, frequently obtained in a fairly complex manner, on reaction with diamines only gave low-molecular-weight polyamides that were of little use for practical application. This circumstance would appear to have played not an inconsiderable role in causing this promising method to have remained without propert attention being given to it until the beginning of the 1970s.

At the end of the 1960s it was shown that activated esters[74] and "cyclic activated amides" such as benzoylenebenzimidazoles[75] could be used for the synthesis of heterochain polymers. Systematic studies of this modification of activated polycondensation, however, were only started in the 1970s.[76]

Formally the "leaving group" method is similar to traditional low-temperature polycondensation based on the use of acid dichlorides, but it has wider synthetic possibilities because of the use of "leaving groups" of varied nature and structure as well as "single-channelling", namely, the absence (or minimal contribution) of side reactions.

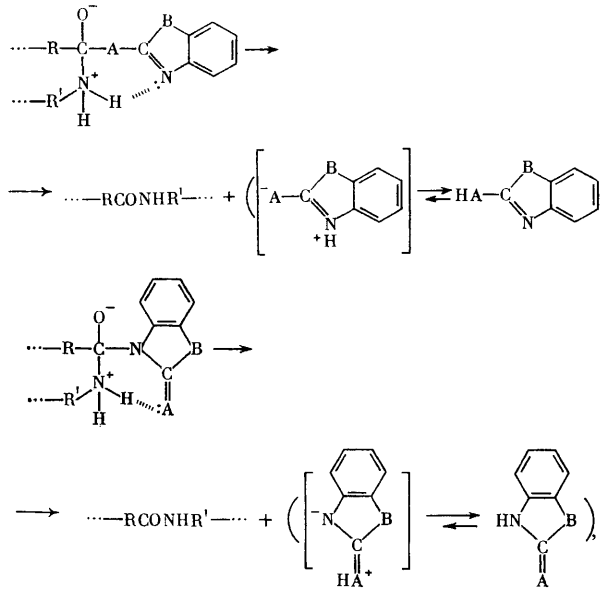
The activation of the monomers (biselectrophiles) in the "leaving group" method is achieved as follows:

1) by introduction of electron-withdrawing substituents into the leaving group or by the use of sulphur-containing leaving groups (thioesters), which are more active than those containing oxygen because of the lower basicity (better stabilisation of the negative

charge in the leaving anion X^-)† resulting from the larger radius of the sulphur atom;

2) by using nitrogen-containing leaving groups (activated amides), which when having the same pK_a values are approximately 10^4 times more reactive than oxygen-containing leaving groups;[77]

3) by making use of anchimerically assisting leaving groups



A, B = 0.5.

Anchimeric assistance

Thus, activated diamides of dicarboxylic acids, in particular those with anchimerically assisting leaving groups, have high acylating potential and are used for the synthesis of high-molecular-weight polyamides under mild conditions (see the study of Katsarava[76] and the references in it). However, they are characterised by a number of disadvantages, which can be mainly classified as: 1) the relatively high cost and complexity of obtaining the activating agents—various benzazoles and other nitrogen-containing heterocycles; 2) the synthesis of activated diamides, mainly via the corresponding acid dichlorides, which imposes certain synthetic restrictions on the method (the synthesis of only activated diamides of dicarboxylic acids and hence a single class of heterochain polymers—polyamides—is described in the literature).

In relation to the above, activated diesters have greater potential as monomers, displaying the following advantages: 1) availability and economical price of the activating agents XH (substituted phenols, etc.);[76] 2) simple "direct" syntheses of activated diesters that achieve complete independence of the method of activated polycondensation; 3) the possibility of controlling the reactivity of activated diesters and hence the polycondensation processes over a wide range by varying the leaving groups together with the low tendency of diesters to undergo side reactions; and, what is particularly important, 4) the ready availability of activated esters of different classes and hence the possibility of synthesising various heterochain polymers (Scheme 1) using activated polycondensation.

It is appropriate to mention here that, starting in the middle of the 1950s, the "activated ester" method has been successfully used in peptide chemistry for obtaining both pure peptides[78–81] and poly(amino acids)[82,83] and regularly alternating polypeptides.[84–87]

In drawing a parallel between peptide chemistry and activated polycondensation, the considerable differences between them should be pointed out. In peptide synthesis the problem of the retention of optical purity is central. Of course, single-channelling of the reaction is of considerable importance in multistage peptide synthesis, but the small contribution from side reactions (1–5%) is not so significant. In polycondensation single-channelling of the reaction acquires particular significance—activated monomers (or low-molecular-weight reaction products) should not undergo side reactions with monomers of an opposite kind, solvents, or products being formed. At the concluding stages of polycondensation the rate of reaction (fundamental act) is of crucial significance—it must be high so as to achieve chain propagation with the vanishingly small concentrations of terminal functional groups.

Scheme 1

Activated diesters of dicarboxylic acids XCORCOX	→	Polyamides Polyesters Polybenzazoles
Activated biscarbonates of diols XCOOROCOX	→	Polyurethanes
Activated carbonates XCOX Activated biscarbamates XCONHRNHCOX	→	Polyureas

Therefore the questions relating to the synthesis, structure, and reactivity of activated diesters, as well as their tendency to undergo side reactions, are key ones in activated polycondensation and in the present review considerable attention is given to them.

II. Synthesis, structure, and reactivity of monomers. Model reactions

1. Synthesis of activated diesters

The reactions which form the basis of the synthesis of different classes of activated diesters are shown in Scheme 2. These monomers can, of course, be readily obtained via the corresponding traditional forms of activated monomers—acid dichlorides, bischloroformates, and diisocyanates—a genetic link being retained between activated polycondensation and traditional low-temperature polycondensation. This approach is justified in a number of cases. It can be used to change to monomers of a "milder" nature, leading to better results in the synthesis of polymers (see below). However, for a number of reasons, as mentioned above, direct methods of synthesising activated diesters have greater future potential.

Activated diesters of dicarboxylic acids are synthesised using free dicarboxylic acids and condensing agents according to reaction (1*b*) or transesterification agents according to reaction (1*c*)[76,88–91] (see Scheme 2).

Activated biscarbonates of diols can be obtained by the reaction of diols with suitable chloroformates [reactions (2*b*) and (2*c*)] or carbonates [reaction (2*d*), and the former, depending on the synthetic requirement, can be carried out even in the absence of an acceptor of HCl (B_N).[76,92]

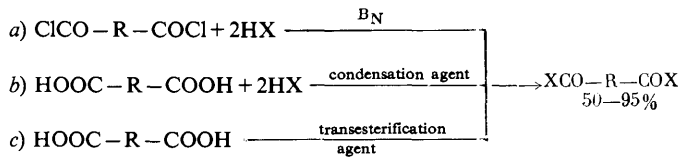
† For the reaction mechanisms, see below.

The "direct" method of synthesising activated biscarbamates involves the treatment of free diamines with a chloroformate or carbonate [reactions (3*b*) and (3*c*), Y = H]. Bis(trimethylsilyl) derivatives of the diamines (Y = $SiMe_3$) can be used successfully in these reactions. In this case there is no need for an acceptor of HCl (B_N), which would cause the dissociation of the resulting carbamate to a diisocyanate (see below).

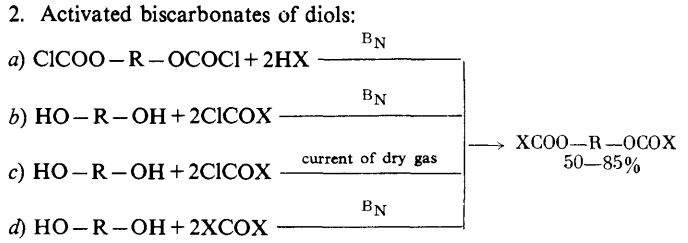
Scheme 2

Syntheses of different classes of activated diesters

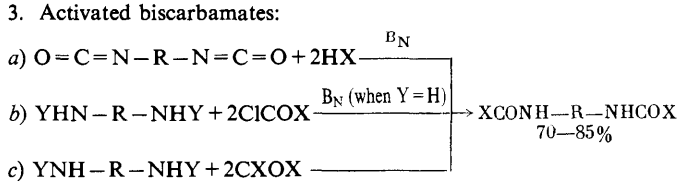
1. Activated diesters of dicarboxylic acids:



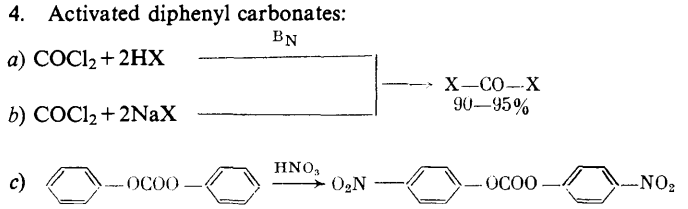
2. Activated biscarbonates of diols:



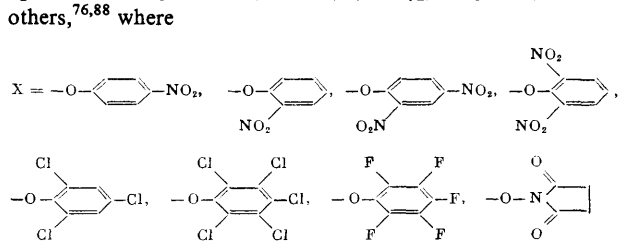
3. Activated biscarbamates:



4. Activated diphenyl carbonates:



Note. Condensation agents are: dicyclohexylcarbodiimide, PCl_3, $SOCl_2$, TsCl, $COCl_2$ $(CF_3CO)_2O$, and others.[45,76] Transesterification agents are: X_3P, X_2SO, X_2CO, $(XCO)_2$, CF_3COX, ClCOX, and others,[76,88] where

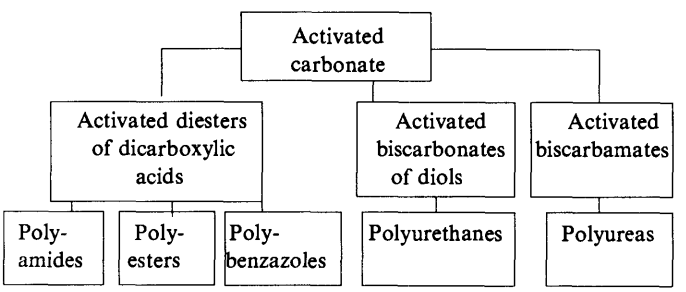


and others (Ref.76). Y = H, $SiMe_3$, B_N = tertiary amine.

Activated diphenyl carbonates (which are also of interest as transesterification agents) are obtained by reaction of phosgene (diphosgene and triphosgene, which are more convenient to handle, can also be used) with a suitable phenol in the presence of B_N [reaction (4*a*)] or a phenoxide [reaction (4*b*)] (Scheme 2). Activated diphenyl carbonates can also be synthesised by nitration of diphenyl carbonate.[93] The latter, in turn, is obtained by a phosgene-free method using CO_2 and phenol as the starting materials.[94] This opens up a route to a new phosgene-free scheme for the synthesis of polyurethanes and polyureas.

Many of the methods that have been developed lead to activated diesters in high yield and it is possible to standardise their syntheses. For example, by using a single transesterification agent it is possible to synthesise an almost unlimited number of diesters of dicarboxylic acids. Similarly, a variety of activated biscarbonates of diols and biscarbamates can be obtained from a single activated phenyl chloroformate. When starting from an activated carbonate X_2CO, it is possible to standardise the syntheses of virtually all classes of monomers and their corresponding polymers (Scheme 3).

Scheme 3

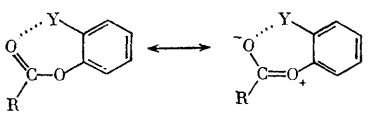


At the same time because of the wide choice of esterification and condensation agents it is possible to vary flexibly the strategy and tactics of designing macromolecular systems, in particular the so-called functional polymers, taking into account both economic and ecological requirements.

2. Structure and reactivity of activated phenyl esters

From IR and ^{13}C NMR spectroscopic studies of *ortho*-, *para*-, and poly-substituted phenyl esters in solution[95–98] it was possible to assign a *trans*-conformation to them, with the torsion angle (φ) of the plane of the ester group relative to the plane of the benzene ring of the phenol residue close to 90° (Fig. 2*a*). The literature data on the conformation of esters also attest to this.[99–102]

With such a conformation of the ester there is no through conjugation between the substituents of the phenyl residue and the carbonyl group, although an interaction occurs through space (in the case of *ortho* substituents), which gives rise to a reduction in contribution from the canonical structure (*K*2).



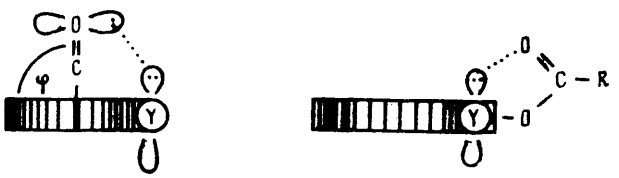
(*K*1) (*K*2)

This, in turn, leads to an increase in the double-bond character of



and a reduction in polarity of the π-bond, which manifests itself (especially strong when halogen atoms are present in *ortho*-positions) in an increase in frequency of the carbonyl stretching vibration and in an upfield displacement of the chemical shift of the $^{13}C=O$ group.[98] The "ortho effect" which occurs on reaction of activated esters with nucleophiles, as will be demonstrated below, leads to a reduction in the apparent rate constant of reaction.

The dependence of the reactivity of esters on the nature of the leaving groups has been studied in the case of the anilinolysis of activated adipates in hexamethylphosphoramide (HMPA).[103] The leaving groups can be arranged in the series given in Table 1 in accordance with the values of the second-order rate constants of reaction (k_2^{app}) (with decreasing activity of the respective esters).



a *b*

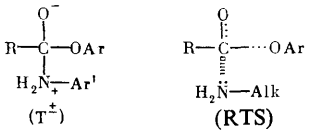
Figure 2. Conformation of *ortho*-substituted phenyl esters of carboxylic acids in solution: *a*, front view; *b*, side view.

On the basis of these results the following conclusions can be made:

1. By changing the nature of the leaving groups it is possible to vary the activity of the diesters over a wide range (in this case by a factor of 10^6). This factor—one of the most important advantages of the activated ester method—clearly suggests the possibilities for controlling the reactivity of electrophilic monomers and hence polycondensation processes without external influences (changes in properties of the medium, temperature, use of a catalyst, etc.).

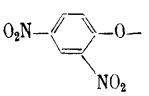
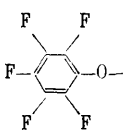
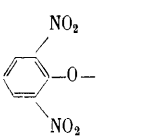
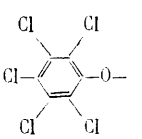
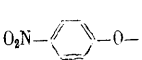
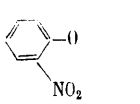
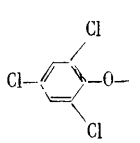
2. The most active esters are 2,4-dinitrophenyl esters, and they are superior to their pentafluorophenyl analogues in every case regardless of the nature of the acyl residue, reacting amine, and reaction medium,[98] which is inconsistent with the results of Covacs et al.,[111] obtained for α-amino acid derivatives.

3. There is no correlation between the apparent rate constants (k_2^{app}) and the pK_a values of the leaving groups (phenols—conjugate acids to the base); the magnitude of the pK_a characterises the stability of the leaving phenoxide anion and correlates with the Hammett σ-constants.[109] Consequently, there is a lack of that kind of correlation between the activity of the esters and the Hammett σ-constants which usually occurs for esters substituted only at the *para* position[112] and which suggests that the leaving groups become detached at the rate-determining stage. It is known that if pre-barrier processes—the formation of intermediate complexes—are rate-determining (see below), the rate constant must correlate with the Taft σ^0-constants because of the virtually orthogonal structure of the esters and the absence of "through resonance". The frequencies of the carbonyl stretching vibrations of esters correlate well with the σ^0-constants.[98-100] If decomposition of the intermediate complexes is rate-determining, the rate constant correlates with the Hammett σ-constants.[99,112] It is appropriate to note that according to Oleinik et al.,[113] a zwitterionic tetrahedral intermediate $T^{\pm}$ is formed in the reaction between esters and arylamines: with alkylamines the reaction occurs via a reactant-like transition state (RTS), which is shifted to the left on the reaction coordinate as the electrophilicity of the ester increases (i.e. with an increase in electrophilicity of the ester the barrier decreases).



$(T^{\pm})$ (RTS)

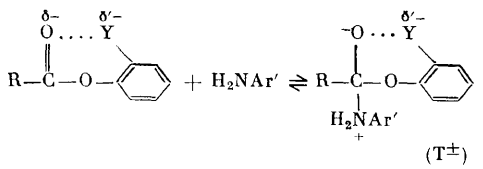
Table 1. Kinetics of the reaction of $ArOOC(CH_2)_4COOAr + H_2NPh$ (molar ratio of 1 : 2) in HMPA at 30 °C.[103]

ArO–	k_2^{app}, litre mol^{-1} s^{-1}	pK_a in water	σ (or Σσ)	σ^0 (or $\Sigma\sigma^0$)
	>1.05	4.0 [104] 4.1 [105–107] 4.39 *	2.48	2.00
	$1.3 \cdot 10^{-2}$	5.3 [106] 5.5 [104] 5.86 *	1.82	2.09
	$6.9 \cdot 10^{-3}$	3.7 [105] 4.39 *	2.48	2.54
	$5.4 \cdot 10^{-4}$	4.5 [108] 5.3 [104. 106] 4.72 *	2.33	2.33
	$2.6 \cdot 10^{-4}$	7.16 [104] 7.15 [109]	1.24	0.73
	$3.9 \cdot 10^{-5}$	7.21 [104]	1.24	1.27
	$3.6 \cdot 10^{-6}$	6.42 [108] 7.59 [104] 6.37 *	1.59	1.57

* The pK_a values calculated according to the study of Barlin and Perrin[109] are given because of discrepancies in the experimental pK_a values (H_2O). According to Bykova and Petrov,[110] the acidity series in water for acids of a single group (phenols in this case) is also retained in organic solvents.

An analysis of the results of Table 1 using the Taft equation indicates[98] that the apparent steric constants have lower values (calculated using Hammett σ-constants) than those reported in the literature (given in brackets): $E_{S_{app}}^{F} = 0.22$ (0.46); $E_{S_{app}}^{Cl} < -1$

(0.18); $E_{S\,app}^{NO_2}$ = −1.56 (−0.75) [calculated for bis(2,4-dinitrophenyl) adipate] [a value of −0.75 has also been adopted for bis-(*o*-nitrophenyl) adipate in calculations]. The reduction in $E_{S\,app}$, which is particularly noticeable when there are two *ortho* chlorine atoms,‡ may be related to the above-mentioned "ortho effect", which creates additional difficulties in the formation of $T^{\pm}$ and shifts this equilibrium to the left, increasing the apparent shielding effect of the *ortho* substituents.



($T^{\pm}$)

Table 2. Apparent constants k_2 for alcoholysis reactions of activated esters at 30 °C.

Ester	Alcohol	Reaction medium	$k \times 10^4$, litre mol^{-1} s^{-1}
p-Nitrophenyl acetate	phenol	chlorobenzene	4.7±0.3
o-Nitrophenyl acetate	»	»	1.6±0.2
Pentafluorophenyl acetate	»	»	5.5±0.4
Pentachlorophenyl acetate	»	»	(1.2±0.1)·10^{-1}
2,4,5-Trichlorophenyl acetate	»	»	1.8±0.2
2,4,6-Trichlorophenyl acetate	»	»	(4.8±0.2)·10^{-2}
2,4-Dinitrophenyl acetate	»	1,2-dichloroethane	(3.2±0.7)·10
	n-butanol	»	3.8±0.5

Note. Catalyst — triethylamine (TEA); initial ratio (mol litre^{-1}) of ester : alcohol : TEA = 0.6 : 0.6 : 0.6

Results obtained on the alcoholysis and phenolysis of model acetates (Table 2) may also provide an indication of the reality of the "ortho effect". In these reactions an RO^- anion is the nucleophile, so the intermediate has an anionic character (T^-) without intramolecular balance of charge. This enhances the role of this interaction and leads to a substantial change in the relative reactivity of the esters compared to aminolysis reactions. The difference in activity of *p*-nitro- and pentafluoro-phenyl esters is levelled out, the *p*-nitrophenyl ester is more reactive than its *o*-nitro-substituted analogue (in the reaction with aniline in the same medium the opposite occurs, see below) and 2,4,5-trichloro-substituted analogue (according to the literature data the latter is more active in aminolysis)[114] and pentachlorophenyl acetate is less active than *p*-nitrophenyl acetate by a factor of approximately 40 (in the reaction with aniline in chlorobenzene the former is 13 times more active, see Table 3).

‡ While the reduction in $E_{S\,app}$ (increase in steric hindrance) by a factor of 2 in the case of 2,6-dinitro- and pentafluoro-phenyl esters can be attributed to the presence of two *ortho* substituents, the large reduction in $E_{S\,app}^{Cl}$ is difficult to explain solely on the basis of two *ortho* atoms.

However, depending on the properties of the medium, *ortho* substituents can have the opposite effect—a catalytic action on aminolysis processes. Thus, for example, in the reaction with aniline in a weakly polar, proton-inert medium, *o*-nitrophenyl esters are 2–4 times more active than their *para*-substituted analogues,[98] which may be related to the formation of an intramolecular hydrogen bond which stabilises $T^{\pm}$.

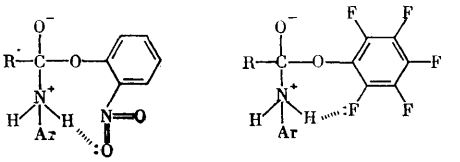


Table 3. Relative reactivity of activated diesters (C_0 = initial concentration of reactants in mol litre^{-1}).

Ester pair (A + B) (C_0)	E_{LUMO}^{*}, eV	Amine (C_0)	Reaction medium (T, °C)	k_1, s^{-1}	k_1^A/k_1^B
A. *p*-Nitrophenyl acetate (0.1)	−0.04	aniline	C_6H_5Cl	1.3·10^{-6}	3.1
B. Methyl *p*-nitrophenyl carbonate (0.1)	−0.95	(4.0)	(30)	0.4·10^{-6}	
A. *p*-Nitrophenyl acetate (0.1)		»		6.5·10^{-4}	3.2
B. Methyl *p*-nitrophenyl carbonate (0.1)			HMPA (30)	2.0·10^{-4}	
A. *p*-Nitrophenyl acetate (10^{-4})		n-butyl amine	C_6H_6 (28)	1.2·10^{-3}	0.3
B. Methyl *p*-nitrophenyl carbonate (10^{-4})		(0.2)		3.7·10^{-3}	
A. 2,4-Dinitrophenyl acetate (10^{-4})	−0.62	t-butyl amine	C_6H_6	3.5·10^{-3}	0.7
B. Methyl 2,4-dinitrophenyl carbonate (10^{-4})	−1.35	(0.2)	(28)	5.1·10^{-3}	
A. *p*-Nitrophenyl acetate (0.05)	−0.04	aniline	HMPA	5.5·10^{-4}	15
B. *p*-Nitrophenyl benzoate (0.05)	−0.07	(2.0)	(30)	3.6·10^{-5}	
A. *p*-Nitrophenyl acetate (0.5)		»	C_6H_5Cl	0.5·10^{-6}	13
B. Pentachlorophenyl acetate (0.5)			(30)	6.3·10^{-6}	

* Energy of the lowest unoccupied molecular orbital calculated by the MINDO/3 method.

In a proton-active medium such as HMPA, where the formation of strong hydrogen bonds is possible, the catalytic effect from an *ortho*-nitro group is absent (only an inhibiting "ortho effect" seems to occur), and in this case *para*-substituted esters are more active (by a factor of approximately 8).[98] We should note that an intramolecular catalytic effect can be exhibited by *ortho*-fluorine atoms, which may partly explain the high activity of pentafluorophenyl esters in aminolysis reactions (in contrast to reactions with ROH, Table 2).

The nature of the acyl residue has a considerable effect on the relative activity of esters (Table 3). According to the data obtained, esters make up the following series of decreasing activity (other

conditions being equal):

a) Reaction with an arylamine: acetate > methyl phenyl carbonate > benzoate;

b) Reaction with an alkylamine: methyl phenyl carbonate > acetate > benzoate.

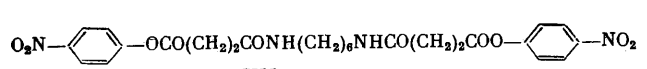
The experimental data obtained can be interpreted on the basis of the above-mentioned mechanism.[113] In a reaction with an arylamine that occurs via the intermediate formation of $T^{\pm}$, carbonates are less active since they correspond to a lower ground state energy (because of the mesomeric interaction between the methoxyl oxygen and the carbonyl group),[115] which results in an increase in the energy barrier. In reactions with alkylamines the transition state is reactant-like and in the case of carbonate (which according to the E_{LUMO} value is more electrophilic than acetate, Table 3) is shifted more to the left along the reaction coordinate, thus reducing the barrier. It follows from the results obtained that the difference in rates of aminolysis on changing from an alkylamine to an arylamine is greater for carbonates.

The medium has a considerable effect on the rate of aminolysis, and it was found that the most important of the properties of solvents is their ability to form strong hydrogen bonds (characterised by the value of pK_{HB}, Table 4). Thus, for example, the rate of reaction of *p*-nitrophenyl acetate with aniline is higher by a factor of about 10^3 in DMSO and HMPA than in the proton-inert chlorobenzene and even acetonitrile, which is comparable to the former in terms of polarity and dielectric constant but has a considerably lower pK_{HB}.

Table 4. Effect of medium on apparent pseudo-first-order rate constants (k_1) of reaction between *p*-nitrophenyl acetate (C_0 = 0.05 mol litre^{-1}) and aniline (C_0 = 2.0 mol litre mol^{-1}) and rate constants of imidisation (k_{im}) of the bis(*p*-nitrophenyl) ester of *N,N'*-hexamethylenedisuccinamide (VII) at 30 °C.

Medium	Properties of medium			k_1, s^{-1} (Ref.103)	k_{im}, s^{-1} (Ref.91)
	μ	ε	pK_{HB} (Ref.116)		
C_6H_5Cl	1.69	5.62	–	$4.7\cdot10^{-7}$	does not cyclise
CH_3CN	3.92	36.2	1.05	$5.2\cdot10^{-7}$	»
HMPA	5.37	30.0	3.56	$5.5\cdot10^{-4}$	$4.0\cdot10^{-6}$
DMSO	3.96	49.0	2.53	$1.4\cdot10^{-4}$	$1.6\cdot10^{-6}$

Similarly, the bis(*p*-nitrophenyl) ester of *N,N'*-hexamethylenedisuccinamide (VII)



(VII)

undergoes cyclisation (imidisation) at an appreciable rate only in a medium with a high pK_{HB} value (Table 4). The experimental data obtained can be accounted for by the considerable catalytic effect of these solvents on the aminolysis of esters. We have established that a single molecule of HMPA and three molecules of DMSO participate in catalysis. The reason for the unusual behaviour of DMSO is apparently related to the formation of a solvent-separated ion pair (the formation of which is supported by UV spectroscopy) involving an acyloxysulphonium ion:

$$R{-}COOAr + O{\leftarrow}SMe_2 \longrightarrow R{-}CO{-}O{\leftarrow}\overset{+}{S}Me_2 \ldots O{\leftarrow}SMe_2 \ldots ArO^-.$$

The third DMSO molecule, as with HMPA, participates in proton transfer in $T^{\pm}$.

In proton-inert organic solvents the reaction is catalysed by the amide that is formed[117] (amides have high values of $pK_a \approx 2$)[116] and the initial amine. Under pseudo-first-order reaction conditions (excess amine) the apparent rate constant is given by the familiar equation $k_1 = \sum k_{i+1}[A]^i$, where $i = 1, 2$.[112,113] However, in *n*-heptane the high order term $k_4[A]^3$, with $i = 3$ (Table 5) was first found, which suggests associated (trimeric) forms of the amine take part in the reaction. This result confirms the mechanism according to which catalysis by amine is no different from the action of a specific solvent[117,118] that is capable of forming a strong hydrogen bond, and is given by:

$$R'NH_2 + B \rightleftharpoons R'NH_2 \ldots B,$$

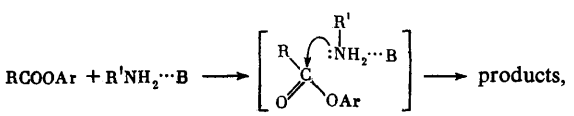


Table 5. Kinetics of the aminolysis of activated *p*-nitrophenyl esters *p*-RCOO–C_6H_4–NO_2 in proton-inert media.

R	(A)	Variation in [A], mol litre^{-1}	Reaction medium	$k_2\times10^2$ litre mol^{-1} s^{-1}	$k_3\times10^2$ litre^2 mol^{-2} s^{-1}	$k_4\times10^2$ litre^3 mol^{-3} s^{-1}
CH_3	BA	0.02–0.35	n-heptane	–	1.3	22.2
	BA	0.04–0.40	benzene	–	3.1	–
	BA	0.01–0.50	1,2-dichloroethane	0.2	9.8	–
	AN	1.5–4.0	chlorobenzene	$1.6\cdot10^{-5}$	$0.4\cdot10^{-5}$	–
CH_3O	BA	0.01–0.42	n-heptane	–	4.6	81.8
	BA	0.04–0.34	benzene	–	9.4	–
	BA	0.04–0.48	1,2-dichloroethane	0.5	22.5	–
	AN	2.0–4.0	chlorobenzene	$0.3\cdot10^{-5}$	$0.2\cdot10^{-5}$	–
CH_3NH	BA	0.05–0.67	n-heptane	–	0.4	2.6
	BA	0.07–0.50	benzene	–	0.16	0.7
	BA	0.04–0.54	1,2-dichlorobenzene	–	1.4	3.7

Note. The reaction with aniline (AN) was carried out at 30 °C, that with *n*-butylamine (BA) at 28 °C. Initial concentrations of esters were 0.05 mol litre^{-1} (reaction with AN) and 10^{-4} mol litre^{-1} (reaction with BA).

where B is a molecule of proton-active solvent or the amine itself.

It was established that activated alkyl aryl carbonates react with amines with removal exclusively of a phenoxide ion ArO^- and

formation of the required urethane [route (*a*)]; the alternative route (*b*) does not occur:

$$ROCOOAr + H_2NR' \begin{cases} \xrightarrow[-ArOH]{(a)} ROCONHR' \\ \xrightarrow[-ROH]{(b)} R'NHCOOAr \rightleftharpoons R'-NCO + ArOH \text{ etc.} \end{cases}$$

In other words, aminolysis of activated esters of carboxylic acids and alkyl aryl carbonates occurs by the same "direct" mechanism—either via the formation of $T^{\pm}$ or via a RTS.

In contrast to activated esters, activated carbamates react with amines by a more complicated mechanism, forming an intermediate isocyanate:

$$RNHCOOAr + (H_2NR')_{i-1} \xrightarrow[-ArOH]{} R-NCO \xrightarrow{H_2NR'} RNHCONHR'$$

An indication of this is provided in particular by the constantly occurring term $k_4[A]^3$, regardless of the properties of the medium (see Table 5).

The mechanism of aminolysis of activated diphenyl carbonates consists of a unique combination of both mechanisms

$$ArOCOOAr \xrightarrow{H_2NR} \begin{bmatrix} T^{\pm} \text{ or} \\ RTS \end{bmatrix} \rightarrow ArOCONHR \xrightarrow[-ArOH]{(H_2NR)_{i-1}}$$

$$\rightarrow RNCO \xrightarrow{H_2NR} (RNH)_2CO\ .$$

Thus, aminolysis of activated esters is a complex process and is susceptible to various intra- and inter-molecular influences, which have a considerable effect on the formation of macrochains in activated polycondensation.

3. Possible side reactions

Studies have been conducted on the tendency of activated esters to undergo various side reactions in which traditional activated forms of the monomers are fairly readily involved and which constitute the reason for the restriction on chain propagation and the unit heterogeneity.

It has been established that the majority of activated diesters do not react with alcohols (methanol, ethanol) even on boiling. In the absence of an amine only the most active 2,4-dinitrophenyl esters undergo appreciable alcoholysis.[119,120]

Activated esters are also stable towards amide solvents. Only 2,4-dinitrophenyl esters exhibit relatively low stability; in HMPA at 30 °C about 10% of the ester groups have decomposed after 6 h (when their initial concentration is 0.1 mol litre^{-1}).

Activated esters also exhibit high hydrolytic stability in these weakly basic solvents even in the presence of considerable quantities of water (up to 9%) (see Table 6), with pentafluoro- and *p*-nitrophenyl esters considerably surpassing their 2,4-dinitro-substituted analogues in this respect. It is worth noting that when triethylamine (TEA) is introduced into solution, the pentafluorophenyl ester is the least susceptible to its catalytic action, which may be attributed to the above-mentioned inhibitory effect from two *ortho*-fluorine atoms in attack on an ester by OH^- ions. Alkyl aryl carbonates have similar hydrolytic stability to that of their ester analogues (Table 6).

In contrast to the "conventional" esters (adipates) examined above, the catalytic effect of TEA is absent in the hydrolysis of diester (VII) and only an acceleration of imidisation occurs (see Table 6). This may be related to structural features of diester (VII).

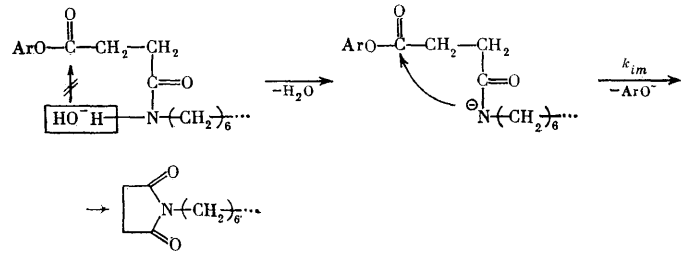


Table 6. Apparent pseudo-first-order rate constants ($k_1^{H_2O}$) of the hydrolysis of activated diesters at 30 °C (not catalysed and catalysed by TEA).

Ester	Solvent	$k_1^{H_2O}$, s^{-1} noncatalytic	$k_1^{H_2O}$, s^{-1} catalytic	$\frac{k_1^{H_2O}(cat)}{k_1^{H_2O}(noncat)}$	$\frac{k_1(aminolysis)^*}{k_1^{H_2O}(noncat)} \cdot 10^{-3}$
$ArOCO(CH_2)_4COOAr$, $ArO = 2,4-(NO_2)_2C_6H_3O-$	HMPA	$1.3 \cdot 10^{-4}$	$4.5 \cdot 10^{-3}$	36	16
$ArO = C_6F_5O-$	HMPA	$8.5 \cdot 10^{-6}$	$2.7 \cdot 10^{-5}$	3	3
$ArO = 4-NO_2C_6H_4O-$	HMPA	$3.5 \cdot 10^{-7}$	$3.2 \cdot 10^{-6}$	9	0.6
	DMSO	$5.2 \cdot 10^{-7}$	$1.6 \cdot 10^{-6}$	3	–
Diester (VII)	DMSO	$1.2 \cdot 10^{-6}$	$1.2 \cdot 10^{-6}$	1	–
		(k_{im} = $1.6 \cdot 10^{-6}$) **	(k_{im} = $5.8 \cdot 10^{-6}$) **	–	–
$CH_3OCOO-C_6H_4-NO_2$	HMPA	$3.8 \cdot 10^{-7}$	$5.3 \cdot 10^{-6}$	14	0.5

Note. Initial concentration of ester groups = 0.1 mol litre^{-1}; molar ratio of [COOR]:[TEA]:[H_2O] = 1:1:50.

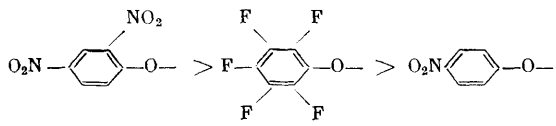
*For k_1 values (aminolysis), see Tables 1 and 3.

**k_{im} = apparent rate constant for imidisation of ester (VII).

In inert organic solvents activated esters hardly react at all with TEA (molar ratio of ester:TEA = 1:2) at 30 °C over a period of more than 24 h. The stability of activated esters towards highly basic tertiary amines is of considerable significance in terms of the synthesis of high-molecular-weight linear heterochain polymers and makes it possible to carry out a number of new polycondensation schemes using a highly basic proton acceptor (see below).

On the whole it may be concluded from the combined results obtained from studying reactions catalysed by TEA that of the possible mechanisms of catalysis—1) nucleophilic catalysis, 2) formation of an intermediate ketene, and 3) general-base catalysis—the latter is the most probable.

We should note that the hydrolysis of $ArOCO(CH_2)_4COOAr$ occurs at a considerably slower rate than even the slowest of its aminolysis reactions—the reaction with aniline. The ratio of constants k_1 (aminolysis)/$k_1^{H_2O}$ is as high as the order of $10^3-10^4:1$ (see Table 6) and decreases as ArO varies in the series



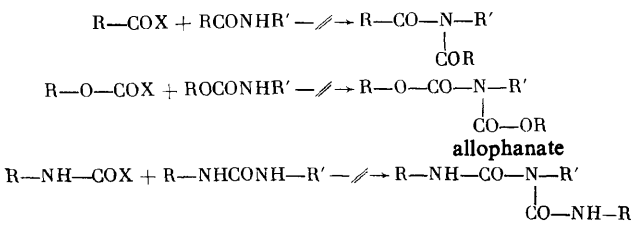
In other words, an increase in activity of the ester helps to suppress hydrolysis. This is consistent with the results of Menger and Smith,[112] according to which aminolysis is more sensitive to the nature of the leaving group than is hydrolysis. An increase in basicity of the amine has a similar effect; the rate of aminolysis increases by a factor of 10^3-10^5 (see Tables 3 and 5) while side reactions (catalysed by amine) are only accelerated by a factor of 10^1 (see Table 6).

Acid-base processes are of considerable importance in relation to polycondensation in an organic medium. It has been established that the phenols used in weakly polar aprotic media mainly form with amines either molecular complexes $ArOH\cdots H_2NR$ without significant charge separation or hydrogen-bonded ion pairs (in the case of the most acidic phenols) in equilibrium with molecular complexes $ArO^-\cdots H_3N^+R \rightleftarrows ArOH\cdots H_2NR$.[121,122] In weakly basic aprotic media with a high value of pK_{HB} (HMPA, DMF, DMSO) the ion pairs are in equilibrium with strong $ArOH\cdots$solvent complexes.[123,124] All of this makes it possible to carry out the aminolysis of activated esters in any organic medium freely and quantitatively without the use of a proton acceptor.

In contrast to phenols, *N*-hydroxysuccinimide forms with primary and secondary amines strong complexes that are insoluble in organic solvents, including polar aprotic ones.[125] However, the amino groups in these complexes are readily acylated by highly active esters. *N*-Hydroxysuccinimide does not form an insoluble complex with tertiary amines.

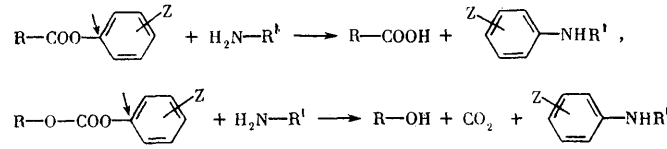
In addition to what has been mentioned, the absence of a reaction between these esters and their aminolysis products should also be considered as an advantage of activated esters (Scheme 4):

Scheme 4



Thus, activated esters differ favourably from the traditional forms of activated polycondensation monomers because of their low tendency to undergo side reactions, which are typical for the latter and lead to a restriction on chain propagation and to unit heterogeneity in the polymers.

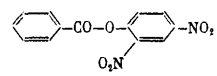
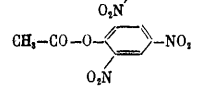
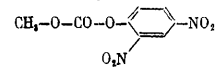
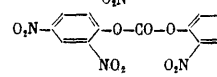
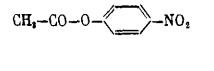
It was found by Katsarava et al.[126] that nucleophilic substitution resulting in the loss of ester groups and a restriction on chain propagation, is of considerable significance in the aminolysis of activated phenyl esters



where Z is an electron-withdrawing substituent.

This reaction occurs to the greatest extent when two nitro groups are present in the phenol residue, the yield of product being dependent on the nature of the acyl residue and the amine (Table 7). It was established that a reduction in temperature, dielectric constant and pK_{HB} of the medium helps to suppress nucleophilic substitution.[127]

Table 7. Yield of product obtained from nucleophilic substitution in the aminolysis of activated esters in HMPA.

Ester	Amine	Temperature, °C	Yield of product, mol%
	benzylamine	30	1.29
	aniline	80	0.44
	benzylamine	30	0.28
	aniline	80	0.08
	benzylamine	30	1.50
	aniline	30	2.60
	benzylamine	30	0.14
	aniline	30	0.28
	benzylamine	30	trace amounts
	aniline	80	not detected

Note. Initial concentration of ester = 0.6 mol litre^{-1}; molar ratio of ester : amine = 1 : 1.2.

As has been mentioned, the activating groups considered above (see Table 1) make it is possible to control the reactivity of esters over a wide range. A further increase in reactivity of phenyl esters through the introduction of additional electron-withdrawing substituents, in our view, is inappropriate because of the sharp increase in the contribution from nucleophilic substitution.

III. Polycondensation

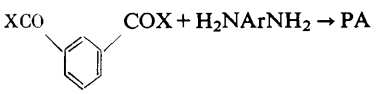
1. Synthesis of polyamides and polybenzazoles

Bifunctional monomers can be divided into four groups according to their nature and reactivity (see Section II). The effect of the nature of the leaving group of an ester on the molecular weight of

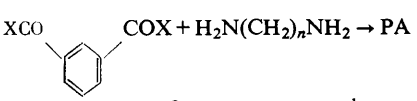
required polyamide (PA) during polycondensation in HMPA has been studied (the conditions of synthesis are given in brackets):[128]

$$XCO(CH_2)_4COX + H_2NArNH_2 \rightarrow PA$$

II-I (80 °C; 0.6 mol litre^{-1})



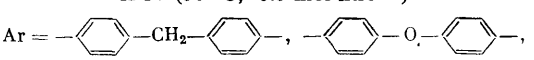
II-II (80 °C; 0.6 mol litre^{-1})



II-III (30 °C; 0.6 mol litre^{-1})

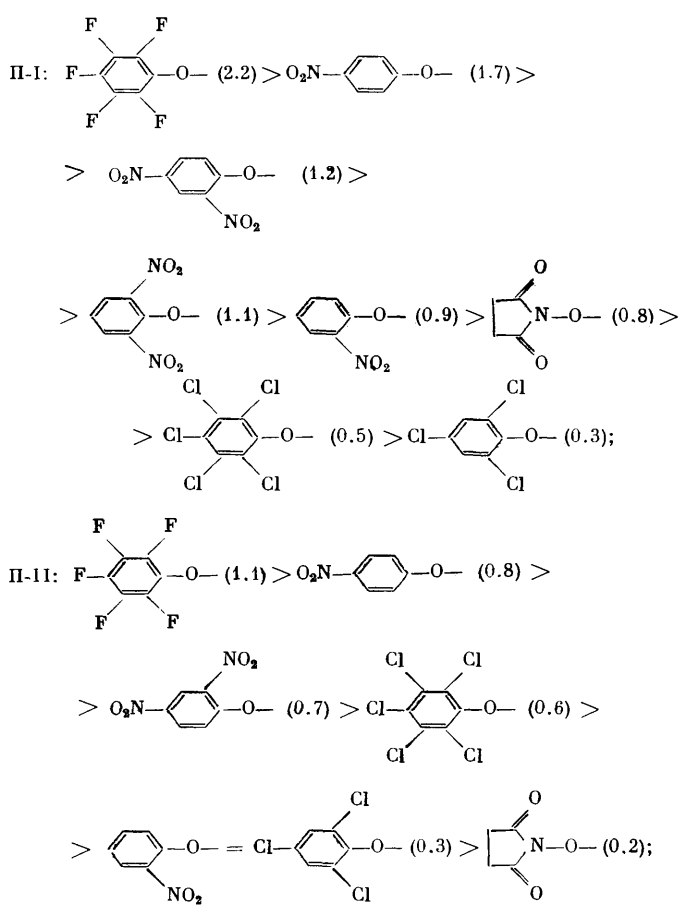
$$XCO(CH_2)_4COX + H_2N(CH_2)_nNH_2 \rightarrow PA$$

II-IV (30 °C; 0.3 mol litre^{-1})



$n = 6, 12$; PA – polyamide .

Polycondensation of pairs II-I to II-III occurs homogeneously, while that of pair II-IV is heterogeneous (polyamide separates out). According to the data obtained, the leaving groups (X) make up the following series with respect to their tendency to form high-molecular-weight polyamides (values of intrinsic viscosity η_{int} at 25 °C and a concentration of polymer solution of 0.5 g dl^{-1} are given in brackets):



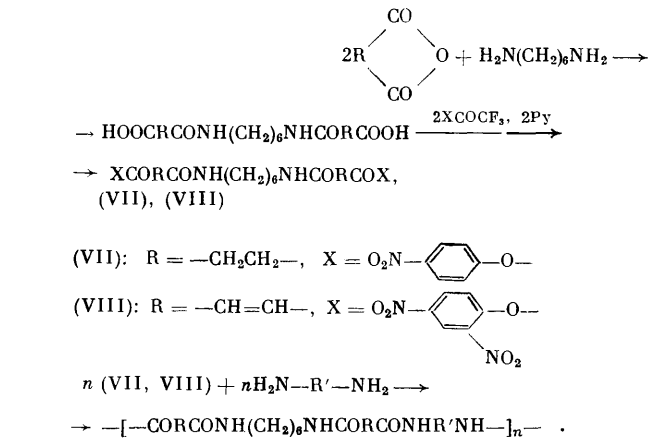
The series obtained do not correlate with the reactivity of the diesters. Under these conditions the pentafluorophenoxide leaving group proved to be more effective in the synthesis of polyamides starting from aromatic diamines (pairs I-II, and II-II), although 2,4-dinitrophenol derivatives lead to good results. When aliphatic diamines are used, one of the best leaving groups is *p*-nitrophenoxide, while in the synthesis of completely aliphatic polyamides the *N*-oxysuccinimide group is one of the best.

A study of the kinetics of polycondensation of pairs II-I to II-III (homogeneous reactions) showed[103] that on the whole its rate is consistent with the reactivity of the monomers [bis(pentachlorophenyl) adipate constitutes an exception, see below]. At the same time the polycondensation of diesters with aliphatic diamines is virtually complete after 1–2 h (at 30 °C), while with aromatic diamines polycondensation lasts from 4 to 40 h depending on the activity of the diester (at 80 °C). The lack of correlation between reactivity of the monomers and the η_{int} value of the resulting polyamides is mainly due to the occurrence of nucleophilic substitution as a side reaction (see Section II.3), resulting in chain termination.

Polycondensation of the monomer pair II-IV, which takes place heterogeneously, is also complete after 1–2 h. The resulting polymers are readily soluble in organic solvents (trifluoroethanol, *m*-cresol), which suggests the absence of intermolecular imide cross-linking which arises when the corresponding acid dichlorides are used.[129]

On the basis of the high stability of intermediate activated amidoesters of the type (VII), which are not very susceptible to imidisation (see Tables 4 and 6), high-molecular-weight polysuccinamides were obtained by reaction of activated succinates with hexamethylenediamine (HMDA) and dodecamethylenediamine (DMDA).[91] The best leaving group for the pair, like II-IV, proved

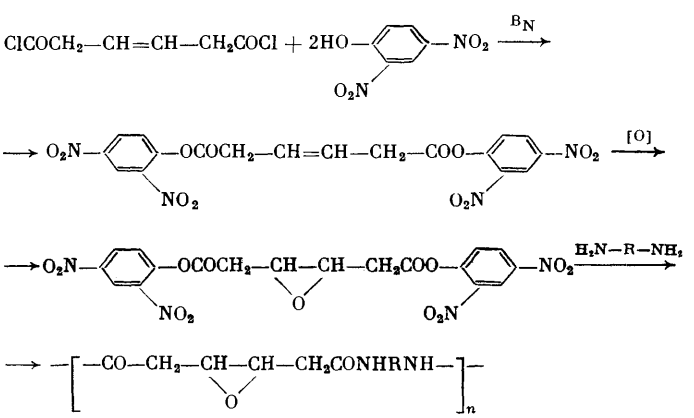
to be *N*-oxysuccinimide. Polysuccinamides were also obtained by a different route using the pure activated bisamidoester (VII):



Polyamides with a strict alternation of two diamine residues can be synthesised by this route, and it can be used to prepare polyamides based on "cyclising" dicarboxylic acids (for example, maleic acid) whose activated diesters are difficult to obtain. Thus, polycondensation of diester (VIII) with hexamethylenediamine in HMPA gave polyhexamethylenemaleimide with η_{int} = 0.67 dl g^{-1}).

The use of activated diesters proved fruitful in the synthesis of polyamides starting from indole-containing dicarboxylic acids,[130,131] whose dichlorides in the presence of an acceptor (triethylamine) undergo intermolecular cyclisation to form diketopyrazinoindole residues.[132]

The synthesis of high-molecular-weight epoxypolyamides via an activated diester has been achieved:[19]

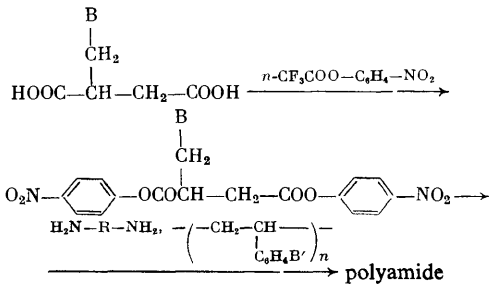


η_{int} = 0.42 – 0.48 (R = Alk) and 0.73 – 3.62 (R = Ar) dl g^{-1}.

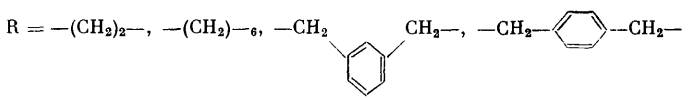
Lower molecular-weight polyamides ($\eta_{int} \leqslant 0.15$ dl g^{-1}) are formed using the corresponding acid dichloride.

The latter two examples provide support for the view expressed above (see Section II.1) that in a number of specific cases the synthesis of activated diesters is worthwhile even if carried out via the corresponding acid dichlorides.

Activated diesters containing nuclei bases have been used in matrix polycondensation reactions:[59]



where



B = adenine, theophylline, thymine/uracil

B′ = adenine/theophylline.

It was established that in the presence of a polystyrene matrix containing a complementary base B′, polyamidation is accelerated by a factor of more than ten.

We should note that the development of activated polycondensation methods opens up a means of studying matrix polycondensation—a relatively new and little-studied process compared to matrix polymerisation.[133]

We have successfully utilised the highly selective acylating capacity of activated diesters to synthesise soluble polybenzimidazoles. Polycondensation of activated isophthalates with aromatic tetraamines in *N*-methylpyrrolidone gave high-molecular-weight polybenzimidazoles, the best results being achieved when 2,4-dinitrophenyl (η_{int} = 2.2 – 2.4 dl g^{-1}) and 2-mercaptobenzthiazole (η_{int} = 1.1 dl g^{-1}) esters were used. The synthesis of polybenzimidazoles occurs under mild conditions (70 – 100 °C), the polymers obtained form golden-brown coloured films with a tensile strength σ_f = (10 – 12) × 10^7 Pa. The corresponding polybenzoxazoles and polybenzthiazoles (η_{int} = 1.1 – 1.2 dl g^{-1}) were obtained under similar conditions by reaction of bis(2,4-dinitrophenyl) isophthalate and aromatic dihydroxy- and dimercaptodiamines.

2. Synthesis of polyesters

"Activated polyesterification" processes have been carried out in dichloroethane at 25 – 60 °C using trimethylamine as a catalyst (4 moles [Sic. Ed. of Translation) per mole of diol).[134,135] It was established that high-molecular-weight, film-forming polyesters ($\eta_{int} \leqslant 0.9$ dl g^{-1}) are only formed by the polycondensation of activated esters of aliphatic dicarboxylic acids with bisphenols. We should note that it is this class of polyesters that is the most difficult to obtain by means of traditional polycondensation methods using the corresponding aliphatic acid dichlorides, which actively undergo various side reactions, including that with the acceptor (tertiary amine).[5] The best leaving group in the synthesis of the polyesters proved to 2,4-dinitrophenoxide. It was concluded from the results of studying polycondensation and model reactions that "activated polyesterification" occurs by a mechanism involving general base catalysis.

Thus, on the one hand, "activated polyesterification" extends the synthetic opportunities of the polycondensation method for

synthesising polyesters, while on the other hand, it opens up interesting prospects for studying acceptor-catalytic polyesterification processes (usually occurring by two catalytic channels—nucleophilic and general-basic),[136] since it makes it possible to distinguish the general-basic channel in a "pure form".

3. Synthesis of polyurethanes and polyureas

The polycondensation of activated biscarbonates of diols with diamines was carried out according to the scheme:[92]

$$n\ \mathrm{ArOCOO{-}R{-}OCOOAr} + n\ \mathrm{H_2N{-}R'{-}NH_2} \longrightarrow$$
$$\longrightarrow\ \mathrm{-[-COO{-}R{-}OCONHR'NH-]_n-}\ ,$$

where

$$\mathrm{R' = -(CH_2)_6-,\ -(CH_2)_{12}-,\ -NHCO(CH_2)_8CONH-,}$$
$$\mathrm{-C_6H_4-CH_2-C_6H_4-,\ -C_6H_4-O-C_6H_4-.}$$

The effect of the nature of the leaving groups has been studied in the case of the reaction of activated biscarbonates of propane-1,3-diol with hexamethylenediamine in DMF (the best solvent for this monomer pair) at 110 °C and a monomer concentration of 0.6 mol litre^{-1}. According to the results obtained the ArO^- leaving groups make up the following series with respect to their tendency to form high-molecular-weight polyurethanes (the η_{int} values in *m*-xylene, dl g^{-1}, are given in brackets):

$$\mathrm{O_2N{-}C_6H_4{-}O{-}\ (1.4) > O_2N{-}C_6H_3(NO_2){-}O{-} = Cl{-}C_6H_2Cl_2{-}O{-}\ (0.7) >}$$
$$\mathrm{> Cl{-}C_6H_3Cl{-}O{-} = C_6H_4(NO_2){-}O{-}\ (0.6) > C_6H_5{-}O{-}\ (0.3)}\ .$$

Branched butane-1,3-diol derivatives proved more sensitive to the nature of the leaving groups. Thus, for example, while activated carbonates of propane-1,3-diol form high-molecular-weight polyurethanes with virtually all leaving groups, in the case of butane-1,3-diol high-molecular-weight polyurethanes ($\eta_{int} \leqslant 3.8$ dl g^{-1}) are only obtained when the *p*-nitrophenol derivative is used.

Polycondensation of bis(*p*-nitrophenyloxycarbonyl)butane-1,3-diol with hexamethylenediamine in amide solvents (DMF, *N*-methylpyrrolidone) occurs homogeneously at 30 °C, and a high-molecular-weight polyurethane is formed after only 1–2 h, but subsequently the process slows down slightly and the increase in viscosity ceases within 12–24 h depending on the concentration of the initial monomers (1.2–0.3 mol litre^{-1}). The occurrence of a "slow stage" in this case may be related to the reduced activity of the carbonate group formed by the secondary hydroxyl as a result of the shielding effect of the methyl group. The "slow stage" virtually disappears when the temperature is increased to 70 °C.

It is appropriate to note that this example [like the increase in molecular weight of a polyamide that continues for several hours at the fairly high temperature of 80 °C (see Section III.1)] additionally and clearly suggests that activated esters have high stability in an amide solvent (see Section II.3).

The nature of the diamine has a considerable effect on "activated polyurethane formation". Polyurethanes with $\eta_{int} \leqslant 0.5$ dl g^{-1} are obtained with aromatic diamines (at the same time polyamides are formed equally effectively with diamines of both classes, see Section III.1). This may be due to a greater reduction in rate of aminolysis on changing from an aliphatic amine to an aromatic one (see Section II.2).

Activated polyurethane formation occurs by "direct" aminolysis (via $T^{\pm}$ or RTS) without the formation of an intermediate isocyanate (see Section II.2), which excludes the formation of anomalous urea residues, allophanate and biuret branches, and intermolecular cross-linking. It was also established that this reaction is irreversible (like the "activated polyamidation" examined above), and the urethane bond does not react with terminal carbonate groups (see Scheme 4). All this assists the formation of linear polyurethanes. An additional advantage of this method is the lack of necessity for using a proton acceptor or catalyst.

In contrast to urethane formation, the aminolysis of activated carbonates (see Section II.2) occurs via the formation of an intermediate isocyanate:

$$n\ \mathrm{ArOCOOAr} + n\ \mathrm{H_2N{-}R{-}NH_2} \xrightarrow[-\mathrm{HOAr}]{} [\mathrm{ArOCONH{-}R{-}NH_2}] \underset{+\mathrm{HOAr}}{\overset{-\mathrm{HOAr}}{\rightleftharpoons}}$$
$$\rightleftharpoons [\mathrm{O{=}C{=}N{-}R{-}NH_2}] \longrightarrow \mathrm{-[-CONH{-}R{-}NH-]_n-}, \qquad (1)$$

where

$$\mathrm{R = -(CH_2)_6-,\ -C_6H_4-O-C_6H_4-;}$$

$$\mathrm{ArO = O_2N{-}C_6H_4{-}O-,\ O_2N{-}C_6H_3(NO_2){-}O-}\ .$$

Of the two leaving groups—2,4-dinitro- and *p*-nitrophenoxide—the latter proved more effective in the synthesis of polyureas according to the above Scheme.[137] In the polycondensation of bis(*p*-nitrophenyl) carbonate with hexamethylenediamine in dimethylacetamide (DMAA) (containing 15% LiCl) at 90–100 °C, a polyurea with $\eta_{int} = 0.75$ dl g^{-1} was obtained. Under these conditions a high-molecular-weight polyurea is formed even when an aromatic diamine is used ($\eta_{int} = 1.34$ dl g^{-1}). The use of bis(2,4-dinitrophenyl) carbonate in these reactions leads to poorer results (a polymer with $\eta_{int} = 0.2-0.4$ dl g^{-1} is formed), which may be due to its tendency to undergo nucleophilic substitution as a side reaction (see Table 7).

The synthesis of polyureas is also carried out by another method, using the "intermediate" of the aminolysis of a carbonate—the activated carbamate (IX)—as a monomer:[138]

$$n\mathrm{O_2N{-}C_6H_4{-}OCONHRNHCOO{-}C_6H_4{-}NO_2} + n\mathrm{H_2NR'NH_2} \longrightarrow$$
(IX)
$$\longrightarrow \mathrm{-[CONHRNHCONHR'NH-]_n-}$$
$$\mathrm{R, R' = -(CH_2)_2-,\ -(CH_2)_4-,\ -(CH_2)_6-,\ -(CH_2)_{12}-\ \text{etc.}} \qquad (2)$$

Polycondensation of (IX) with diamines occurs under the same conditions as the synthesis of polyureas according to Eqn. (1), giving polymers with $\eta_{int} = 0.5-0.7$ dl g^{-1}.

We should note that the formation of the intermediate isocyanate in the synthesis of polyureas according to Eqns. (1) and (2) does not hinder the preparation of linear soluble polymers. Cross-linked polymers are not formed in this case apparently because of the equilibrium nature of the reaction at the stage involving regeneration of isocyanate. The *p*-nitrophenol that separates out in an amide solvent vigorously reacts with the isocyanate [the equilibrium constants of the dissociation of (IX) with R = $-(CH_2)_6-$ and the

reaction of hexamethylenediisocyanate with *p*-nitrophenol in DMAA are very close to each other and at 30 °C are equal to $(4.5 \pm 0.5) \times 10^{-3}$. This does not prevent the latter reacting with an amino group but it suppresses the formation of biuret.

Thus, the use of the activated polycondensation method considerably simplifies the processes involving formation of linear polyurethanes and polyureas. In terms of synthetic possibilities they are also superior to traditional methods and can be used to obtain polymers in solution under mild conditions without resorting to the synthesis of the corresponding diisocyanates or bischloroformates, which are often difficult or completely impossible to obtain. This circumstance is of particular importance for the preparation of polymers with special properties from those diamines and diols for which the traditional polycondensation methods cannot be used.

4. Some general characteristics of activated polycondensation

We have established in the case of the reaction of activated diesters of dicarboxylic acids and activated biscarbonates of diols with diamines that, in activated polycondensation, polymers with a maximum molecular weight are obtained when there is a strictly equimolar ratio of monomers, regardless of whether the process is homogeneous or heterogeneous.

The dependence of the molecular weight of the polymer in the synthesis of polyamides and polyurethanes on the concentration of monomers for homogeneous processes at 25–30 °C is extremal in nature with a maximum at monomer concentrations of 0.6 and 0.8–1.0 mol litre^{-1} respectively. At higher temperatures (100–120 °C) the results of polycondensation over the concentration range studied (0.2–1.2 mol litre^{-1}) are virtually independent of the initial concentration of the monomers. In heterogeneous polycondensation (the synthesis of aliphatic polyamides in HMPA) the maximum molecular weights are achieved when the reaction solution is diluted to 0.15 mol litre^{-1}, regardless of the nature of the dicarboxylic acid (succinic, adipic) or diamine (hexamethylenediamine, dodecamethylenediamine). The reason for this dependence should be sought in the improved swelling of the polymers when they are diluted, since the polymer grain size decreases on dilution, assisting chain propagation in the heterophase.

The use of amide solvents and DMSO, in which reactions involving both aromatic and aliphatic diamines can occur successfully, as the reaction medium proved the most fruitful. In the case of the latter, other organic solvents such as acetone, dioxan, THF, dichloroethane, etc., in which high-molecular-weight polyamides (regardless of the heterogeneous nature of the process) were obtained at 25–30 °C, are also suitable. Under these temperature conditions in HMPA, diesters with 2,4-dinitro-, 2,6-dinitro-, and pentafluoro-phenoxide leaving groups readily react with aromatic diamines. For esters with other leaving groups the optimum temperature is 80 °C. On comparing these results with the data in Table 1, it may be assumed that for activated polycondensation to be effective the apparent rate of reaction (fundamental stage) must be of the order of $\sim 10^{-2}$ litre mol^{-1} s^{-1}.

While the synthesis of polyamides and polyurethanes from aliphatic diamines occurs successfully at 25–30 °C, for the preparation of high-molecular-weight polyureas it is necessary to increase the temperature to 90–100 °C in order to change the reaction to homophase conditions. This is due to the equilibrium nature of the process at the stage involving dissociation of the intermediate carbamate to isocyanate. In the swollen precipitate the equilibrium is shifted towards unreactive carbamate, which inhibits chain propagation. After homogenisation of the solution the viscosity of the polyureas increases considerably (from 0.5 to 0.75 dl g^{-1}).

In the synthesis of polyamides and polyurethanes, where equilibrium stages do not occur, separation of the polymer out of solution apparently assists chain propagation through a local increase in concentration of the functional groups and their favourable relative position in space (resembling "liquid-crystalline polycondensation"). If the process occurs in a weakly polar proton-inert solvent, catalysis by an amide (see Section II.2) assumes considerable significance. In the condensed state this catalysis should only have a slight effect because of the high local concentration of the amide groups. The polyamide chain may also fulfil the role of an acceptor of HX (strong hydrogen complexes are formed), although in weakly polar solvents this problem is not so important since salt-like complexes (inactive ammonium cations) are hardly formed at all (see Secton II.3).

Thus, in certain specific cases of activated polycondensation the separation of the polymer out of solution may constitute one of the reasons for a restriction on chain propagation. In other cases, such as in the polycondensation of diamines with pentachlorophenyl diesters of adipic and isophthalic acids in HMPA, the poor solubility of the diesters results in considerable inhibition of the process at the initial stages.[103] After homogenisation of the solution the rate of polycondensation of bis(pentachlorophenyl) adipate with 4,4′-diaminodiphenylmethane is still low and considerably slower than the rate of polycondensation involving bis(*p*-nitrophenyl) adipate, which does not correspond to the expected reactivity of the diesters (see Table 1). The reason for this discrepancy should be sought either in the "immuring" of the terminal ester groups inside the macromolecular coil because of their low affinity for HMPA ("lyophobic effect") or in an increase in the inhibitory "ortho effect" through a reduction in the local dielectric constant of the medium.

Of the other causes of a restriction on chain propagation in the aminolysis of activated diesters, we can single out nucleophilic substitution. The results of model reactions (see Section II.3) are supported by the presence of terminal 2,4-dinitroaniline groups in the corresponding polymers (a characteristic absorption occurs in the region 355–365 nm) at a level of 0.6–1.8 mol%.[126] The contribution of nucleophilic substitution in the reaction between 2,4-dinitrophenyl esters of carboxylic acids, in particular aliphatic acids, and an aromatic amine is comparatively low (see Table 7). The successful synthesis of high-molecular-weight polyamides in the reaction between dinitrophenyl diesters and aromatic amines is considerably dependent on this (see series II-I and II-II). The same diesters actively undergo a nucleophilic substitution reaction with aliphatic diamines and form polyamides that are considerably inferior in terms of viscosity to the samples synthesised via other diesters (series II-III and II-IV). 2,4-Dinitrophenyl diesters have improved behaviour in the synthesis of polyesters and polybenzazoles, which is also an indication of the low contribution of nucleophilic substitution in these processes. In the reaction between 2,4-dinitrophenyl carbonates and an aromatic amine, on the other hand, the yield of the product obtained from nucleophilic substitution is higher than in the reaction with an alkylamine (see Table 7), which inhibits the formation of high-molecular-weight polyurethanes and polyureas based on aromatic diamines ($\eta_{int} \leqslant 0.2–0.4$ dl g^{-1}).

Protonation of the amino groups by low-molecular-weight products of an acidic nature which separate out is known to result in chain termination during low-temperature polycondensation. However, as was demonstrated in Section II.3, in the case of the

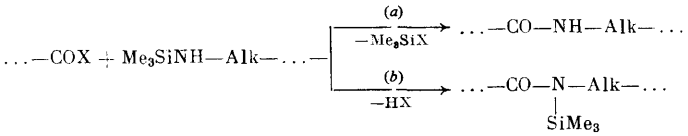
weak acids which we have used as phenols, this reaction is not critical. An indication of this is provided by the results given above on polycondensation involving aliphatic diamines without using a proton acceptor in different media—both proton-active and proton-inert.

Polycondensation involving *N*-oxysuccinimide esters occurs in a distinctive manner.[139] The ability of *N*-hydroxysuccinimide to bind with primary aliphatic amines, giving strong insoluble complexes (see Section II.3) has a considerable effect on polycondensation; it inhibits, for example, the reaction between the corresponding isophthalate and hexamethylenediamine. Polycondensation of hexamethylenediamine with a more active adipate readily occurs with the formation of a high-molecular-weight polyamide (series II-IV). In this case triethylamine cannot deprotonate the primary amino group and has no significant effect on the course of the reaction. An increase in temperature to 80–120 °C leads to a marked acceleration of the reaction, but at the same time the side reaction between *N*-hydroxysuccinimide itself and the aliphatic diamine is intensified.[125]

Thus, the various processes for restricting chain propagation are primarily responsible for the lack of a clear relationship between the reactivity of activated diesters and the viscosity properties of the resulting polymers. The role of these processes may be reduced through a choice of suitable reaction conditions or leaving groups.

5. Syntheses using trimethylsilylated derivatives and diamine salts

As an alternative to free aliphatic diamines, their *N,N'*-bis-(trimethylsilyl) derivatives have been used successfully in polycondensation with activated diesters.[90,91,125,137,138,140,141]

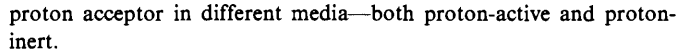


Despite the lower nucleophilicity of trimethylsilylated amino groups,[142,143] polycondensation of these derivatives with various activated diesters occurs at sufficiently high rates, resulting in the formation of heterochain polymers that are comparable in terms of molecular weight to the corresponding polymers obtained via the free bases.

Polycondensation of activated diesters with trimethylsilylated diamines mainly takes place with the formation of a "normal" amide [route (*a*)][141] (the eliminated phenol HX acts as a desilylating agent). Even if route (*b*) does occur in this reaction, the number of trimethylsilylated amide groups are either insufficient for formation of cross-linked polymers or the rate of their acylation by activated esters is much lower than the rate of desilylation.[142] Activated diesters differ in this respect favourably from acid dichlorides, which on reacting with trimethylsilylated diamines give cross-linked polymers in a number of cases.[141]

The stability of trimethylsilylated amino groups towards alkyl esters of carboxylic acids (which is important when diamines containing ester groups are used, see below) and also the elimination of the low-molecular-weight silylated reaction product Me_3SiX, which is incapable of protonating an amino group, should be included amongst the advantages of nucleophiles of this class. This is an important factor in the case of polycondensation systems for which a powerful inhibitory reaction between acidic by-products and diamines is typical, such as when bis(*N*-oxysuccinimide) esters of dicarboxylic acids are used as monomers (see Section III.4).[125]

Because of the high stability of the activated diesters towards triethylamine, we were able to use stable diamine salts as monomers in polycondensation.



Y = Cl, CH_3COO.

The reactions examined in this Section are especially useful for the design of macromolecular systems based on diamines that are unstable as free bases. In particular, they have been used successfully for the synthesis of functional heterochain polymers of different classes—polyamides, polyurethanes, and polyureas—from alkyl esters of the natural diaminocarboxylic acids—lysine and cystine—which are of practical interest for medical and biological applications.[144,145]

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In summarising the above material we may conclude that during the last 10–15 years another versatile method for the synthesis of heterochain polymers has been developed. With this method a standardised approach can be made towards the synthesis of heterochain polymers of different classes and to design novel, functional macromolecular systems that were previously unobtainable, including biomedical polymers. This makes the new method particularly promising and attractive for the "fine chemistry" of polymers with special properties. With regard to large-scale production, problems of a practical nature may arise in the future, stimulating the development of new technologies based on the reactions examined above, including efficient methods of regenerating the low-molecular-weight polycondensation products, and corresponding to economic and ecological requirements.

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Translated from *Uspekhi Khimii* **60** 1449–1472 (1991) U.D.C. 541.64; 547.8; 547.64; 542.953

Reactions using nitro-containing monomers for the synthesis of aromatic polymers

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ABSTRACT. The progress made in the synthesis of aromatic polymers based on nitro-containing monomers is reviewed. It is shown that the main processes for the synthesis of aromatic polymers using nitro-containing monomers are nucleophilic aromatic polynitrosubstitution reactions, which are effectively used to obtain polymers containing ether groups in the main macromolecular chains. A group of novel reactions that includes thermal and chemical conversion of nitro-containing heterochain polymers is examined.

The bibliography includes 98 references.

Contents

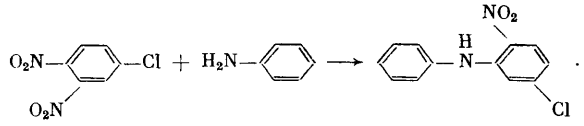
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I. Introduction

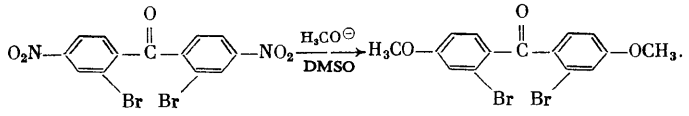
Research into novel functional groups used in polycondensation and the modification of condensation polymers is a topical question in the chemistry of high-molecular-weight compounds. Such groups should establish a sufficiently high reactivity of the monomers, without limiting their availability or increasing their toxicity. Up until recently nitro compounds, which are widespread in organic chemistry,[1,2] have not been used to any appreciable extent in polycondensation processes; however, developments that have occurred over the last 15 years have considerably changed the position in this area. The present review is devoted to an analysis of the principal advances made in the synthesis of condensation polymers based on nitro-containing monomers.

II. Nucleophilic aromatic polynitrosubstitution reactions

Reactions involving nucleophilic substitution of aromatic nitro groups have been known for a long time.[3] Thus, Laubenheimer[4,5] in 1876 described the replacement of the nitro group in 3,4-dinitrochlorobenzene by aniline to form 2-nitro-5-chlorodiphenylamine:



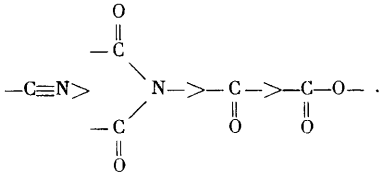
It is interesting to note that very little attention was subsequently given to the application of nitrosubstitution reactions until Gorvin[6] demonstrated the successful reaction between 2,2′-dibromo-5,5′-dinitrobenzophenone and methoxide ion:



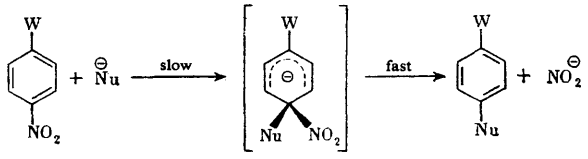
The reaction occurred almost quantitatively, indicating the higher reactivity of nitro groups compared to bromine atoms.

The successful achievement of this reaction was related to the use of a dipolar aprotic solvent. In general the use of dipolar solvents is a necessary condition for the preparation of products in high yield at moderate temperatures.

Subsequent studies[7–17] showed that nitrobenzene derivatives containing other electron-withdrawing groups undergo nitrosubstitution. The following series constitutes the rectivity of activating groups:

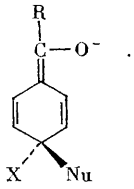


Nucleophilic substitution of a nitro group from an activated system usually occurs by a two-stage addition–elimination mechanism. The first stage is usually, but not always, limiting (determining the rate of the overall process).

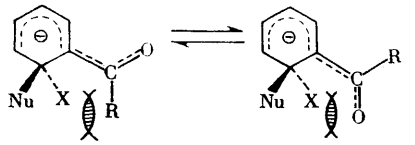


When strong electron-withdrawing substituents are present in the ring, nucleophilic substitution reactions occur under mild conditions. The presence of electron-withdrawing groups of the type $-\overset{\overset{O}{\|}}{C}-R$ at

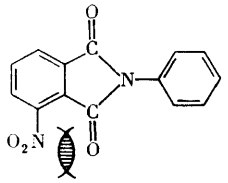
para positions relative to the leaving groups causes the substitution reactions to occur readily because of stabilisation of the Meisenheimer complex as a result of their acceptance of negative charge from the ring:



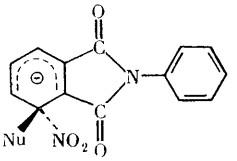
On the other hand, any electron-withdrawing groups situated at *ortho* positions cause a reduction in the rates of the substitution reactions as a result of the formation of high-energy conformers of a Meisenheimer complex:



Steric interactions in the Meisenheimer complexes are less clearly reflected in the case of activated systems containing condensed rings (nitro-substituted *N*-arylphthalimides) where the *ortho* isomers are much more reactive than *para* isomers as a result of the inductive effect, and also the relief of the *peri* interaction



and the absence of steric interaction in the Meisenheimer complex



Moreover, the formation of conformers of the Meisenheimer complex does not occur as a result of ring condensation.

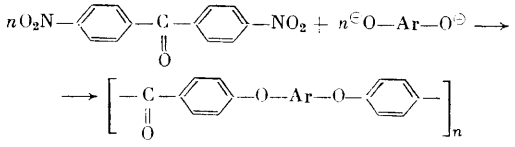
The higher rates of reaction found for nitro groups compared to chlorine groups are due to the greater electrophilicity of the carbon atoms on which substitution occurs, since the nitro group is a stronger electron acceptor than chlorine.

Substitution reactions obey second-order kinetics, being first-order with respect to both the aromatic substrate and the nucleophile.

In general the phenoxides used in nitrosubstitution reactions must be free of moisture. In the presence of the latter, derivatives containing ester and imide groups are readily deactivated as a result of hydrolysis and ring opening respectively. However, it should be noted that derivatives containing nitrile and ketone groups are less sensitive to the presence of small quantities of water. In these cases free phenols can be used in the presence of carbonates or alkali metal hydroxides. Under normal reaction conditions, alkali metal nitrites which are by-products of the reactions do not undergo undesirable conversions. Nevertheless, on increasing the time of the reactions—especially at higher temperatures—nitrite ions can attack other nucleophilic sites of the initial compounds or by-products.[17,18]

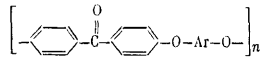
The efficiency of activation of the nitro groups by carbonyl "bridges" predetermined the theoretical possibility of using nucleophilic aromatic polysubstitution processes to obtain polyether containing carbonyl groups.[19,20]

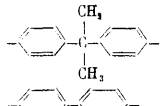
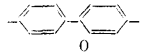
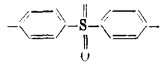
It was demonstrated for the first time by Radlmann et al.[21] and by Heath and Wirth[22] that nitrosubstitution reactions occur sufficiently productively to be able to extend them to the synthesis of high-molecular-weight aromatic polyethers. Reaction of 4,4′-dinitrobenzophenone with bisphenols gave different polyetherketones,



whose individual properties are given in Table 1.

Table 1. Polyetherketones obtained by nitrosubstitution.[21]



—Ar—	Temperature of polycondensation	Solvent	η_{int} in MP	mp of polymer, °C
	65	DMSO/C_6H_5Cl	1.32	195–220
	145	DMSO	1.18	236–255
	140	DMSO	1.07	201–228

Clendinning and Kwiatkovski[23] also used polynitrosubstitution reactions to obtain polyetherketones.

Because of the strong activation effect of the nitrile groups, the two nitro groups in 2,4- and 2,6-dinitrobenzonitriles readily undergo substitution. This make it possible to obtain high-molecular-weight polyethers containing nitrile substituents as a result of the reaction between dinitrobenzonitriles and salts of different bisphenols:[11]

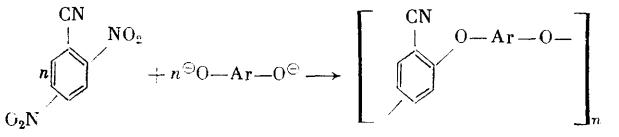
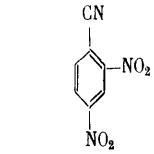
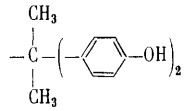
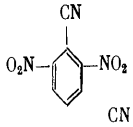
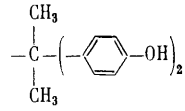
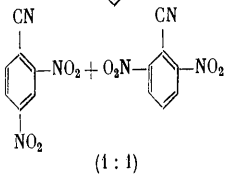
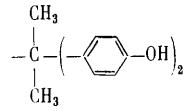
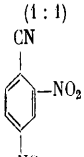
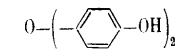
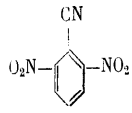
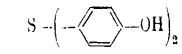
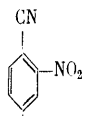
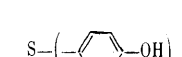
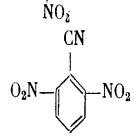
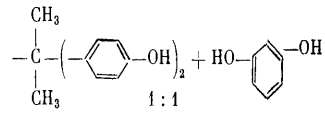
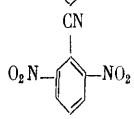
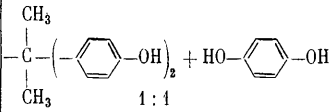
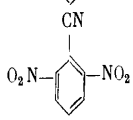
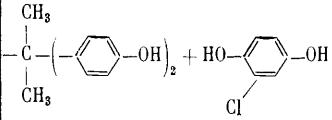
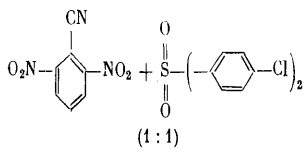
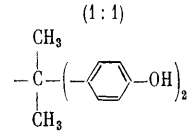


Table 2. Synthesis of polyethers by nitrosubstitution of dinitrobenzonitriles with bisphenol salts.[11]

Dinitro compounds	Bisphenols	Reaction conditions			Thermal properties of polymers		
		solvent/T, °C	yield, %	$[\eta]$, dl g^{-1}	T_g, °C*	T_1, °C**	
						air	N_2
		DMSO/115	81	0,68	141	430	430
		DMSO/145	75	0,51	173	385	420
 (1 : 1)		DMSO/140	89	0.60	160	420	425
		DMSO/140	70	0.24	136	360	380
		DMSO/115	75	0.40	147	450	450
		DMSO/115	85	0.32	134	450	450
	 1 : 1	DMSO/115	75	0.34	155	390	400
	 1 : 1	DMSO/114	—	0.55	176	415	430
	 (1 : 1)	DMSO/115	88	0.50	174	430	410
 (1 : 1)		DMSO/150	91	0.38	178	430	420

* Glass-transition temperature as determined by differential scanning of calorimetry.

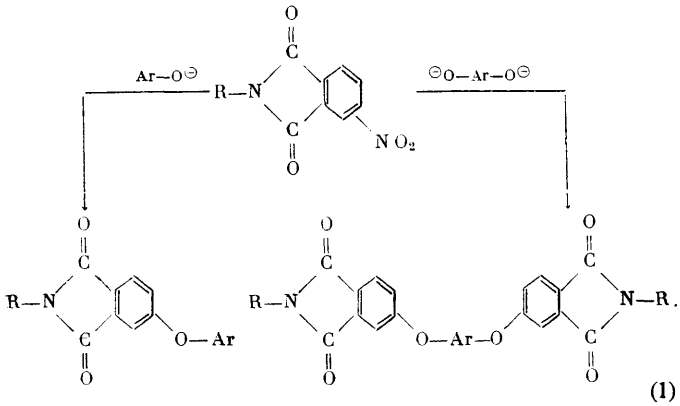
** Temperature of loss of 1% weight as determined by thermogravimetric analysis.

Some properties of the polyethers synthesised are given in Table 2.

The majority of the nitrile-substituted polyethers obtained are soluble in chlorinated solvents; strong and flexible films are obtained from their solutions. The high glass-transition and thermal-degradation temperatures are caused by the aromaticity of these polymers and the high polarity of the nitrile groups.

The second large family of polymers obtained with the use of polynitrosubstitution processes comprises aromatic polyetherimides.[19]

According to several studies,[10,24–27] nitro groups that are activated by two carbonyls undergo nucleophilic substitution. Activation of nitro groups by the two carbonyls contained in cyclic imides is particularly effective.[26,28] Thus, *N*-substituted 3- and 4-nitrophthalimides were converted to mono- and bis-etherimides by reaction with different mono- and bis-phenoxides by means of nitrosubstitution:

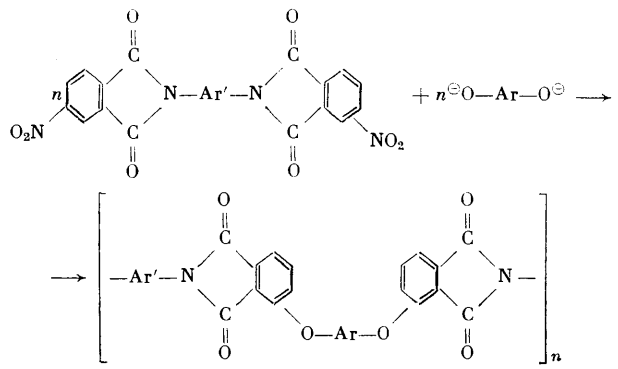


(1)

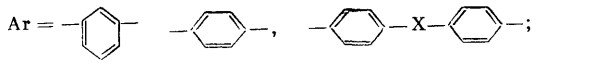
These nitrosubstitution reactions must be carried out in the complete absence of water, since *N*-substituted nitrophthalimides are readily deactivated as a result of hydrolysis and ring opening. Anhydrous solutions of phenoxide salts can be obtained from sodium hydride and the respective phenols or by azeotropic dehydration of aqueous phenoxide salts in DMSO–toluene in a similar manner to the techniques used in the synthesis of polysulphones.[29]

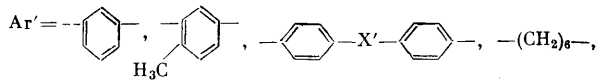
The synthesis of imidoethers is carried out under mild temperature conditions (25–60 °C), it occurs sufficiently rapidly (the reaction time varies from 5 min to several hours), and results in formation of the required products in high yield (>95%).[26]

The high yields of bis(etherimides) predetermined the possibility of extending the reactions depicted in Scheme (1) to the synthesis of polymers, namely, to the preparation of polyetherimides using nitrosubstitution processes[28,30–35]



where

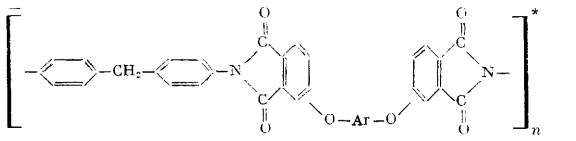




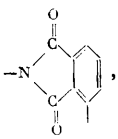
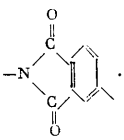
$X' = -CH_2-, -O-, -SO_2-$.

The synthesis of polyetherimides by means of polynitrosubstitution was carried out under modified conditions[29] in the complete absence of moisture.[31,32] The conditions for the synthesis of polyetherimides starting from the dinitrodiphthalimide derivative of 4,4′-diaminodiphenylmethane are given in Table 3 together with certain properties of the polyetherimides.

Table 3. Synthesis conditions and some properties of polyetherimides with the general formula[31,32]



Compound	—Ar—	Synthesis conditions			$[\eta]$, dl g^{-1}	Yield, %
		solvent	T, °C	time, h		
1	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	DMSO	40	1.0	0.28	91 **
2	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	DMSO/toluene	40	1.0	0.39	91
3	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	"	40	22.0	0.56	–
4	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	DMF	50	2.0	0.43	–
5	*p*-C_6H_4–C_6H_4-*p*	DMSO	40	0.5	0.36	98 ***
6	*p*-C_6H_4–$C(CF_3)_2$–C_6H_4-*p*	DMSO	50	1.0	0.19	77
7	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	DMSO/toluene	60	17.0	0.42	89

* Compounds 1–6:  , compound 7:  .

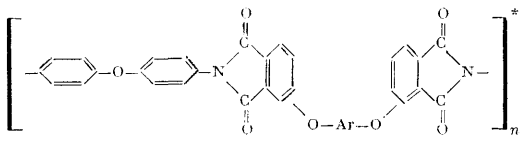
** T_g = 230 °C, T_{deg} = 380 °C.
*** T_{deg} = 400 °C.

Polyetherimides based on other dinitrophthalimides were obtained under similar or fairly similar conditions. Some properties of the polymers synthesised are given in Tables 4 and 5.

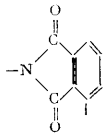
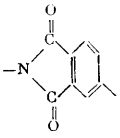
On the whole, polynitrosubstitution reactions occur rapidly even under comparatively mild conditions. When dipolar aprotic solvents or their mixtures with toluene are used, polymers with relatively high molecular weights are formed (M_w up to 123 × 10^3, M_n up to

23×10^3).[32] The most frequently used solvents are DMSO + toluene and DMF, the choice of solvent being determined by the method of obtaining the anhydrous bisphenoxide. The reactivity of dinitrophthalimides used is determined primarily by the position (3- or 4-) of the nitro groups rather than by the nature of the Ar residue. Monomers that contain nitro groups at the 3-position are more reactive than systems containing nitro groups at the 4-position.[26] Consequently, the synthesis of polyetherimides using dinitrophthalimides that contain nitro groups at the 4-position are carried out at higher temperatures and for a longer time. A factor that affects the rate of reaction is the rate of solution of the monomers; this gives rise to the possibility of polymers with relatively high molecular weight being formed when there is some departure from equimolarity of the monomers. The low solubility of bisphenoxides (and/or a low rate of their solution) can be compared with a slow feeding of these monomers into the reaction zone.

Table 4. Synthesis conditions and some properties of polyetherimides with the general formula[31,32]



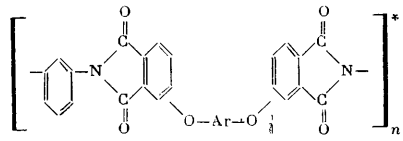
Compound	—Ar—	Synthesis conditions: solvent	T, °C	time, h	$[\eta]$, dl g^{-1}	Yield, %	T_g/T_{deg}
1	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	DMSO/toluene	45	0.25	0.61	97	–
2	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	"	40	17	0.33	89	226/385
3	*m*-C_6H_4–	DMF	60	1	0.18	100	226/–
4	*p*-C_6H_4–	DMSO	50	1	0.45	76	237/430
5	*p*-C_6H_4–S–C_6H_4-*p*	DMAA	60	1	0.37	100	234/–
6	*p*-C_6H_4–O–C_6H_4-*p*	DMF	60	1	0.80	100	239/400
7	*p*-C_6H_4–C_6H_4-*p*	DMSO	50	0.8	0.60	95	277/380
8	*p*-C_6H_4–$C(CH_3)_2$–C_6H_4-*p*	DMSO/toluene	55	14	0.41	94	196/420
9	*p*-C_6H_4–O–C_6H_4-*p*	DMF	60	1	0.44	96	215/–

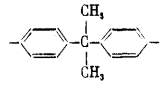
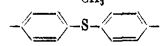
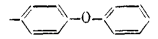
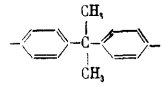
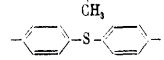
* Compounds 1–7:  , compounds 8 and 9: 

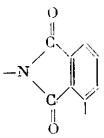
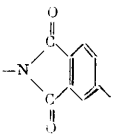
It is advisable to carry out the synthesis at elevated temperatures in order to increase the solubility of the monomers. However, it was found in a number of cases that an increase in temperature and duration of reaction resulted in the formation of products with a lower molecular weight.[32] It is possible that this occurs as a result of side reactions with nitrite ion,[26,28,36] which is eliminated during polynitrosubstitution. Consequently, the optimum temperature for reactions involving 3,3′-dinitrophthalimides is 50 °C, while for reactions involving 4,4′-dinitrophthalimides the optimum temperature is 10 °C higher.[32]

Increasing the concentration of the monomers generally assists the formation of polyetherimides with higher molecular weights, but on reaching very high concentrations (~50%) the rates of solution of the initial compounds decrease—as a result of saturation and an increase in viscosity—which also slows down polynitrosubstitution. The most frequently used concentration range is 20–25%.[32]

Table 5. Synthesis conditions and some properties of polyethermides with the general formula[31,32]



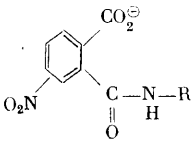
Compound	—Ar	Synthesis conditions: solvent	T, °C	time, h	$[\eta]$, dl g^{-1}	Yield, %	T, °C
1		DMSO/toluene	55	5.25	0.23	87	227
2		DMAA	60	1	0.16	100	209
3		DMAA	60	1	0.22	95	232
4		DMF	70	2.5	0.29	82	227
5		DMAA	60	1	0.1	80	–

*Compounds 1–3:  , compounds 4 and 5:  .

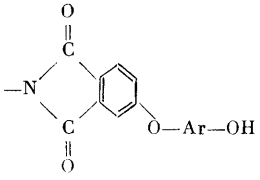
In a number of cases sodium phenoxide or sodium 4-methylphenoxide were introduced into the reaction mixtures after completion of the synthesis processes of polyetherimides in order to replace the terminal nitro groups and increase the thermal stability of the required polymers. At the same time careful control over the course of the reactions was necessary in order to decrease the contribution of exchange reactions between the phenols and the diarylether groups[26] which reduce the molecular weight of the polymers.

By analogy with the synthesis of mono- and bis-etherimides, reactions for the synthesis of polyetherimides by means of polynitrosubstitution are especially sensitive to the presence of moisture in the reaction system. The moisture remaining after formation of a bisphenol and also that contained in the reactants or solvents leads to poor reproducibility of results and to formation of low-molecular-weight polymers. The moisture remaining in the system is in equilibrium with the bisphenoxide, which gives rise to the presence of hydroxide ions in the reaction mixture. The latter

attack the imide rings[37] in the monomers and in the polymers formed. As a result of ring opening, an amino acid

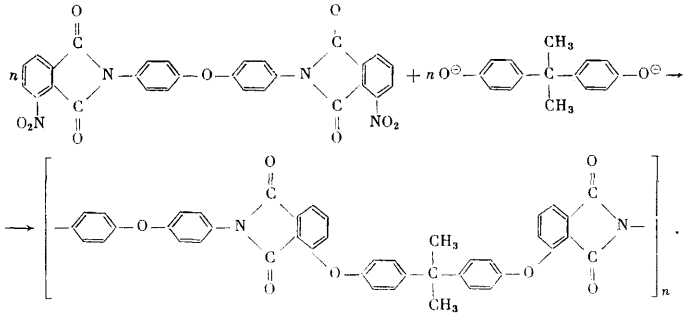


is formed, disrupting the stoichiometry during synthesis of the polymers and causing chain termination, since the nitro group in it is insufficiently activated to undergo substitution.[37] The presence of a hydroxide ion also opens up the possibility of formation of structures of the type



in which the hydroxyl group no longer behaves as a nucleophile.

The effect of moisture on the synthesis of a polyetherimide was demonstrated in the case of the synthesis of a polymer in accordance with the following scheme through the addition of a controlled amount of water to the system

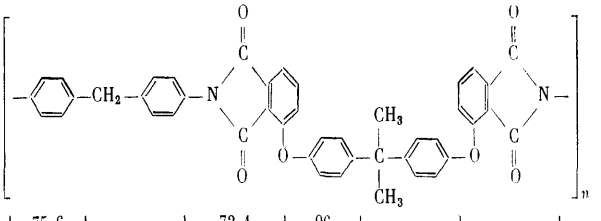
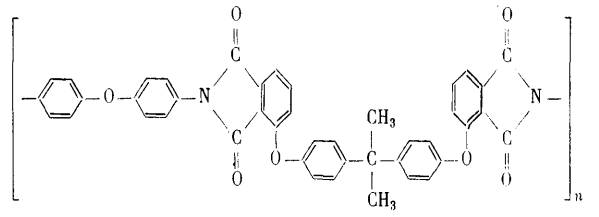
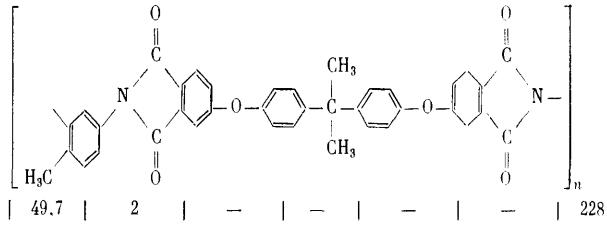


It transpired that when the process was carried out in the driest system in DMSO, a polymer with [η] of not less than 0.44 dl g^{-1} was formed, whereas addition of 0.03% water to the solvent (10 mol.% based on the reactants) assists the formation of a polymer with [η] = 0.25 dl g^{-1}, while addition of 0.09% water (30 mol.%) leads to the formation of a polymer with [η] = 0.18 dl g^{-1}.[32]

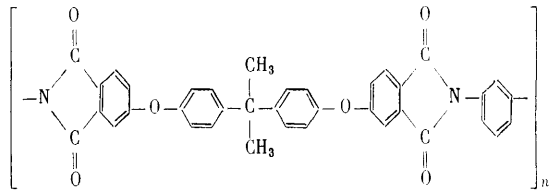
A study of polyetherimides using gel permeation chromatography showed that they have wide molecular weight ranges, which may also be due to the presence of water in the reaction mixtures. It is this factor that may determine the presence of "open" rings in chains and at the ends of the macromolecules, leading to the possibility of strong carboxylic acids being formed during processing.

Polyetherimides are amorphous in the majority of cases. This factor in combination with the asymmetry of their macromolecular structure and the presence of a considerable number of ether bonds in the latter governs the solubility of the polymers in solvents such as chlorinated hydrocarbons, phenols, and dipolar aprotic solvents. A further characteristic of polyetherimides, which is clearly illustrated in Tables 3–5, is the considerable difference between the glass-transition and degradation temperatures of these polymers, thus making it possible to process them into articles by moulding under pressure. Materials based on polyetherimides have high deformation strength characteristics. Some properties of polyetherimide films obtained from solutions and also those of moulding materials derived from them are given in Table 6.

Table 6. Mechanical properties of materials based on polyetherimides obtained by polynitrosubstitution.[32]

[η], dl g^{-1}	Yield point, MPa	Elongation at yield, %	Break point, MPa	Elongation at break, %	Ultimate flexural strength, MPa	Flexural modulus, MPa	Thermal stability, °C
							
0.42	75.6	—	72.1	96	—	—	—
0.49	78.4	5.5	—	—	—	—	223
0.70	93.7	6.8	—	—	147.7	3080	217
							
0.38	93.7	7	86.1	65	—	—	204
							
0.36	49.7	2	—	—	—	—	228

Of polyetherimides that have been synthesised, the polyetherimide which corresponds to the structural formula



is of the greatest interest in terms of the availability of the starting compounds, processability, and deformation-strength and thermal properties of materials based on it. This polyetherimide, for which 4-nitrophthalic anhydride, *m*-phenylenediamine, and bisphenol A are

the starting compounds, is manufactured by General Electric (USA) under the name Ultem®.[10,34,38–47] Some properties of this polyetherimide are given in Table 7.

Table 7. Properties of Ultem® polyetherimide.[11]

Mechanical properties	
Stress at yield point (yield point)	105 MPa
Modulus of elasticity	3000 MPa
Elongation at break	60–80%
Ultimate flexural strength	145 MPa
Flexural modulus	3300 MPa
Ultimate compressive strength	140 MPa
Compressive modulus	2900 MPa
Gardner impact strength	36 N m
Izod impact strength	
notched sample	50 J m^{-1}
unnotched sample	1300 J m^{-1}
Thermal properties	
Glass-transition temperature	217 °C
Heat-deflection temperature under load	
1.85 MPa	200 °C
0.46 MPa	210 °C
Oxygen index	47
Inflammability by UL-94 method (vertical sample)	V–O at 0.64 mm Hg
Smoke evolution by NBS (National Bureau of Standards) method	
D_s after 4 min	0.7
D_{max} after 20 min	30

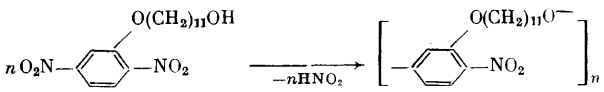
Ultem® is one of the best engineering thermoplastics known at the present time.[40–47] Its distinctive merits are good processability on standard equipment,[43–47] high tensile strength and modulus of elasticity,[34,38,40–43,46,47] good preservation of mechanical properties at elevated temperatures,[38,40,41,43,46,47] valuable electrical properties that remain stable over wide temperature and frequency ranges.[34,38,40,41,43,46,47] The material is distinguished by its high heat resistance and low smoke density. With regard to the latter property it is superior to all known unfilled thermoplastics.[38,40,41,43,44,46,47] The polyetherimide is stable towards solvents[41,45,47] and has high chemical stability.[38,46,47]

Because of the unique properties of Ultem®, in particular the possibility of using it to obtain articles with a complex configuration, it can be successfully used as a construction material in electrical engineering, electronics, the aerospace industry, ship building, and transportation, including the manufacture of components in the car industry.[38,41,46–48] Moreover, Ultem® and other polyetherimides can be used as heat-resistant adhesives,[50] layers and films for the electronics industry,[51] and foamed plastics for use in heat insultion and vibrational absorption.[52]

Mixtures of polyetherimides with other heterochain and heterocyclic polymers are of considerable interest. Thus, composites based on aromatic polyamides and polyetherimides were obtained with improved impact strength and stability towards chlorinated solvents.[53] Attempts have been made to produce mixtures of polyetherimides and polybenzimidazoles.[54]

On the whole polyetherimides have attracted the attention of consumers, and according to several studies[3,13,38–49] constitute a significant achievement in the chemistry and technology of condensation polymers.

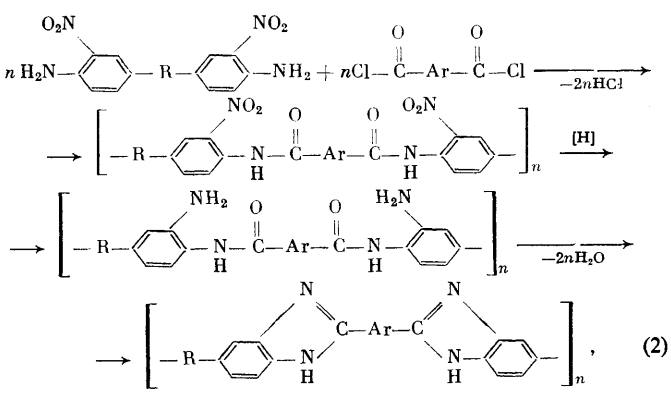
It was shown by Schaeffer in recent studies[55,56] that not only phenol groups but also aliphatic hydroxyl groups can be used in nitrosubstitution reactions. Thus, polycondensation of 1,4-dinitro-2-(n-hydroxyundecyloxy)benzene in a mixture of THF : DMSO (3 : 1) using phase-transfer catalysts gave polyethers with molecular weights of up to 32 000.



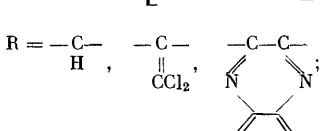
III. Reductive polyheterocyclisation reactions

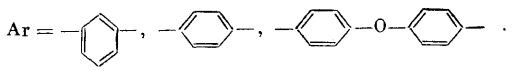
In contrast to nucleophilic aromatic polynitrosubstitution processes, reductive polyheterocyclisation reactions[57–60] do not assume substitution of nitro groups contained in the monomers used. The nitro groups are retained as *o*-substituents in heterochain polymers, but after their reduction to primary amine groups they participate in processes for the formation of the required aromatic heterocycles.

The evolution of reductive polyheterocyclisation processes in recent years has been due primarily to the development of novel polybenzimidazoles. Novel unsubstituted poybenzimidazoles have been obtained[61–65] from novel bis(*o*-nitroanilines) that are derivatives of chloral and DDT [66–68] by a route that had been proposed previously[57–60,69–71] and which involves the mild reaction between bis(*o*-nitroanilines) and aromatic dicarboxylic acid dichlorides in NMP followed by reduction/cyclisation of the poly(*o*-nitroamides):



(2)



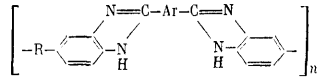


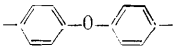
Some properties of the unsubstituted polybenzimidazoles synthesised, which are soluble in MP, DMF, DMAA, and DMSO, are given in Table 8.

It is evident from the properties listed that the majority of the unsubstituted polybenzimidazoles are non-softening polymers with relatively low values of the temperatures of loss of 10% of initial

weight (T_{10}) during differential thermogravimetric analysis (air, ΔT = 5 °C min^{-1}). The unusual series of thermal stability of the polybenzimidazoles in relation to the dicarboxylic acid residue may be due to incomplete reduction of the nitro groups and the subsequent ring-closure reactions of (*o*-nitro)amide residues at high temperatures (see below).

Table 8. Some properties of unsubstituted polybenzimidazoles with the general formula[61,65]



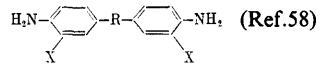
—R—	—Ar—	η_{int} in NMP, dl g^{-1}	T_{soft}, °C	T_{10}, °C
—C(=O)—		0.44	–	360
—C(=O)—		0.30	–	350
—C(=O)—		0.28	300	410
—C(=CCl$_2$)—		0.28	–	380
—C(=CCl$_2$)—		0.46	–	360
—C(=CCl$_2$)—		0.30	–	410
		0.28*	–	475
		0.10*	–	425

*Viscosities determined in *m*-cresol.

Another characteristic feature of unsubstituted polybenzimidazoles synthesised by means of reductive polyheterocyclisation is provided by their low viscosities and hence molecular-weight characteristics, caused by the lower basicity (Table 9) and correspondingly lower nucleophilicity of bis(*o*-nitroanilines) compared to unsubstituted diamines containing the same "bridging" groups.

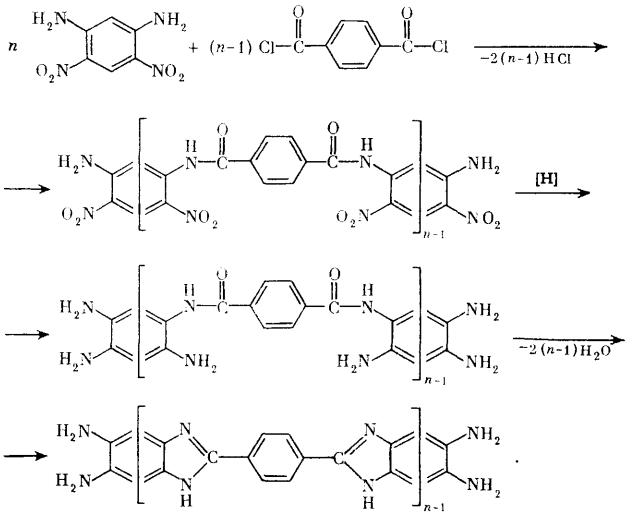
The outcome of this situation is evident in the use of reductive polyheterocyclisation processes for the synthesis of oligomeric benzimidazoles rather than polymeric forms,[72] for which it is most suitable to carry out polycondensation with a certain excess of bis(*o*-nitroanilines).

Table 9. Ionisation constants of bis(*o*-nitroanilines) and unsubstituted diamines with a corresponding structure, having the general formula

 (Ref.58)

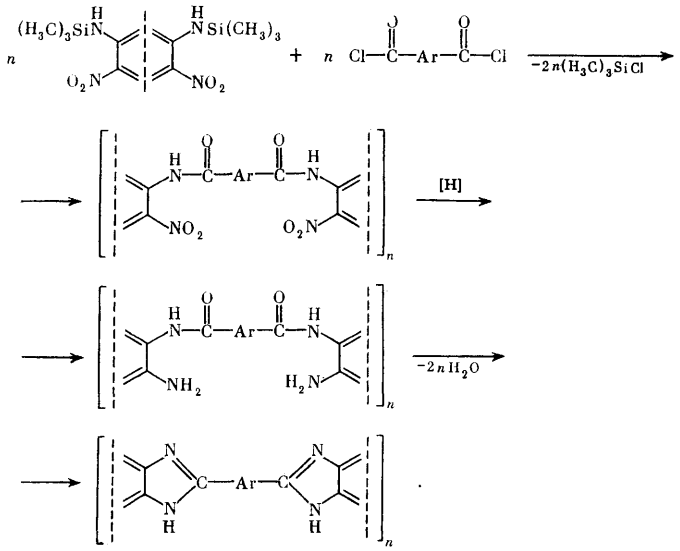
—R—	—X	pK_{a1} (DMF)	pK_{a2} (DMF)	ΔpK_a
—C(=CCl$_2$)—	–H	3.65	3.20	0.45
—C(=CCl$_2$)—	–NO$_2$	2.75	2.50	0.25
—C(=O)—	–H	3.02	2.72	0.30
—C(=O)—	–NO$_2$	2.75	2.45	0.30
	–H	2.95	2.62	0.33
	–NO$_2$	1.88	1.76	0.12

Such an approach is of particular interest in relation to the synthesis of rod-like oligobenzimidazoles starting from 1,3-dinitro-4,6-diaminobenzene and terephthalyl chloride:[72]

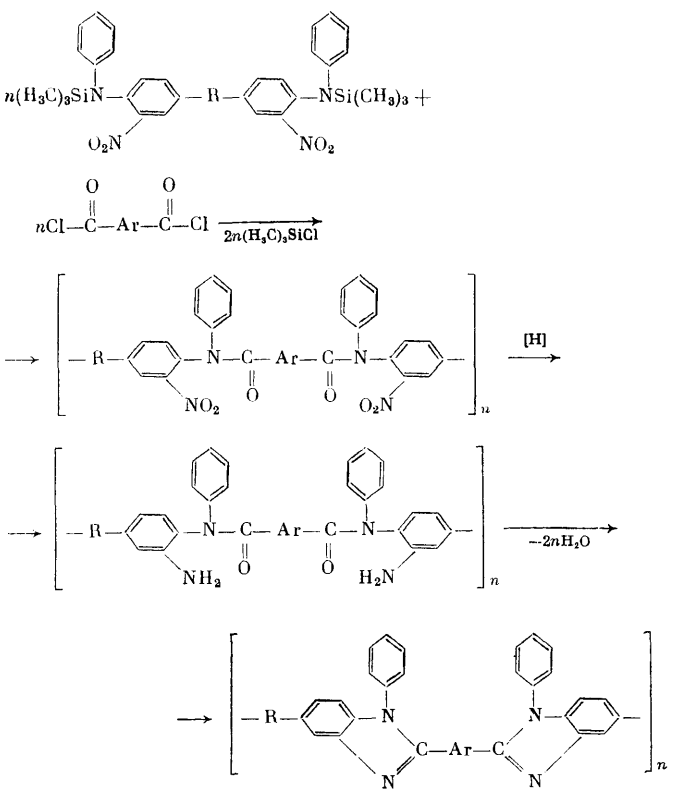


Rod-like oligobenzimidazoles containing *o*-phenylenediamine terminal groups can be used, according to Gordon et al.[73–76] to obtain molecular composites, which have stimulated considerable interest amongst research workers recently.[77–80]

An alternative approach to the use of bis(*o*-nitroanilines) to obtain benzimidazole-containing systems involves increasing the basicity of the amino groups of these monomers by trimethylsilylating them:[81,82]

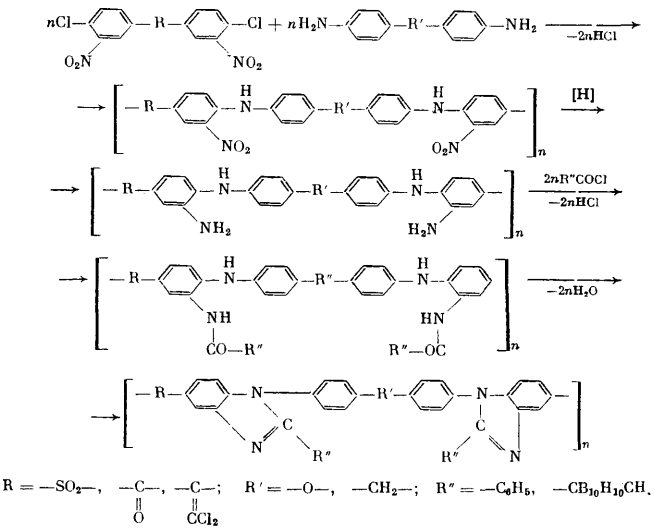


According to Rusanov and Tugushi,[72] a similar approach can yield relatively high-molecular-weight polybenzimidazoles containing phenyl substituents on the nitrogen atom in the benzimidazole rings, which are synthesised from very weakly basic bis(*o*-nitrodiphenylamines):



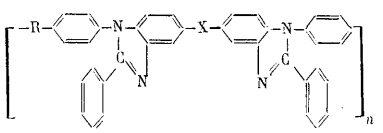
R = $-SO_2-$, $-\overset{\overset{O}{\|}}{C}-$, $-\overset{\overset{CCl_2}{\|}}{C}-$.

Novel poly(*C*-substituted) benzimidazoles[83–86] were obtained by means of modified reductive polyheterocyclisation processes. According to Rusanov et al.,[87,88] these involved the reaction of activated bis(*o*-nitrohalo)arylenes with aromatic diamines, reduction of the nitro groups in the resulting poly(*o*-nitro)imines to amino groups, acylation of the latter, and catalytic cyclisation of polyimines containing *o*-acylamine substituents:



R = $-SO_2-$, $-\overset{\overset{O}{\|}}{C}-$, $-\overset{\overset{CCl_2}{\|}}{C}-$; R′ = $-O-$, $-CH_2-$; R″ = $-C_6H_5$, $-CB_{10}H_{10}CH-$.

Table 10. Fundamental properties of poly(*C*-phenyl)benzimidazoles with the general formula[83–85]



—R—	—X—	η_{int}, dl g^{-1}	T_{soft},** °C	T_{10}^{*}, °C
$-\overset{\overset{CCl_2}{\|}}{C}-$	—O—	1.30	360	450
$-\overset{\overset{CCl_2}{\|}}{C}-$	$-CH_2-$	1.00	330	410
$-\overset{\overset{O}{\|}}{C}-$	—O—	1.50	310	510
$-\overset{\overset{O}{\|}}{C}-$	$-CH_2-$	1.20	280	470

* Determined from thermomechanical curves.
** Differential thermogravimetric analysis, air, ΔT = 4.5 °C min^{-1}.

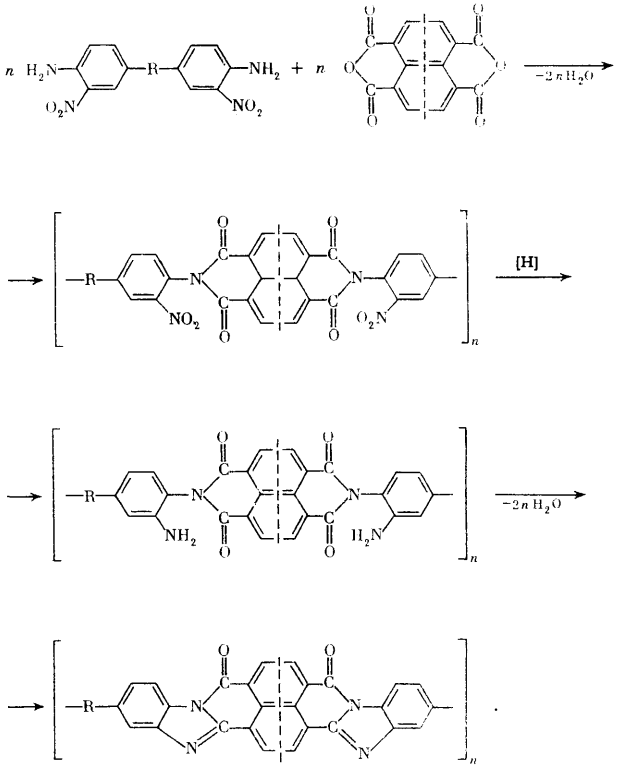
C-phenyl-substituted polybenzimidazoles that combine high viscosity and thermal properties with solubility in phenolic solvents, MP, and DMF have been obtained using 3,3′-dinitro-4,4′-dichloro-

benzophenone and 1,1-dichloro-2,2-bis(3-nitro-4-chlorophenyl)-ethylene,[83–85] which are derivatives of chloral and DDT,[66–68] as activated bis(*o*-nitrohalo)arylenes. Some properties of these polymers are given in Table 10.

C-Carborane-substituted polybenzimidazoles were obtained[86] by reaction of 3,3′-dinitro-4,4′-dichlorodiphenylsulphone with 4,4′-diaminodiphenyl oxide, reduction of the nitro groups in the resulting poly(*o*-nitro)imine to amino groups, acylation of the latter with *m*-carborane-1-carboxylic acid chloride, and catalytic cyclisation of the systems obtained to the required polybenzimidazoles. It is interesting to note that the carborane-containing polybenzimidazoles obtained in this manner are superior in terms of their viscosity and thermal properties as well as the strength of their films to poly(*C*-phenyl)benzimidazoles obtained from *m*-carborane-dicarboxylic acid dichloride.[86]

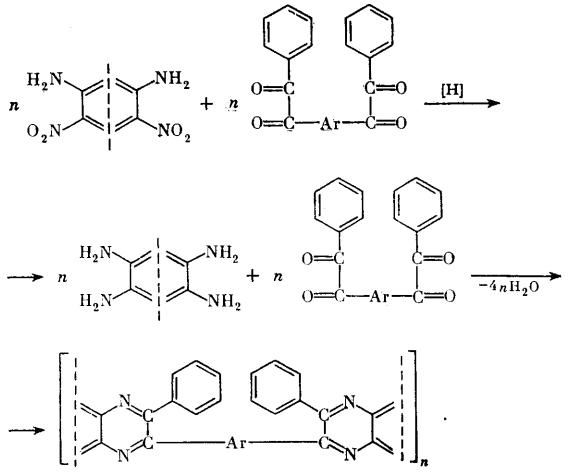
As well as increasing the range of polybenzimdazoles obtained by means of reductive polyheterocyclisation, the attention of research workers in recent years has been focussed on the possibility of using this process to obtain classes of polyheteroarylenes such as polynaphthoylenebenzimidazoles and polyphenylquinoxalines.

The synthesis of polynaphthoylenebenzimidazoles was carried out in accordance with following scheme:[89]



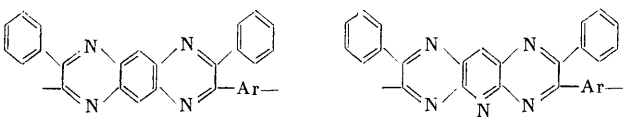
An advantage of this approach to the synthesis of polynaphthoylenebenzimidazoles, in addition to those already known,[57–60] is the possibility of decreasing the number of isomers of the required structures by means of acylation reactions exclusively on the amino groups at the early stages of the reactions. In turn, a decrease in the number of isomers opens up a route to the creation of more regularly formed systems, which have correspondingly higher thermal properties.

The synthesis of polyphenylquinoxalines was carried out in accordance with the following scheme:[90]



This process differs from the previously developed reductive polyheterocyclisation reactions[57–60] in that the stage involving the formation of linear nitro-containing polymers is absent — bis(*o*-nitroanilines) do not react with bis(α-diketones) even under very severe conditions. In actual fact this process essentially involves the reduction of bis(*o*-nitroanilines) to bis(*o*-phenylenediamines) in the presence of bis(α-diketones) and, owing to the specific nature of the reactions leading to polyphenylquinoxalines,[91–94] a polycondensation reaction *in situ* of the resulting bis(*o*-phenylenediamines).

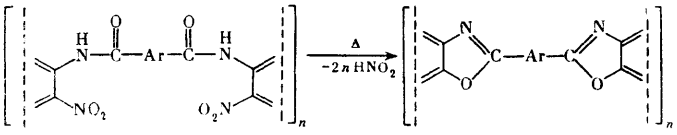
The scheme put forward is attractive as it opens up the possibility of obtaining polyphenylquinoxalines with high heat stability (T_{soft} ~ 400 °C) containing condensed heterocycles starting from 1,3-dinitro-4,6-diaminobenzene instead of the unstable 1,2,4,5-tetraaminobenzene and 3,5-dinitro-2,6-diaminopyridine instead of the unstable 2,3,5,6-tetraaminopyridine.

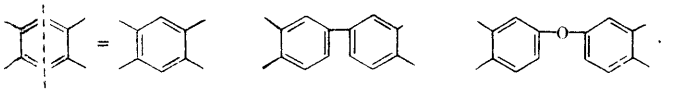


It was reported by Korshak et al.[90] that when processes involving the catalytic reduction with hydrogen over Raney nickel or the reduction with activated iron mixed with HCl were used, only low-molecular-weight polymers ($\eta_{init} \leqslant 0.2$ dl g^{-1}) were obtained. It would appear that under these conditions either the selectivity of reduction is disrupted, i. e., not only is bis(*o*-nitroaniline) reduced but also the bis(α-diketone) is partially reduced, or the reduction of bis(*o*-nitroaniline) to bis(*o*-phenylenediamine) is not quantitative. Further research into the optimum process conditions will most likely lead to considerable progress in the synthesis of polyphenylquinoxalines.

IV. Thermal polyheterocyclisation reactions of poly(*o*-nitroamides)

Poly(*o*-nitroamides) obtained in accordance with Scheme (2) can, according to Kim and Pearce,[95] be regarded as prepolymers for the preparation of polybenzoxazoles:





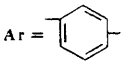
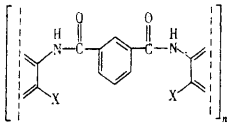
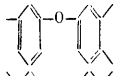
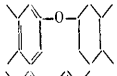
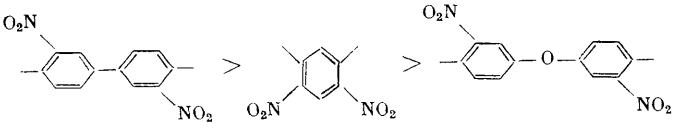


Table 11. Thermal stability and yield of carbon of aromatic polyamides with the general formula:[95]

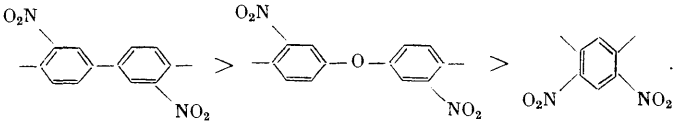


	–X	T_{sd}, °C	$T_{mr}I$, °C	$T_{mr}II$, °C	Yield of carbon, %
	–H	425	460	–	42
	$-NO_2$	336	351 373	650	35
	–H	440	470	588	37
	$-NO_2$	291	325 390	592	45
	–H	505	542	–	38
	$-NO_2$	386	405	660	52

The series of thermal stability of poly(*o*-nitroamides) in relation to the bis(*o*-nitroaniline) residue takes the following form:



while the yield of carbon is given by the series:



The respective temperatures of start of degradation (T_{sd}), temperatures of maximum rate of weight loss (T_{mr}), and yields of carbon of poly(*o*-nitroamides) and unsaturated polyamides are given in Table 11.

An analysis of the data listed in Table 11 indicates that the temperatures of start of thermal degradation for poly(*o*-nitroamides) are lower than for unsubstituted polyamides in all cases. At the same time, the yield of carbon in the majority of cases is higher for poly(*o*-nitroamides), which confirms that reactions leading to more stable systems occur in poly(*o*-nitroamides).

The occurence of two maxima for the rate of weight loss is a conspicuous feature. In the opinion of Kim and Pearce[95] it is due to the differing ease of elimination of the first and second nitro groups from each fundamental unit of the polymer.

The formation of polybenzoxazoles from poly(*o*-nitroamides) occurs more readily than from the corresponding poly(*o*-chlorophenyl)amides[96–98] and may be regarded as a promising method for the synthesis of these polyheteroarylenes.

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Translated from *Uspekhi Khimii* **60** 1473–1493 (1991) U.D.C. 541.64;541.128;547.7;542.953

Donor-acceptor interactions in polycondensation processes

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ABSTRACT. **The results of studies on the role of donor-acceptor interactions in polycondensation processes are correlated. The thermodynamic and kinetic aspects of the problem, the features of the reaction mechanism, structure and properties of the resulting polymer that are related to donor-acceptor interactions are examined in examples of the curing of epoxide oligomers.**

The bibliography includes 84 references.

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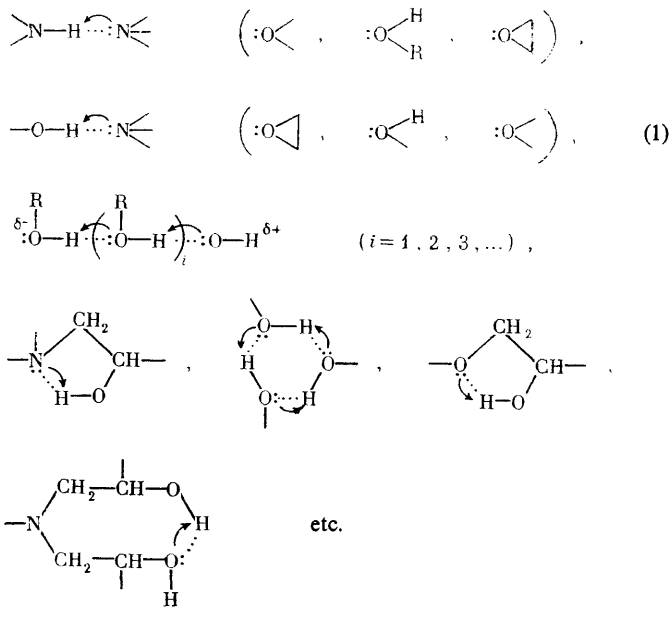
I. Introduction

Monomers containing reactive functional groups of an electrophilic and nucleophilic nature are usually employed as starting compounds in polycondensation processes. These groups can undergo different donor-acceptor interactions between themselves and with other compounds of the reaction system (polymer, solvent, catalyst, impurities or specially introduced components), forming homo- or hetero-associates of a linear or cyclic nature. Thus, both initial and developing systems have a well-defined structural organisation. Although the very fact of such donor-acceptor interactions occurring between polar groups has been known for a long time in organic chemstry, their role in polycondensation processes during the formation of linear and cross-linked polymers, as in similar reactions of low-molecular-weight organic compounds, has until recently remained unclear. Only comparatively recently has this question become the subject of systematic studies, mainly through the efforts of two groups of research workers at the Semenov Institute of Chemical Physics, USSR Academy of Sciences. The first group has studied this question in the case of reactions involving formation of urethanes,[1–12] the second group has studied epoxide curing processes.[13–31] On the basis of these studies it has been possible to formulate sufficiently well-argued ideas about the role of donor-acceptor interactions in the kinetics and mechanism of the processes studied and also in the formation of the structure and properties of the resulting polymers.

The aim of the present article is to classify the results of studies on the effect of donor-acceptor interactions on polycondensation processes, mainly by considering examples of the curing of epoxide oligomers and to draw the attention of research workers to this problem. Elucidation of the role of possible donor-acceptor interactions in the reaction system is a key not only to a more fundamental understanding of the features of the kinetics and mechanism of the formation of a polymer but also to controlling the process and, in individual cases, the structure and properties of the resulting polymer.

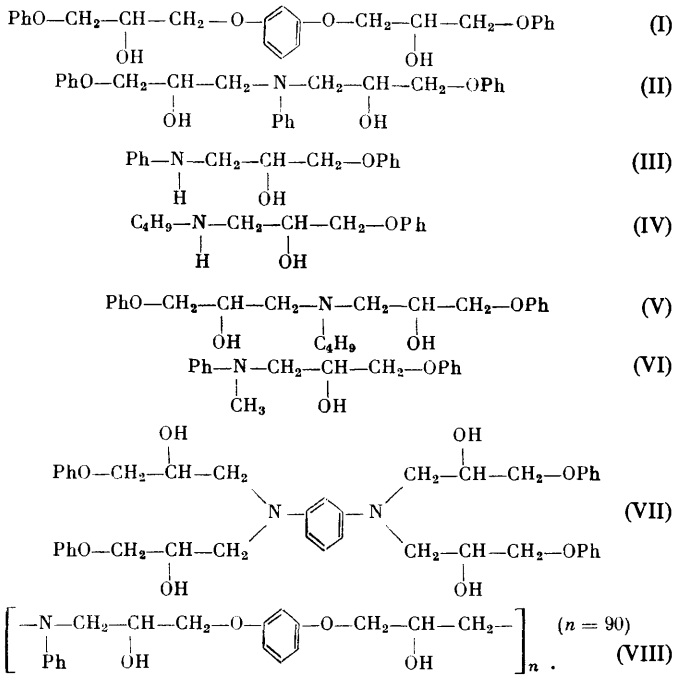
II. Composition of the reaction system

The composition of the reaction system is highly complex because of the occurrence of various donor-acceptor interactions, and linear and cyclic homo- and hetero-associates are contained in the system together with the monomer forms of reactive functional groups. As an example we can illustrate the possible forms of the donor-acceptor complexes for epoxyamine systems containing primary, secondary, and tertiary amino groups as well as epoxide, secondary hydroxyl, and ether groups.



The occurrence of such donor-acceptor interactions as described above was demonstrated using specially synthesised and certain other model compounds by means of IR spectroscopic studies over a

wide concentration range in CCl_4 solution.[13,20,26,27] The model compounds that were synthesised are depicted below:



The values of thermodynamic parameters for the respective complexation reactions have been determined by means of calorimetry and IR spectroscopy (Tables 1 and 2).[13,20,26,31–33]

Table 1. Thermodynamic parameters of reactions for the formation of model donor-acceptor complexes.[20]

Reaction system	$-\Delta H$, kJ mol^{-1}	$-\Delta S$, J mol^{-1} K^{-1}	K_e*, litre mol^{-1}	K_e**, litre mol^{-1}
Cyclohexanol–cyclohexanol (HH)	27.2	98.6	–	–
Cyclohexanol–phenyl glycidyl ether (EH)	14.2	46.0	1.3/0.5	1.5/0.6
Cyclohexanol–aniline (A_1H)	18.8	67.0	1.9/0.5	2.0/0.5
Cyclohexanol–ethylaniline (A_2H)	11.7	41.8	1.4/0.7	1.2/0.6
Cyclohexanol–diethylaniline (A_3H)	3.8	8.4	0.6/0.6	0.3/0.3

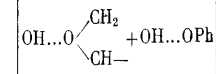
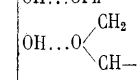
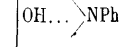
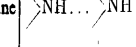
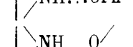
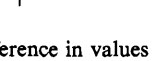
* The equilibrium constants K_e (determined by calorimetry) at 22 °C are given by the numerator, while the values of K_e at 98 °C are given by the denominator.

** The values of K_e (determined by IR spectroscopy) at 28 °C are given by the numerator, while the values of K_e at 98 °C are given by the denominator.

Five-membered rings constitute a characteristic form of the cyclic associates. In the molecules of model compounds II and V eight-membered rings with OH...OH hydrogen bonds also occur, but the total proportion of cyclic structures of the associates in the polymer is small and does not exceed 1–2%. A similar conclusion was also drawn from kinetic studies.[20,30]

It is interesting to note that NH groups participate in the formation of hydrogen bonds in both the crystalline and amorphous states of the compound not only as electron donors but also as acceptors.[26,32,33]

Table 2. Thermodynamic parameters of model H-complexes.[26,32,33]

Compound	Reaction system	Type of H-bond in the complex	K_e (at 25 °C), litre mol^{-1}	$-\Delta H$, kJ mol^{-1}
I	Isopropanol–isopropanol	OH...OH	2.45	17.0÷21.0
II	Isopropanol–phenyl glycidyl ether		1.08	–
III	Isopropanol–anisole	OH...OPh	0.33	9.6
IV	From the difference between systems II and III*		0.75	12.5
V	Isopropanol–*N*-diethylaniline		0.38	9.2
VI	*N*-Methylaniline–*N*-methylaniline		0.45	7.5
VII	*N*-Methylaniline–anisole		0.36	7.5
VIII	*N*-Methylaniline–di-n-propyl ether		0.29	13.0

* K_e calculated from the difference in values for systems II and III.

It can be seen from Table 2 that autoassociation of the hydroxyl groups is the predominant form of association at room temperature. As estimates have shown,[26] the proportion of hydroxyl group autoassociates in epoxyamine networks with a stoichiometric composition constitutes 85–90%. Autoassociation of hydroxyl-containing compounds (alcohols, phenols, acids) has been well studied. The extensive literature data, which have been classified in three reviews,[31,33,34] indicate that it is quite a complex process, resulting in the formation of an equilibrium mixture of different linear and cyclic *n*-dimensional autoassociates. With respect to the question that interests us concerning the participation of such structures in the catalysis of the nucleophilic addition of amines to an epoxide ring, the cyclic associates usually exist as trimers and it follows from their structure [see scheme (1)] that they are actually inactive in this process, whereas in linear associates the activity increases significantly relative to the activity of a monomeric hydroxyl-containing compound.

The question as to how information about the thermodynamics of low-molecular-weight model compounds can be applied to real cross-linked epoxyamine polymers is quite natural. A direct comparison between the IR spectra of model compounds and polymers provides a clear answer.[28] The frequencies of the absorption maxima, the line

half-widths, and the relative intensities of vibration bands due to groups participating in the formation of hydrogen bonds for model compounds (melt or glass) virtually match those of linear and cross-linked polymers in a vitreous state. This means that the composition and average values of the hydrogen bond energies for polymer and low-molecular-weight epoxyamine systems are similar. A similar conclusion can be made by comparing the thermodynamic parameters of the model and polymer systems (Tables 1–3).

Table 3. Thermodynamic parameters of complexation reactions for a number of epoxyamine systems.[13,17,18,23,24]

System	$-\Delta H$, kJ mol^{-1}	$-\Delta S$, J mol^{-1} K^{-1}
Phenyl glycidyl ether–aniline (Refs.20, 23)		
EH	9.6	29.3
A_1H	14.2	35.5
A_2H	9.2	27.2
Phenyl glycidyl ether–*N*-ethylaniline (Ref.24)		
EH	10.4	33.4
A_2H	10.4	41.8
A_3H	4.6	5.0
Resorcinol diglycidyl ether–2,5-diaminopyridine (Refs.17, 18, 21)		
EH	16.3	33.4
A_1H	14.2	31.3
A_2H	10.4	41.8
A_3H	4.6	5.0

The processes involving formation of donor-acceptor complexes in oligooxypropylene glycols, hydroxyoligobutadienes, and oligourethanes have been studied using IR spectroscopy and calorimetry.[34–36] It was shown that the thermal parameters of the H-complex in these systems (HO:...H–O, OH...:O<, OH...π-bond, NH...π-bond, NH...:O=C<) do not depend on the molecular weight of the oligomers and almost match those for low-molecular-weight model compounds.

All these results suggest that the approach using model systems to study donor-acceptor interactions is fully justified. Moreover, only with its application is it possible to determine quantitatively the thermodynamic and kinetic properties of the numerous complexes that are formed in a reaction system. At the present time we have only just begun to study the thermodynamics and kinetics of complex systems. For the time being, in fact, it is only possible to determine the apparent values of the thermodynamic and kinetic parameters in the systems (see Section III). The development of an algorithm for both experimental and theoretical approaches to the study of such systems remains an important task.

In studying the thermodynamics of these reactions another problem arises—a correct determination of the exothermicity of opening the epoxide ring and the justification for using calorimetry to study the kinetics of the process.

In fact, during the complexation reactions in the system with constantly varying concentrations of donor and acceptors, the apparent quantity of heat liberated (Q) may have a non-linear dependence on the degree of conversion (α) since in general

$$Q = q\alpha + \sum q_i(\alpha), \qquad (2)$$

where q is the exothermicity of opening the epoxide ring: $\Sigma q_i(\alpha)$ is the total exothermicity of all the donor-acceptor interactions in the system, which depends non-linearly on the degree of conversion $\alpha = (E_0 - E)/E_0$ (E and E_0 are the current and initial epoxide concentrations respectively).

However, it usually transpires that there is a well-defined linear relationship between Q and α, determined chemically or by means of IR spectroscopy (it is represented graphically as a straight line starting from the origin). Consequently, $\Sigma q_i(\alpha) \to 0$ and $q\alpha \gg \Sigma q_i(\alpha)$, namely, there is a balancing out of the heats of formation and heats of decomposition of the different complexes in the systems during the process. This in turn means that calorimetry can be used as a tool to study the kinetics of these reactions.

III. Donor-acceptor interactions and reaction kinetics

It is clear that formation of the complexes described above must lead to a change in the reactivity of the initial reactant molecules. At the same time, because the concentrations of the functional groups and hence donor-acceptor complexes are constantly changing throughout polycondensation, the nature of the kinetic effects must also vary with the conversion.

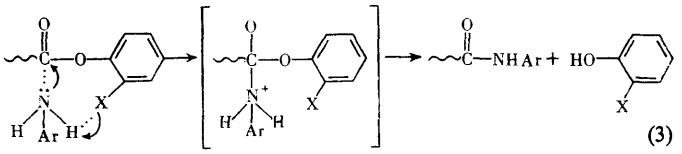
Only on the basis of ideas about the decisive role of complexation processes is it possible to understand such characteristics of the reactions of epoxy compounds with primary and secondary amines as the simultaneous occurrence of autoacceleration and autoinhibition effects, which is very unusual in terms of kinetics,[13,20,30] the catalytic and inhibitor effect of different solvents,[13,20,27–40] the well-defined ortho effect of electron-donating substitutents in aromatic amines and the anomalously low activity of polyoxyethylene primary amines,[37,41] the accelerating effect of added quantities of tertiary amines,[19,42] the high reactivity of aromatic *N*-diglycidylamines and *o*-diglycidyl ethers,[43,44] and certain others.[20,29,45–49]

A very typical kinetic feature of polycondensation systems that is related to the occurrence of donor-acceptor interactions is the markedly non-linear, and sometimes even non-monotonic, dependence of the rate of reaction on the concentration of the reactants with a considerable variation of the latter.[3–6,46,48]

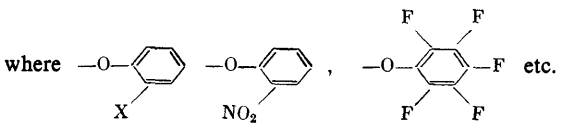
In the formation of urethanes during reaction between isocyanates and alcohols catalysed by tetravalent tin compounds, the effect of donor-acceptor interactions manifests itself in the extremal nature of the dependence of the catalytic rate constant on the strength of the complex between catalyst and alcohols,[50] the sharp reduction in the Hammett ρ constant compared to that for a non-catalytic process,[51] and the levelling out of the reactivity of hydroxyl groups that are different in nature.[3,4]

In reactions of the so-called "activated" polycondensation the high activity of *o*-substituted phenyl esters is due not only to and even not so much to stabilisation of the leaving group, which increases with a decrease in pK_a of the corresponding acid, but mainly to the catalytic effect of the *o*-substituent through formation

of an intramolecular hydrogen bond with amines in the preparation of a polyamide:[52,53]

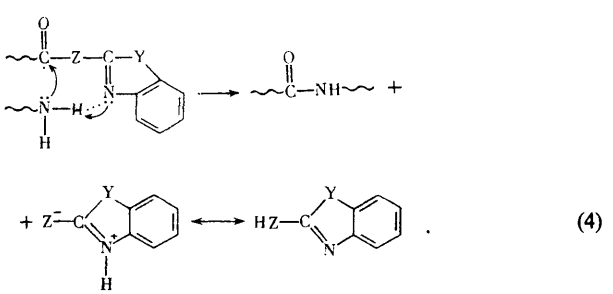


(3)

where  etc.

As expected, the catalytic effect of an *o*-substituent (such as NO_2) is particularly well defined in a proton-inert or weakly proton-accepting medium (chlorobenzene, benzene), where the *o*-nitrophenyl ester is two to four times more active than its *p*-substituted analogue. In a strong proton-donating medium (HMPA), which inhibits the formation of an intramolecular hydrogen bond, the reverse occurs—the *p*-nitrophenyl ester is eight times more active than the *o*-substituted isomer.[53]

It was established in a similar manner that benzene derivatives are very effective as leaving groups because of the formation of an intramolecular hydrogen bond in the reaction between activated esters and amines:[54]

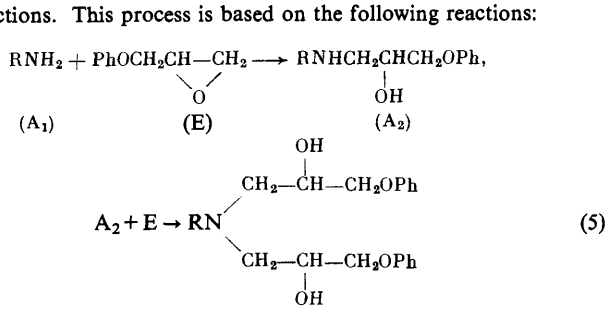


(4)

(Y, Z = —O—, —S—)

In a recently published monograph[55] a large number of examples are given to illustrate the determining role of an intramolecular hydrogen bond and other types of donor-acceptor interactions of reacting groups in the catalysis of different nucleophilic substitution-addition reactions.

Let us examine in greater detail the features of the kinetics of the curing of epoxides by amines that are related to donor-acceptor interactions. This process is based on the following reactions:

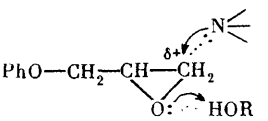


(5)

(R = Ar or Alk).

A tertiary amino group that is formed during curing of epoxides by aliphatic amines can in individual cases catalyse the polymerisation of epoxide groups. If aromatic amines are used as curing agents, this reaction does not occur at temperatures below ~150 °C.

It is widely known that added quantities of hydroxyl-containing compounds (water, alcohols, phenols, acids) substantially accelerate the reaction between epoxides and amines and other nucleophilic reactants.[18–24,56–63] In this case considerable activation of the carbon atom of the epoxide ring towards nucleophilic attack takes place. The reaction occurs via a trimolecular transition state, first described by Smith[62,63] for the interaction between epoxide compounds and amines: †



(6)

It is as a result of the build-up of hydroxyl groups during the reaction [see scheme (5)] that the curing of epoxide oligomers by amines has a well-defined autocatalytic nature.

By using a special method for the efficient removal of traces of moisture and other hydroxyl-containing compounds[22] from the initial materials and reaction vessels, it was possible to reduce the concentration of hydroxyl-containing impurities on the basis of water to 10^{-6} mol litre^{-1} or less.

It transpired[22] that under these conditions a reaction occurs between phenyl glycidyl ether (PGE) and aniline, but the initial rate is 40–50 times slower than in the reaction catalysed by proton donors and the dependence on the aniline concentration is quadratic rather than linear. The presence of even small amounts of moisture reduces the order of reaction with respect to amine.

The quadratic dependence of the rate of reaction on the concentration of amine (A_1) signifies that the latter acts both as an electrophile, forming an intermediate complex (A_1E) with an epoxide compound (E)

$$A_1 + E \underset{K_-}{\overset{K_+}{\rightleftharpoons}} (A_1E), \qquad (7)$$

and as a nucleophilic reagent

$$(A_1E) + A_1 \xrightarrow{K_1} A_2 + A_1,$$

are a result of which an addition product (A_2) is obtained.

The decrease in the order of reaction with respect to amine in the presence of hydroxyl-containing impurities is related to its taking place partly by a catalytic mechanism, when the hydroxyl-containing compound, which is considerably more acidic than the amine, acts as a proton donor. It should be noted that in the usual method of purification of the reactants and the vessels used, the content of moisture in the reaction mixture is still sufficiently high and the order of reaction with respect to amine is considerably different from quadratic.[23,24] Thus, it was shown by Mutin et al.[25] that the reaction of PGE with butylamine has a fractional order ($1 \leqslant n \leqslant 2$) that is dependent on the reaction temperature. This case is effectively represented if account is taken of the fact that two reactions are taking place simultaneously in the system—one that is first-order with respect to amine (catalytic reaction) and one that is second-order with respect to amine (non-catalytic reaction). The

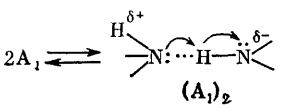
† Not only monomeric but also associated forms of hydroxyl-containing compounds and amines can act as proton donors and nucleophilic reagants.

contribution of each of these to the apparent rate is dependent on temperature, since their energies of activation are different, and on the concentration of the proton-donating impurities.

We should note that on the whole there are no fundamental differences‡ between the catalytic reaction, when activation of the epoxide ring is effected by the hydroxyl-containing component, and the non-catalytic reaction, where the amine itself acts as an electrophilic reagent (proton donor). It is important to note that electrophilic assistance is needed for opening of the epoxide ring by such weakly nucleophilic reagents as amines. This conclusion was also extended to other known nucleophilic addition reactions to an epoxide ring,[13] and it is essential for an understanding of the kinetic mechanisms of such processes.

Let us examine in greater detail the mechanism of addition of amines to the epoxide ring. The catalytic addition of amines takes place in two stages: initial formation of quite stable donor-acceptor complexes between the epoxide compound and the hydroxyl-containing reactant; and subsequent nucleophilic attack by amine on this complex, i.e., this quasi-termolecular reaction in fact comprises two successive bimolecular reactions with a push-pull mechanism occurring in the transition state. We should stress that in the donor-acceptor complexes between amine and hydroxyl-containing compounds ($A_i \ldots HOR$) formed in this process the amine is actually deactivated as a nucleophilic reagent and only free, uncomplexed molecules of amine act as the latter.

The question of the detailed mechanism of the non-catalytic reaction between epoxide compounds and amines still remains an open one. Apart from the mechanism shown in scheme (7), we can also put forward an alternative one which involves the initial formation of a more reactive amine dimer



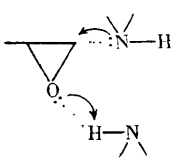
(8)

According to scheme (8) an increase in both the electrophilic and nucleophilic activity of the dimer compared to monomeric amine is to be expected. The kinetic scheme in this case can be given in the form:

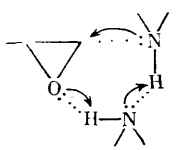
$$2A_1 \rightleftharpoons (A_1)_2,$$

$$(A_1)_2 + E \rightleftharpoons [(A_1)_2E] \rightarrow A_2 + A_1. \qquad (9)$$

The respective transition states for the alternative mechanisms (7) and (9) are shown in schemes (10) and (11):



(10)



(11)

‡ There is only a difference in the degree of activation of the epoxide ring.

It is impossible to distinguish between these mechanisms from the experimental data that are available at the present time. However, the second [scheme (11)] seems preferable to us, since according to this scheme addition of amine occurs via a cyclic transition state and is fully concluded in a single stage, whereas a further proton transfer is required in the realisation of scheme (9).

It is not excluded also that different mechanisms [see schemes (7) and (9)] can precede formation of the same transition state [see scheme (11)]. The question of the nature of the transition state in nucleophilic addition of an amine to an epoxide ring will be considered in greater detail below.

The kinetics of the condensation of primary and secondary amines with epoxides are well represented if account is taken of the fact that the main characteristic of these processes is the formation of different hetero- and auto-complexes that have varying reactivity. An interpretation of the physical significance of the apparent values of the termolecular rate constants that are determined still remains very approximate. This situation is evidently typical for liquid-phase reactions, in which different donor-acceptor interactions of all the components of the reaction system play an important part. For example, even the simplest non-catalytic reaction (in the absence of proton donors) of an epoxide compound with an amine should in general be given by a kinetic scheme that takes into account all the donor-acceptor interactions:

$$A_i^1 + A \underset{a}{\overset{K'_{ai}}{\rightleftharpoons}} A_{i+1}^1,$$

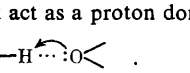
$$A_i^1 + A \underset{b}{\overset{K''_{ai}}{\rightleftharpoons}} (A_iE),$$

$$A_i^1 \underset{c}{\overset{K'''_{ai}}{\rightleftharpoons}} A_i^c,$$

$$A_i^1 + A_i^1 \xrightarrow[d]{K_{ij}} \text{product} + A_{i+j-1}^1, \qquad (12)$$

where A is a primary or secondary amine, the superscripts "l" or "c" indicate linear (reactive) and cyclic (non-reactive) autoassociates respectively. For reactions *a*, *b*, *d*: $i = 1, 2, 3, \ldots$; for reaction *c*: $i = 2, 3, \ldots, j = 1, 2, 3, \ldots$; K''_{ei}, K'_{ei}, K_{ei} are the equilibrium constants; k_{ij} are the true rate constants.

When glycidyl ethers are used as the epoxide compound and the solvent is electron-donating, kinetic scheme (12) will be supplemented by reactions involving complexation between amines and the non-ring oxygen atom in the glycidyl ether molecule and the electron-donating atom of the solvent molecule. In this case the amine must act as a proton donor



(13)

The apparent experimental rate constant of the non-catalytic reaction k_1 is determined from the equation

$$W_0 = k_1 E_0 A_0^2, \qquad (14)$$

where W_0 is the initial rate of reaction, A_0 and E_0 are the concentrations of the respective functional groups: the index "0" relates to the values of the parameters when $t = 0$.

From kinetic scheme (12) the following expression can be derived:

$$W_0 = \sum_{i=1}^{\infty} \sum_{j=1}^{\infty} k_{ij} (A_i^1 E) A_j^1, \qquad (15)$$

where (A_i^1E) and A_j^1 are the equilibrium concentrations of the respective complexes. A solution to this equation, namely, a determination of the composition of the apparent rate constant in general form does not seem possible.

In reality the situation is of course simpler, since the concentration of all the complexes rapidly decreases with an increase in the degree of autoassociation. With regard to the relationship $k_{ij} = f(i, j)$, it can turn out to be non-monotonic since opening of the epoxide ring will occur with the greatest probability via a cyclic transition state that is dependent on the values of i and j.

At the present time a definitive answer to the problem concerning the composition of the apparent rate constant in opening of the epoxide ring by amine is not known. As a first approximation the autoassociation reactions of amine can be neglected. In this case the form of the expression for the apparent rate constant of the non-catalytic reaction assuming that $(A_1E) \ll E_0$ is quite clear [see scheme (7)]:

$$k_{app} = k_{tr}K_e, \tag{16}$$

where k_{tr} is the rate constant for the fundamental reaction of opening the epoxide ring [see schemes (10) and (11)], K_e is the equilibrium constant of the reaction $A_1 + E \rightleftarrows (A_1E)$.

The composition of k_{app} will also be similar if it is assumed that the reaction occurs by scheme (9) via a cyclic transition state [see scheme (11)]. Here K_e is the equilibrium constant of the reaction $2A_1 \rightleftarrows (A_1)_2$, in which $A_{1_0} \gg 2(A_1)_2$ and cyclic forms of the dimers are absent.

The treatment given above indicates that we encounter considerable difficulties in interpreting the physical composition of the apparent rate constant, which are related to the absence of valuable quantitative information on the thermodynamics of the reactions for formation of H-complexes and their reactivity. Further detailed studies of the donor-acceptor interactions in these systems would make it possible to find a more precise solution to this problem than we can offer at the present time.

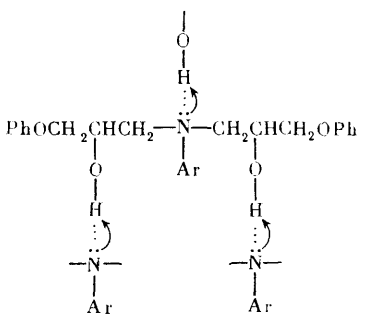
The question of the balancing mechanism which was touched upon above is very closely associated with the problem of the composition of the apparent rate constant. Without establishing this mechanism it is impossible to understand why in a complex system such as the epoxyamine system in question, where many donor-acceptor interactions take place and the reactivity of the H-complexes varies considerably, comparatively simple kinetic mechanisms occur. These are namely: a slight dependence of the apparent rate constant on the degree of conversion, simple dependences of the initial rate on the concentration of reactants, a linear dependence of the total quantity of liberated heat Q on the degree of conversion, and the similarity between the values of Q and the enthalpy for opening the epoxide ring. The latter two problems have been discussed already and the essence of the first two can be revealed, for example, in a study of the non-catalytic reaction.

According to kinetic scheme (12), the initial rate of reaction will decrease compared to that which would occur in the absence of any donor-acceptor interactions as a result of a decrease in the total number of nucleophilic species due to autoassociation of the amino groups and will increase because of an increase in the nucleophilicity of the associated amino groups as well as a certain increase in acidity of the auto-complexes of amine (compared to that for unassociated molecules). This combination of positive and negative factors should lead to a certain levelling out of the role of donor-acceptor interactions in changing the concentrations of reactants and reaction products, namely, a balancing effect. The linear dependence between the current reactant concentrations and the concentrations of their free, uncomplexed forms can also be attributed to its occurrence. In general the magnitude of the balancing effect depends on the nature of the reactants and the specific reaction conditions.

One of the kinetic manifestations of the formation of H-bonds in an epoxyamine system is shown not only in an acceleration but also a deceleration of this reaction at its advanced stages.

The deceleration effect of the advanced stages of conversion is due to the formation of unreactive complexes (A_iH_n). Complexation, on the one hand, reduces the concentration of the reactive complex (EH_n) and, on the other hand, reduces the concentration of free amine and hence leads to a retardation of the process. It should be stressed that deceleration of the reaction can only occur when the basicity of the resulting secondary of tertiary amino groups (or of both of them) is greater than the basicity of the initial primary amino group. Only in this case will a progressive relative decrease in the concentration of free hydroxyl groups, and hence in the rate of overall process, occur.[13,19,20,30]

Complexation of the amino groups with the hydroxyl groups is clearly revealed in the fact that the viscosity of the reaction system at the advanced stages of the processes increases substantially as a result of the formation of a network with labile hydrogen bonds at branch points, since the formation of tertiary amino groups gives rise to a trifunctional reaction occurring in the system (one tertiary amino group and two hydroxyl groups):



(17)

In complete agreement with what is expected, the effect of an increase in viscosity of the system during the reaction increases with a decrease in the ratio of A_{1_0}/E_0, where the index "0" denotes the concentrations of reactants at an initial point in time. In this case the maximum attainable value of the viscosity increases. Thus, when A_{1_0}/E_0 = 1.8; 1.0; 0.45, $\eta_{rel\,t\to 0}$ = 3.5; 14.0; 32.5 respectively. Introduction of a stronger base into the reacting system causes a sharp decrease in viscosity of the system as a result of break-up of the polyfunctional associates.

An increase in reaction temperature leads to a decrease in the proportion of amines associated with hydroxyl groups, and as a result to inhibition of the process starting to occur at a more advanced stage. When the reaction is carried out under adiabatic conditions, 100% conversion of the epoxide groups is achieved without any autoinhibition effect.[23]

Thus, the hydroxyl group has a dual role in this reaction. On the one hand, it leads to considerable activation of the epoxide ring as a result of the formation of a complex (EH_n); on the other hand, in the formation of unreactive complexes (A_iH_n) the rate of reaction is reduced because of a decrease in the concentrations of primary and secondary amines as well as that of free hydroxyl groups not forming (A_iH_n) complexes and which catalyse the reaction. The second factor, naturally, has a much greater effect in reducing the

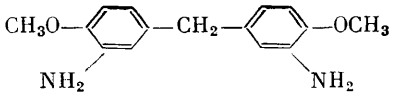
rate than does the first, which is also borne out by the experimental results.[20,30] Additions of a model secondary alcohol—cyclohexanol—lead not only to an increase in the rate of reaction but also to an increase in the degree of conversion at which a marked inhibition of the reaction occurs.

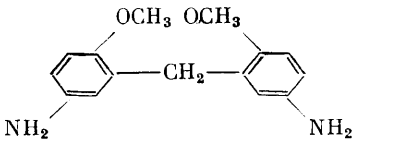
Thus, the results presented above suggest that the mechanism of the reaction of epoxide compounds with amines makes it basically possible for not only autocatalysis but also an autoinhibition effect at advanced stages of the reaction to be exhibited in such systems. However, the latter can only occur when the relative concentration of free hydroxyl groups decreases during the reaction because of the increase in the equilibrium constant for complexation between a hydroxyl group and an amino group on changing from a primary amino group to a secondary and then tertiary amino group.

When electrophilic assistance reagents are introduced into the epoxyamine systems (alcohols, phenols, carboxylic and Lewis acids) in order to activate the epoxide ring, donor-acceptor interactions can cause a dual kinetic effect—both acceleration and inhibition of this reaction depending on the concentration and acidity of the added components.[13,64,65] When activators with quite a high acidity are used (carboxylic and Lewis acids), the dependence of the rate of reaction on the concentration of added component is extremal in nature.

Actually the effect of activating the epoxide ring towards a reaction with nucleophilic reagents increases with an increase in acidity of the electrophilic assistance reagent. At the same time an increase in the acidity and concentration of the added component leads to the amine being bound in an unreactive complex right up to complete inhibition of the reaction when all the amine is bound. This effect is sometimes used to regulate the rate of curing of such systems. These so-called latent systems have considerable viability at low temperatures but start to react at a high rate on heating, which results in decomposition of the unreactive amine–acid complexes.[13]

Consideration of donor-acceptor interactions also makes it possible to understand the kinetic effects related to the structure of the initial reactants. There are a number of facts which attest to the anomalously low reactivity of aromatic amines containing electron-donating groups at the *ortho* position. Thus, the reactivity of an amino group which has SCH_3 as the *ortho* substituent is 21 times lower than for an amino group without this substituent.[56] A similar pattern occurs for aromatic amines with methoxyl groups at the *ortho* position.[37]

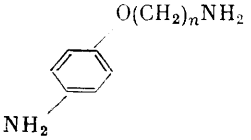

(18)


(19)

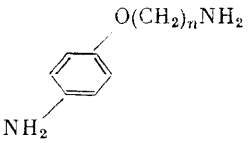
The reactivity of diamine (18) when it reacts with resorcinol diglycidyl ether is approximately 10 times lower than for (19). For both amines containing electron-donating substituents at the *ortho* position the presence of an intramolecular hydrogen bond in which the amine group acts as a proton donor has been established. It would appear that the nucleophilicity of this amino group must increase as a result of both the inductive effect of the electronic substituent and through the formation of an intramolecular donor-acceptor complex, although in reality it decreases. This contradiction can be readily eliminated if it is borne in mind that the hydrogen atoms of the amino group are involved in formation of an associate, namely, the concentration of amine as a proton donor in the reaction system decreases. It is evident that in terms of the ideas being developed concerning obligatory electrophilic assistance for nucleophilic attack on the epoxide ring, this reduction in concentration of proton donors in highly pure systems (when the amine itself acts as a proton donor at the initial stage of the reaction) must lead to a decrease in the rate of reaction. This is what actually occurs.

On the basis of the ideas put forward above, a whole series of aliphatic and mixed (aliphatic-aromatic) liquid oligomers with reduced reactivity was synthesised:[41]

$$ArNHCH_2CH_2(OCH_2CH_2)_mNH_2 \ (m = 1, 2), \tag{20}$$


(21)

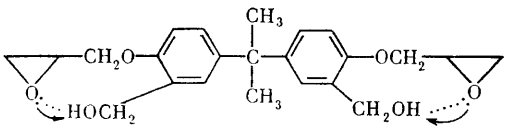
$(n = 2,3)$


(22)

The use of such amines as curing agents has considerable technological advantages, increasing the viability of composite materials.

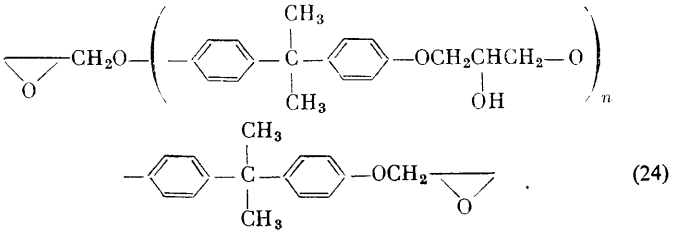
The high reactivity of *o*-diglycidyl ethers of phenols, *o*-diglycidyl esters of aromatic carboxylic acids, and *N*-diglycidylamines can only be explained by assuming that secondary hydroxyl groups, which are present in these compounds as small quantities of impurities, participate in catalysis.[13,43,44,66–67]

The presence of intramolecular hydrogen bonds in the 3,3′-dihydroxymethyl-4,4,′-diglycidyl ether of bisphenol A


(23)

gives rise to its considerably higher reactivity (by a factor of about 10) than that of the diglycidyl ether not containing hydroxymethyl groups at *ortho* positions.[68]

The rate of curing the epoxybisphenol A oligomers (24) increases with an increase in molecular weight of the oligomer, although the concentration of the epoxide groups decreases as this occurs.[13,20,29,45] This result, which appears paradoxical at first glance, is quite obvious when it is borne in mind that with an increase in molecular weight of the oligomer there is an increase in concentration of hydroxyl groups, which leads to an increase in the rate of reaction

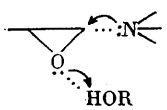

(24)

Determination of the reactivity of the epoxide groups in oligomers with varying molecular weights (taking into account the concentration of the hydroxyl groups contained in them) showed that it is the same and does not depend on the molecular weight of the oligomer.

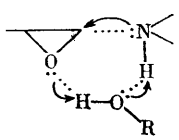
Even in early studies on reactions of epoxides with amines[56–63] it was noted that both proton-donating and electron-donating solvents have a considerable effect on the reaction kinetics. Proton-donating solvents decrease the induction period and increase the rate of reaction to a greater extent the higher the acidity of the solvent, whereas electron-donating solvents reduce both the initial and continuing rate of reaction, and as the degree of conversion of the epoxide groups increases, the inhibition effect increases.[19,20,37,39,40] This type of solvent behaviour is fully consistent with the reaction mechanism considered above. The inhibitory effect of electron-donating solvents is caused by the reduction in concentration of proton donors in the reaction system as a result of their bonding with solvent molecules. At the initial stage amines are bound by solvent while during the reaction hydroxyl groups are bound.[37]

The rate of reaction in strongly associated systems can easily vary over quite a considerable range from the effect not only of the solvent but also of other factors such as temperature and external mechanical or electrical fields, which are capable of changing the degree and nature of association of the reacting groups.[13,69–71]

In concluding this section let us return to the question of the mechanism of addition of amines to an epoxide ring. Possible transition states for non-catalytic opening of the epoxide ring by amine are depicted in schemes (10) and (11). Such schemes can similarly be recorded for a reaction catalysed by any proton donor, such as ROH:



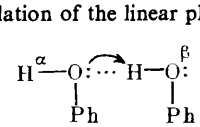
(25)



(26)

It does not appear possible to distinguish these two alternative schemes from the existing kinetic and structural data. At the same time, from detailed kinetic and structural studies of certain other nucleophilic addition reactions to the epoxide ring (phenols and carboxylic acid) it is possible to choose in favour of a cyclic transition state [scheme (26)].[13,46–48]

In the reaction between PGE and phenol[46] a variable order of reaction with respect to phenol was found; at small phenol concentrations it was close to first order, while at large concentrations it increased to fourth order. High values for the order of reaction with respect to the hydroxyl-containing reagent were also obtained in addition of alcohols to propylene oxide[72] or isocyanates,[3] which is due to an increase in reactivity of the hydroxyl-containing compounds on forming autoassociates. A quantum-mechanical calculation of the linear phenol dimer



(27)

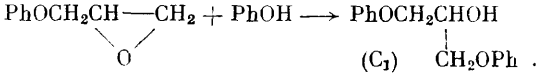
revealed a considerable reduction in electron density on the H^{α} hydrogen atom and an increase in electron density on the O^{β} oxygen atom compared to "monomeric" phenol.[73] Naturally this must result in an increase in proton-donating capacity and nucleophilicity of the phenol dimer. Such changes in the distribution of electron density are even more typical for higher molecular-weight associates.

Taking into account the different possible homo- and hetero-associates, the initial rate of the reaction between phenol (P) and epoxide (E) can be satisfactorily represented by the following simplified scheme, which assumes that all phenol autoassociates have solely a linear structure,

$$P_{i-1} + P \overset{k_i}{\rightleftharpoons} P_i, \quad E + P_i \overset{K_{1i}}{\rightleftharpoons} (EP_i),$$

$$(EP_i) \xrightarrow{k_i} C_1 + P_{i-1}, \qquad (28)$$

where C_1 is the primary product of the addition of PGE to phenol

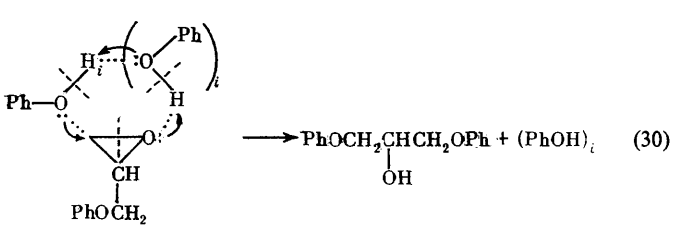


(29)

K_i and K_{1i} are the equilibrium constants for the respective reactions, k_i are the rate constants for formation of C_1.

The unimolecular conversion of the heteroassociates (EP_i) to the reaction product in accordance with scheme (28) in essence assumes a cyclic transition state. The values of the kinetics parameters determined from this scheme showed that the rate of formation of C_1 is mainly determined by processes involving association of the epoxide with higher forms of phenol associates (P_4 and P_5).

The revelation of the determining role of phenol associates can only be understood in terms of kinetic scheme (28), which assumes the unimolecular decomposition of heteroassociate (EP_i) via a cyclic transition state which is more probable sterically for H-complexes of PGE with higher forms of phenol associates.

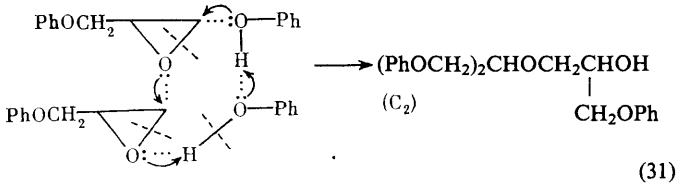


(30)

In the transition state the donor-acceptor bonds indicated by arrows are converted into covalent bonds, while the covalent bonds that are intersected by broken lines are cleaved synchronously to form the final reaction products. The formation of the transition state, which comprises a complex cyclic heteroassociate, is preceded by the process of "assembling" its individual fragments, each of which is a simpler homo- or hetero-associate. In this case the principal determining reaction channel, as kinetic studies have shown, is provided by heteroassociates (EP_i), where $i = 4, 5$.

In achieving a cyclic transition state the formation of reaction products occurs simultaneously with the transfer of a proton from the nucleophilic reagent to the molecule which provides electrophilic assistance. In this case the latter essentially fulfils two functions: it activates the epoxide ring towards nucleophilic attack and increases the activity of the nucleophilic reagent, i.e., bifunctional catalysis takes place and a "push-pull" reaction mechanism occurs. It is evident that such a mechanism predicates a lower energy of activation of the reaction than for a non-cyclic transition state, but imposes stricter limits on the entropy factor.

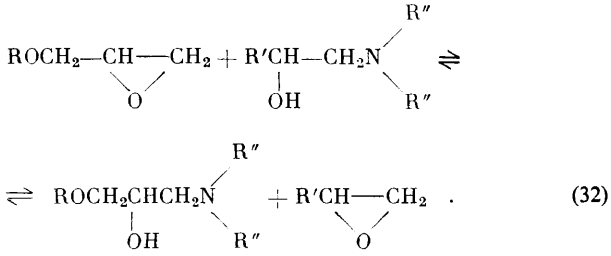
Using the concept of a cyclic transition state it is possible to understand the fact of parallel formation of a secondary addition product (C_2) directly from the initial reactants.[74] This reaction can be depicted as follows:



(31)

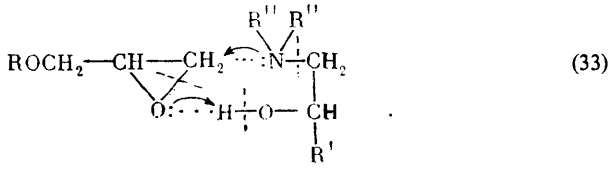
The formation of this type of transition state is evidently preceded by the development of simpler heteroassociates of the type (EP). It is interesting to consider the fact that kinetic studies demonstrate that in all only two molecules of phenol take part in this reaction, and not more as in the formation of C_1.

In fact, similar results were also obtained in the reaction between epoxide compounds and carboxylic acids.[47] Lastly, we shall give two final examples. A novel reaction, namely, amino alcohols on reacting with epoxide compounds can undergo transepoxidation, was recently discovered:[49]



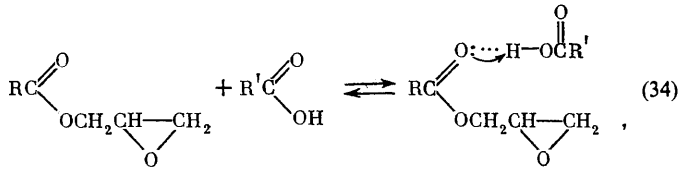
(32)

Evidently the most probable mechanism for this is given by the following:



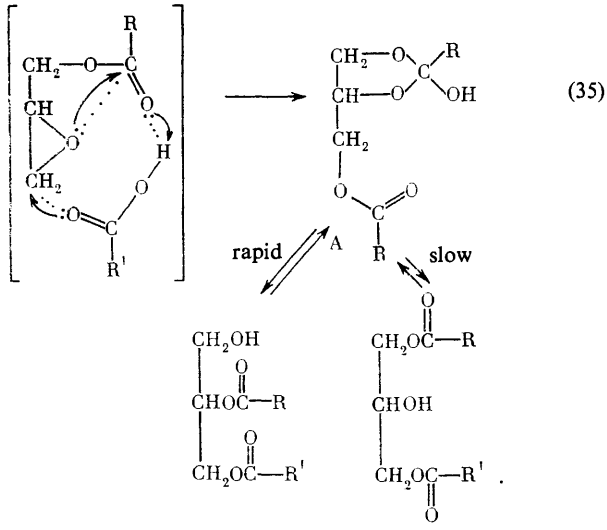
(33)

Without involving the concept of a cyclic transition state it is also impossible to understand the reaction between carboxylic acid glycidyl esters and carboxylic acids, which results in the formation of an "anomalous" addition product;[74] whereas in the reaction between phenol glycidyl ethers and carboxylic acids, "normal" addition products are obtained. In the first case the product of the donor-acceptor interaction between the hydroxyl group of the acid and the carbonyl group of the ester will evidently become an "active" complex:



(34)

which forms a cyclic transition state



(35)

From the scheme presented it is possible to understand not only the formation of the "anomalous" addition product but also the subsequent slow conversion of the latter to the more stable "normal" addition product via the intermediate A.

Thus, the examples of model reactions for the curing of epoxide oligomers considered above indicate that addition of nucleophilic reagents to the epoxide ring occurs in a very complex manner and involves the initial formation of homo- and hetero-associates. The latter in turn can form even more complex reactive cyclic heteroassociates that act as unique microreactors in which the reaction products are obtained through unimolecular rearrangement with synchronous transfer of electrons in the system.[1–4,13]

The presence of a cyclic transition state is very typical of a large number of reactions in the liquid phase in which various donor-acceptor interactions between the components of the system are possible.[55] The structural organisation of this type of reaction system caused by the donor-acceptor interactions of its components (initial reactants and reaction products) governs, on the one hand, the multiplicity of the routes for passage of the reaction and, on the other hand, the few routes for its favourable development.

Further studies directed at finding a link between the kinetic mechanisms of the chemical reactions and the structural organisation of liquid-phase systems involving polar reactants should lead to a re-examination of the mechanism of many reactions which seem to us at the present time to be well studied.

IV. Donor-acceptor interactions and polymer structure

The donor-acceptor interactions which exist in the reaction system not only govern the kinetic mechanism of the process but also can affect the structure of the resulting polymer in individual cases. Thus, the topological structure of an epoxyamine cross-linked polymer depends to a considerable extent on the occurrence of ineffective cyclisation reactions during its derivation, which lead to the formation of so-called monocycles that in the final analysis reduce the concentration of elastically active chains of the network.[13,15,31,44] The proportion of such ineffective rings is

determined by the ratio of rate constants of intra- and inter-molecular reactions, which in turn depends on the ratio of intra- and inter-molecular hydrogen bonds in diepoxides.

It has been shown in a considerable number of studies[13–16,31,43,76–82] that the *o*-diglycidyl esters of diphenols or *o*-diglycidyl esters of aromatic dicarboxylic acids and also *N*-diglycidylamines have a considerable tendency to form ineffective rings. An important factor that assists the development of ineffective rings in these cases is the formation of a strong intramolecular bond in the products of the primary addition of amine to diepoxide, resulting in activation of the neighbouring epoxide group. The effect of increased reactivity of these diglycidyl ethers and the positive effect of substitution in these monomers are precisely related to this phenomenon.[13,43,44]

The formation of cross-linked polymers with a defect topological structure naturally has an effect on their physical and mechanical properties in the hyperelastic and vitreous states.[77–82] A number of interesting observations about the effect of donor-acceptor interactions on the structure and properties of the polymers formed are made in two studies concerning the processes for formation of polyurethanes.[83,84]

Thus, donor-acceptor interactions between the components of a reaction system during polycondensation processes to a considerable extent determine the reactivity of the resulting homo- and hetero-associates and, as a result, the mechanism of the fundamental stages of condensation and the kinetics of the process. In three-dimensional polycondensation, donor-acceptor interactions can have an effect on reactions leading to intramolecular cyclisation, resulting in the formation of ineffective rings, and hence on the structure and properties of the resulting cross-linked polymers.

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Translated from *Uspekhi Khimii* **60** 1513–1531 (1991) U.D.C. 541.128; +542.952; 541.49+541.64

Nontraditional methods of synthesising metal-containing polymers

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ABSTRACT. Complexes of metals with (meth)acrylates and acrylamides are used as examples for examining the application of nontraditional methods for initiating polymerisation of metal-containing monomers: graft, low-temperature, electrochemical, matrix, solid-state (under high pressure with shear deformation), frontal and spontaneous. Such approaches are demonstrated to be very effective for preparing metal-containing polymers with a wide sprectrum of relative molecular masses and with different solubility and stereotacticity. A bibliography containing 39 citations is included.

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I. Introduction

The synthesis and polymerisation of metal-containing monomers (MCM) has recently advanced at such a rapid pace owing to the efforts of scientists in many countries that a new scientific discipline has formed. It is characterised by novel compositions, methods for their polymerisation, and new approaches to studying the structure of the metal-containing polymers formed.[1-3] The ever increasing interest in such polymers is due to their unusual properties, which are determined not only by the metals in them but also the nature of the polymer matrix. The products of MCM polymerisation are composites with new physicomechanical and operating properties, catalytically and biologically active macromolecules, etc.

Furthermore, considerable attention has been given to polymerisation of MCM by traditional methods (primarily polymerisation in solutions with an initiator, usually a radical, at elevated temperatures). Besides difficulties in choosing a suitable solvent and initiator (which might react with the MCM), problems arise with separating the polymer and removing from it residues from the reaction mixture.

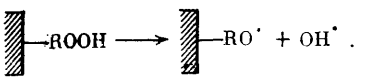
This has led to numerous investigations on nontraditional methods of MCM polymerisation. It was expected that the structures and properties of MCM would facilitate successful application of these methods. Indeed analysis of the data obtained indicates that nontraditional methods of polymerisation have to a large extent been used with nontraditional monomers (MCM are undoubtedly in this class).

Let us recall that MCM are compounds containing an organic moiety with a reactive multiple bond capable of undergoing addition and a metal-containing group chemically bonded to it.[1-3] All MCM can be divided into four groups: monomers with covalent, ionic, donor–acceptor, and π-bonds between the metal and organic part. However, the principal achievements in application of nontraditional methods have involved two groups of MCM: ionic, e.g. metal (meth)acrylates $M(OCOCR=CH_2)_n$ ($R = H$ or CH_3, n is the metal valence), and donor-acceptor, e.g. metal complexes of acrylamides (AAm) $M(H_2NCOCH=CH_2)X_n(H_2O)_p$ ($p = 0$ or 2).

Let us examine the principal nontraditional methods of initiating polymerisation of such MCM.

II. Graft polymerisation of MCM

Graft polymerisation is an effective method for preparing metal-containing polymers that combine properties of the starting polymeric support (film, fibre, powder, etc.) and the grafted polymer. Radiation grafting of MCM, in which the polymer–support is previously irradiated in the presence of oxygen from air, is the most effective approach. This forms hydroperoxide (HP) groups on the surface of the polymer. These can then initiate grafting under the appropriate conditions:



Thus, boiling a suspension of irradiated polyethylene (PE) powder in an alcoholic solution of MCM produces graft polymerisation of acrylates containing the transition metals Cr^{III}, Fe^{III}, Co^{II}, Ni^{II}, and Cu^{II}.[4,5] A distinguishing feature of the grafting of these MCM is the almost complete absence of the homopolymer. Graft polymerisation of potassium acrylate gave 30% homopolymer. A redox-active metal clearly hinders initiation of polymerisation. The kinetic dependences of the process are the same for all acrylates studied. In the first 0.5 h the rate is maximal. It then rapidly drops (Fig. 1). It is interesting that acrylates of divalent metals graft at higher rates than those of trivalent ones. The activity of the acrylates changes in the following order: $Co^{II} > Cu^{II} > Ni^{II} > Cr^{III} > Fe^{III}$. Grafting of Cu^{II} acrylate is characteristically rather effective, in contrast with polymerisation of this MCM in solution. This is obviously due to adsorption of the metal acrylate on the surface of the hydrophobic polymeric support.

The initial rate of graft polymerisation w_0 for all acrylates studied is practically constant for 0.04–0.40 *M* MCM in alcohol. The existence of a limiting rate is probably due to the attainment of a limiting [MCM] on the PE-powder surface. The adsorption isotherm of Co^{II} acrylate confirms this hypothesis (Fig. 2). The amount of adsorbed monomer increases with increasing [acrylate] in solution and reaches the limiting value corresponding to coverage by a monolayer.

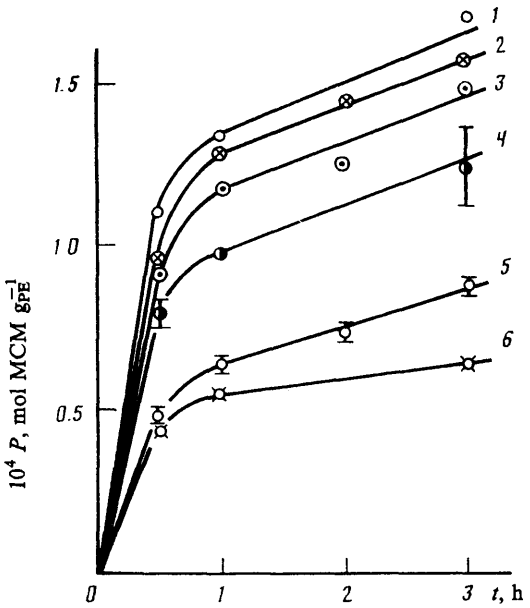


Figure 1. Kinetic curves for yield (*P*) of grafted metal acrylate polymer: *1,3*, Co^{II}; *2*, Ni^{II}; *4*, Cu^{II}; *5*, Cr^{III}, Fe^{III}. The solvent is alcohol. [MCM] = 0.04 mol dm^{-3}, *T* = 79 °C. *1,2,5,6*, *D* = 200 kJ kg^{-1}; *3,4*, *D* = 100 kJ kg^{-1}; *1,3,4*, *I* = 2.8 J kg^{-1} sec^{-1}; *2,5,6*, *I* = 1.4 J kg^{-1} sec^{-1}.

The nature of the transition metal has a substantial influence on the grafting of acrylates. The dependence of the initial rate of grafting on [HP] in irradiated PE can be represented as follows: $w_0 \sim [HP]^{\alpha}$ with α = 0.7, 0.6, 0.5, 1.1 and 1.1 for grafting of Co^{II}, Ni^{II}, Cr^{III}, Cu^{II} and Fe^{III} acrylates, respectively. Such values for α are consistent with predominantly bimolecular termination of the growing chains for Co^{II}, Ni^{II} and Cr^{III} and monomolecular for Cu^{II} and Fe^{III}. The special behaviour of various types of MCM based on Cu^{II} and Fe^{III} has been noted in many other instances[3] and was explained by the increased probability of monomolecular chain termination involving Cu^{II} and Fe^{III}.

Grafting of metal acrylates is characterised by low activation energy E_a from 42 to 55 kJ mol^{-1}. The rate of polymerisation also depends weakly on the presence of radical inhibitors.

The observed dependences are probably general in nature and can be used to examine graft polymerisation of other MCM. Indeed it has been demonstrated that the kinetic curves for grafting of metal chelates of monomers, complexes of metal acrylates with 2,2′-bipyridyl and 1,10-phenanthroline, are analogous.[6] The order of activity for the metals is the same as found in graft polymerisation.

Graft polymerisation after irradiation has been investigated for AAm complexes of metal chlorides and nitrates under conditions analogous to those for acrylates.[5,7] Like for the acrylates, the amount of homopolymer of these MCM in the polymeric products was insignificant. It was 4–8 times less than for grafting of the metal-free analogue, AAm. The only exception was $MnCl_2$, the rate of thermal homopolymerisation of which surpasses that of grafting.

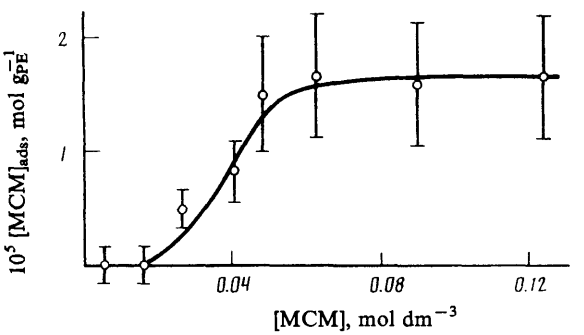


Figure 2. Adsorption isotherm of Co^{II} acrylate on PE powder: MCM in alcohol (15 dm^3), 5 g PE, *D* = 200 kJ kg^{-1}, *I* = 2.8 J kg^{-1} sec^{-1}, *T* = 22 °C.

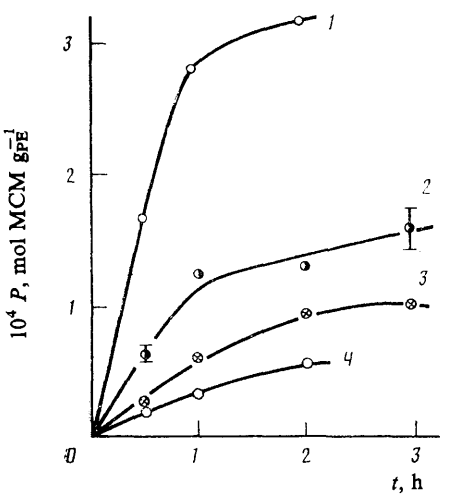


Figure 3. Kinetic curves of yield of grafted polymers of AAm complexes: *1*, $Cr(AAm)_4Cl_3$; *2*, $Co(AAm)_4Cl_2$; *3*, $Ni(AAm)_4Cl_2$; *4*, $Co(AAm)_4(H_2O)_2(NO_3)_2$. In alcohol, [MCM] = 0.1 mol dm^{-3}, *T* = 80 °C, *D* = 200 kJ kg^{-1}, *I* = 1.4 J kg^{-1} sec^{-1}.

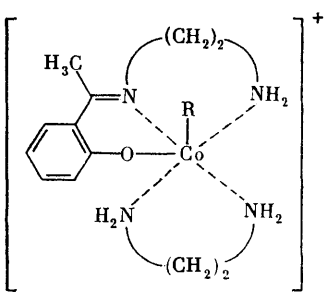
In contrast with graft polymerisation of metal acrylates, the rate of grafting of AAm complexes of metal chlorides varies as follows: Cr^{III} > Co^{II} > Ni^{II} (Fig. 3). This order is opposite that of the metal ion electronegativities. The nature of the anion of the complexant also has a significant effect. Graft polymerisation of

$Co(AAm)_4(H_2O)_2(NO_3)_2$ proceeds with a rate almost three times less than that of $Co(AAm)Cl_2$. Complexes of Cu^{II} with AAm are typically inactive in graft polymerisation.

The rate of grafting of AAm complexes of metals is proportional to [MCM] in solution whereas for grafting of uncoordinated AAm $w_0 \sim [AAm]^{1.7}$. Graft polymerisation of AAm and its complexes is characterised by monomolecular chain termination. The E_a for the complexes $Co(AAm)_4Cl_2$ and $Ni(AAm)_4Cl_2$ are 51 and 60 kJ mol^{-1}, respectively. As in graft polymerisation of acrylates, radical inhibitors had little effect on the reaction of AAm complexes. This is probably due to formation of complexes of the inhibitors with MCM.

III. Low-temperature radical polymerisation

It is difficult to choose an initiator for free-radical polymerisation of MCM at low temperatures. As a rule, traditional initiators are used at elevated temperatures and the redox systems used at low temperatures can lead to side reactions. Therefore, organometallic compounds capable of acting as low-temperature radical initiators are of great interest. For instance, cationic Co^{III} complexes such as



$R = CH_3$, C_2H_5, C_3H_7.

can undergo homolytic cleavage of the Co–R bond.[8] This was used to initiate low-temperature polymerisation of $M[OCOCH=CH_2]_2$, where M = Zn^{II}, Mg^{II}, Pb^{II} and Ba^{II} in methanol.[9] The overall scheme taking into account partial dissociation of the monomer and participation of $[MOCOCH=CH_2]^+$ in the decomposition of the complex can be represented as follows:

$$RCo \xrightarrow{[M(OCOCH=CH_2)]^+} R^{\cdot},$$

$$CH_2=CH + R^{\cdot} \longrightarrow {\sim}CH_2{-}\underset{\displaystyle COOM(OCOCH=CH_2)}{\underset{|}{CH}}{\sim}$$

$$\underset{\displaystyle COOM(OCOCH=CH_2)}{\underset{|}{CH_2=CH}}$$

The kinetics of polymerisation, in addition to the complete inhibition by radical traps, confirm that the process is radical in nature. Such initiators enable polymerisation to be carried out at comparatively low temperatures (from –20 to 10 °C) at sufficiently high rates. The products produced under such conditions are expected to have high relative molecular masses (stereotactic structures may also form).

Another possible method for initiating low-temperature radical polymerisation is irradiation. The post-irradiation polymerisation method has become widespread. The matrix is vitrified, transforming the system from a glass to a supercooled liquid.[10] In a number of instances the process occurs at high rates and the yield of polymers is quantitative. This is due to the sharp change of molecular mobility during phase transitions.

On cooling to –196 °C, Co^{II}, Ni^{II}, Cr^{III}, Mn^{II} and Cu^{II} acrylates in 10% alcohol are completely vitrified. On warming up they devitrify and, with the exception of Ni^{II} acrylate, crystallise and melt (Table 1).[11] On warming up Ni^{II} acrylate that had been vitrified and irradiated at –196 °C in a calorimeter, an exotherm associated with MCM polymerisation is observed immediately after the devitrification step (Fig. 4). The polymer forms a separate phase. As a result, the concentration of monomer decreases. This produces on the calorimetric heating curve an exotherm for crystallisation and an endotherm for melting in addition to the exotherm for polymerisation.

Table 1. Phase-transition temperatures of 10% acrylate salt solutions in ethanol.[11]

Metal acrylate	T_v, °C	T_{cr}, °C	T_m, °C
Ni(II)	–173	–	–
Co(II)	–173	–138	–118
Cu(II)	–171	–143	–118
Mn(II)	–171	–138	–118
Cr(II)	–171	–138	–118

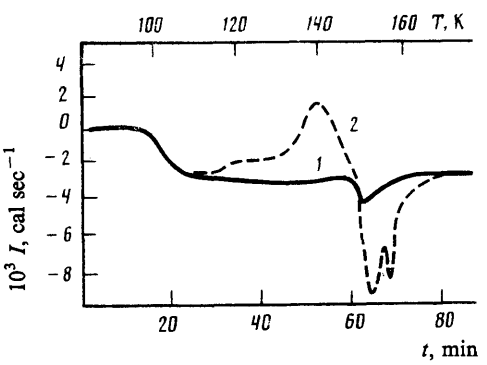


Figure 4. Calorimetric heating curve of 10% Ni^{II} acrylate in alcohol before (*1*) and after (*2*) irradiation. D = 100 kJ kg^{-1}, T = –196 °C.

Post-irradiation polymerisation of AAm complexes of Co^{II} and Ni^{II} chlorides and nitrates proceeds analogously (Fig. 5). It is noteworthy that the calorimetric heating curves of unirradiated MCM differ from the classical curves for the vitreous state. This may be due to the formation and rearrangement of different complexes of the MCM with ethanol. The yield of polymer in this instance reaches 45%. The relative molecular mass was low, $\overline{M}_\eta$ = 5600 (for comparison, $\overline{M}_\eta$ = 8700 for polyacrylamide prepared by polymerisation of AAm under analogous conditions).

Investigation of polymers formed by devitrification of irradiated alcohol matrices revealed that syndiotactic structures are primarily formed. For example, polyacrylic acid prepared by hydrolysis of the product of polymerisation of Co^{II} acrylate contains up to 60% of

the syndiotactic fraction (Table 2). However, the corresponding fraction obtained by polymerisation of acrylic acid under the same conditions gave ony 25–30%.

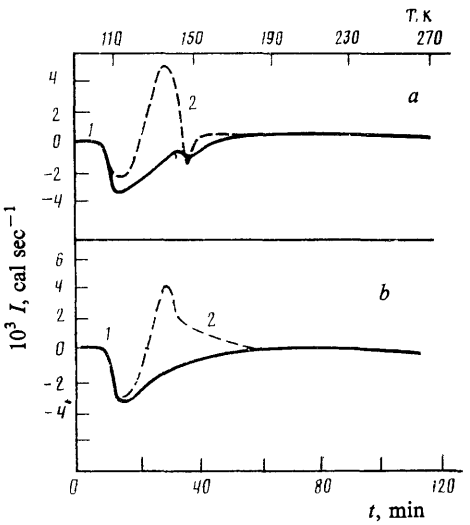


Figure 5. Calorimetric heating curves of 10% $Ni(AAm)_4Cl_2$ (*a*) and $Co(AAm)_4(H_2O)_2(NO_3)_2$ (*b*) in alcohol before (*1*) and after (*2*) irradiation. D = 100 kJ kg^{-1}, I = 100 kJ kg^{-1} h^{-1}, T = –196 °C.

Table 2. Fractional composition of PPA prepared by polymerisation of acrylic acid and isolated from the polymerisation product of Co^{II} acrylate.[11]

Fraction	Selective solvent	Fraction, %	
		PAA	PAA(Co)
Syndiotactic	Dioxane–water (80:20 vol.%)	25–30	45–60
Atactic	Dioxane	60–65	10–20
Insoluble gel	—	10–15	20–30

IV. Solid-state polymerisation under high pressure with shear deformation

Polymerisation under high pressure with shear deformation is performed in a Bridgman anvil cell. It is very effective for converting solid monomers,[12] among which MCM are one of the most interesting. Metal acrylates are so reactive in this process that high degrees of conversion are attained even at pressures from 500 to 1000 MPa and anvil rotation angles from 100 to 200° (Fig. 6).[13,14]

The participation of metal ions in this process was suggested by investigations of the polymerisation of transition metal acrylates under analogous conditions. Thus, the Mössbauer spectrum of Fe^{III} acrylate treated at 2 GPa exhibits two doublets with (shift relative to SnO_2) δ = 1.35 mm sec^{-1} and Δ = 2.22 mm sec^{-1} and δ = 1.44 mm sec^{-1} and Δ = 2.62 mm sec^{-1} (Fig. 7, curves *3* and *4*) in addition to the doublet from starting Fe^{3+} with δ = 0.76 mm sec^{-1} and Δ = 0.65 mm sec^{-1} (Fig. 7, curve *1*).[15] Comparison of Mössbauer spectra of Fe^{3+} and Fe^{2+} demonstrated that the new lines in the spectra of Fe^{III} acrylate that appear after treatment under pressure correspond to Fe^{II} acrylate.

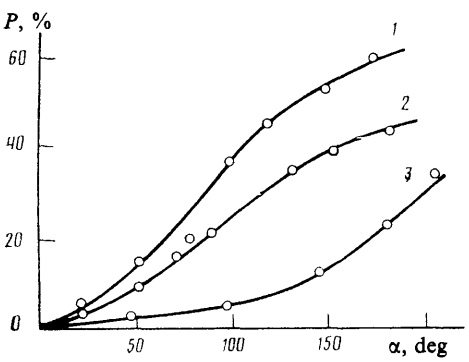


Figure 6. Polymer yield as a function of anvil rotation angle α under high pressure with shear deformation. Pressure, 160 MPa. Metal acrylate monomers: *1*, Ba^{II}; *2*, Pb^{II}; *3*, Zn^{II}.

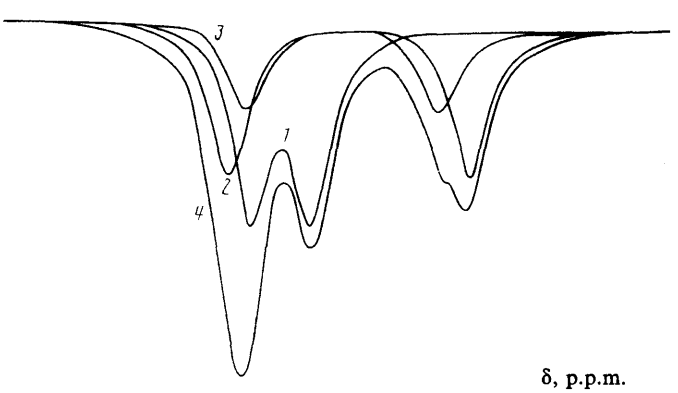


Figure 7. Mössbauer spectra of Fe^{III} acrylate: *1*, before treatment; *2,3*, doublet arising after treatment; *4*, summed spectrum after treatment. Pressure, 2 GPa; anvil rotation angle, 100–200 °C.

As vinyl monomers polymerise during plastic flow under pressure, the flow resistance increases as polymer accumulates.[12] This effect can be used for direct evaluation of the reactivity of monotypic monomers. The flow resistance (σ) as a function of deformation (anvil rotation angle α) for several AAm complexes is plotted in Fig. 8.[16] The data show that the greatest change occurs for $Co(AAm)_4Cl_2$; the least, for $Cu(AAm)_4(NO_3)_2$. The unusual nature of the function for $Fe(AAm)_4(NO_3)_3$ is noteworthy. The AAm complexes can be placed in the following order of

reactivity on the basis of the functions obtained: $Co(AAm)_4Cl_2$ > $Co(AAm)_4(H_2O)_2(NO_3)_2$ > $Ni(AAm)_4(H_2O)_2(NO_3)_2$ > $Mn(AAm)_4$. $.(H_2O)_2(NO_3)_2$ > $Cu(AAm)_4(NO_3)_2$.

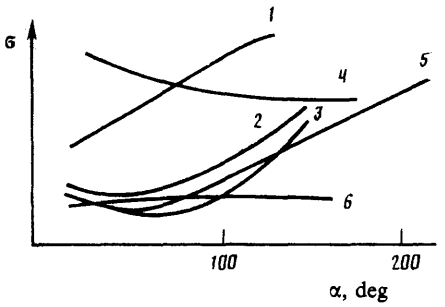


Figure 8. Dependence of flow resistance on deformation for AAm complexes: *1*, $CoCl_2$; *2*, $Co(NO_3)_2$; *3*, $Ni(NO_3)_2$; *4*, $Fe(NO_3)_3$; *5*, $Mn(NO_3)_2$; *6*, $Cu(NO_3)_2$.

This method can also be applied to copolymerisation of MCM. Thus, copolymerisation of acrylates and of AAm complexes of Y^{III}, Ba^{II} and Cu^{II} nitrates is effective.[17] It is noteworthy that high pressure with shear deformation is the only method for introducing into the copolymer MCM based on Cu^{II}, which are usually unreactive in polymerisation. The synthesised ternary copolymers were used as polymeric starting materials for preparing high-temperature superconducting ceramics with good properties.

V. Electrochemical polymerisation

Electrochemical polymerisation of MCM is a unique method for preparing films containing redox centres in each repeating unit. The redox conductivity enables the film to grow continuously since its exterior is active in electron transfer at the film–solution interface.

Electrochemical polymerisation can be examined in more detail using the rather numerous mixed-ligand complexes of Ru^{II}, Os^{II} and Fe^{II} perchlorates and hexafluorophosphates as examples.[18–21] The ligands used were 4-vinylpyridine, other more complicated monomers containing pyridine, derivatives of cinnamates, stilbazole, etc., in addition to unsubstituted polypyridyl ligands (2,2′-bipyridyl, 2,2′,2″-terpyridyl, 1,10-phenanthroline, etc.).

The polymerisation was carried out in 0.1 M tetraethylammonium perchlorate in CH_3CN by repeated cycling of a Pt electrode near the reduction potential of the ligand. Homogeneous even polymer films were formed. For the majority of investigated MCM, the first step of electrochemical polymerisation is formation of the anion–radical by electron transfer into the π^*-orbital of the unsubstituted ligand.

$$[Ru(bipy)_2L_2]^{2+} \overset{+e^-}{\rightleftharpoons} [Ru(bipy)(bipy)^{\cdot-})L_2]^{+} \overset{+e^-}{\rightleftharpoons} [Ru(bipy)^{\cdot-})_2L_2]^{0}.$$

An electron then transfers onto the substituted ligand either by an intramolecular mechanism or by disproportionation. Repetition of these reactions produces the polymer.

Electrochemical polymerisation of complexed AAm is of great interest. However, the majority of studies have been performed using transition metal chlorides such as $ZnCl_2$ and $AlCl_3$.[22–24] Therefore, polymerisation of AAm in aqueous solutions using nitrates, perchlorates and sulphates is impossible. However, effective electrochemical polymerisation of AAm in nonaqueous media in the presence of Co^{II} nitrate and perchlorate was recently reported.[25] The reaction was carried out in DMF, from which the polymer precipitated, and DMSO, in which the reaction mixture remained homogeneous. The rate in DMSO was an order of magnitude greater than that in DMF. The kinetic equation has the following form:

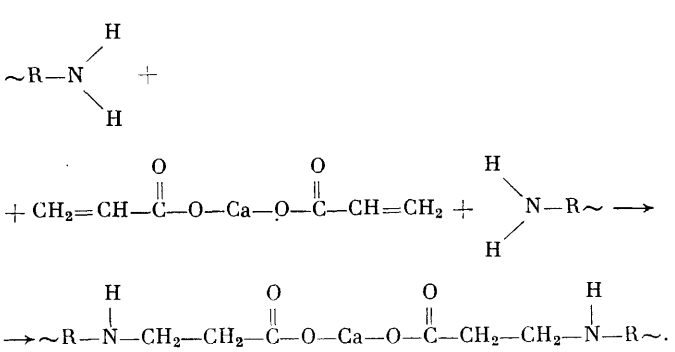
$$w_p = K[AAm]^{1.5}[Co(NO_3)_2]I^{0.5}.$$

This dependence was explained by assuming that two types of monomers, free AAm and that complexed to Co^{II} nitrate, simultaneously participate in chain growth. This was confirmed by the comparatively small amount of $Co(NO_3)_2$ in the polymer, 6–10 mass%. The process can produce polyacrylamide of very high relative molecular mass, greater than 2 500 000. The reaction is inhibited by *p*-benzoquinone, indicative of the radical nature of the process. It is interesting that polymerisation does not occur in the presence of Co^{II}. Most likely this suggests that participation of nitrate in initiation of the process has not been considered.[25]

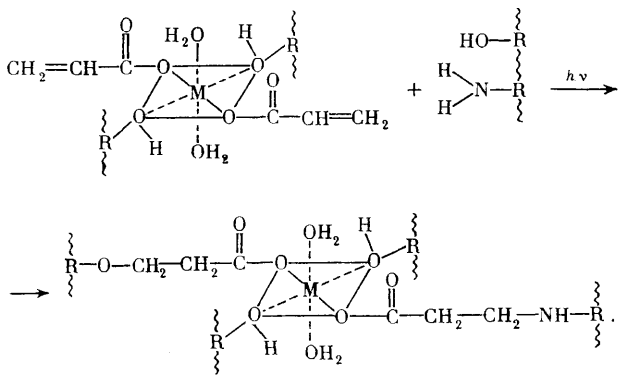
VI. Matrix polymerisation

Polymerisation of MCM in the matrix of a different polymer or compound can lead to dramatic modification of the properties of various materials. Various methods are possible. Among these, polymerisation in the polymer melt is one of the most effective. Thus, polymerisation of acrylates and AAm complexes of Zn^{II} and Ni^{II} nitrates in a high-density PE melt was investigated.[26] The MCM were added to the polymer as a solution in methanol. The mixture was polymerised in a press-form for 5 min at 190 °C and 15 MPa. It was found that adding even 0.5 mass% Zn^{II} acrylate to the PE completely stops the flow at 190 °C. However, adding 10 mass% MCM increases the melting point from 131 to only 135 °C. The crystallinity of the polymer does not change. This is consistent with crosslinking of the amorphous PE during polymerisation of the acrylate. Crosslinking of a polymer is characterised by a sharp drop of the relative expansion (for 0, 2, 5 and 10 mass% Zn^{II} acrylate, its value is 790, 20, 10 and 2%, respectively). The tensile strength of the modified polymer is maximal for 2–5 mass% MCM (Fig. 9).

Interesting results were obtained during investigations of laser-induced polymerisation of Ca^{II}, Co^{II}, Ni^{II} and Cu^{II} acrylates in a gelatin matrix.[27–29] Holographic information can be recorded using laser radiation by adding a metal acrylate to the gelatin matrix. The holograms produced in this manner diffract more efficiently and have better resolution than ordinary holograms. Crosslinking of gelatin by Ca^{II} acrylate can be represented as follows:



The analogous process involving transition metal acrylates is more complicated and includes preliminary formation of macrocomplexes of MCM and gelatin. This is confirmed by IR and electronic spectroscopy. The photochemically induced formation of structures from such complexes is represented by the following scheme:



The sensitivity to absorption of radiation by the macrocomplexes and the degree of crosslinking (number of double bonds reacted) depends on the nature of the transition metal: $Cu^{II} > Ni^{II} > Co^{II}$.

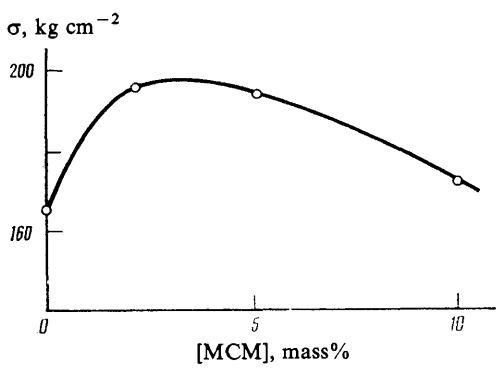
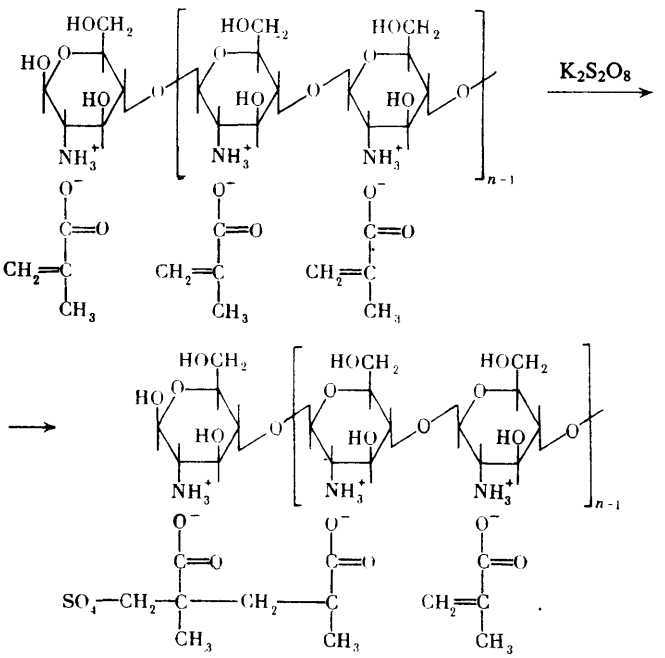


Figure 9. Dependence of tensile strength (σ) of the Zn^{II} polymerisation product in high density PE melt on MCM content.

Matrix effects were detected during an investigation of the polymerisation of aqueous sodium methacrylate in the presence of chitosan acetate (mole ratio chitosan : MCM = 1 : 1) initiated by $K_2S_2O_8$.[30] The rate is described by: $w_p = K[M]^{0.8}[K_2S_2O_8]^0$ up to $[K_2S_2O_8] < 3.5 \times 10^{-3}$ mol dm^{-3} and $w_p = K[M]^{0.8}[K_2S_2O_8]^{1.8}$ for $[K_2S_2O_8] > 3.5 \times 10^{-3}$ mol dm^{-3}. However, w_p changes linearly with initiator concentration in the presence of a chitosan analogue with a low relative molecular mass, glucosamine hydrochloride. The relative molecular mass of the sodium polymethacrylate increases linearly with conversion. The polymerisation is distinguished by a rapid initiation and continuous nature. The polymer contains only one SO_4 group per chain. These data are consistent with the following scheme for matrix polymerisation of MCM owing to inclusion of acrylate bound through ionic and hydrophobic bonds to the polymeric chain of chitosan residues:



VII. Frontal polymerisation in the melt

During an investigation of the properties of $M(AAm)_4 \cdot (H_2O)_2(NO_3)_2$, where M = Mn^{II}, Co^{II}, Ni^{II} and Zn^{II}, it was unexpectedly discovered that these monomers readily undergo polymerisation in a self-propagating (frontal) regime without addition of any initiators or activators.[31] In the frontal polymerisation method, the bottom of the vessel containing the MCM is briefly heated. After the "ignition" is stopped, the boundary where the substance changes colour, the polymerisation front, continues to advance of itself. This effect is the first documented instance of thermally initiated frontal polymerisation. The reaction proceeds under the most mild conditions of any known for such processes: monomer powders pressed at low pressures, the lack of specially added initiator or activator, comparatively low ignition temperature temperatures (120 – 180 °C), and a reaction at normal pressure. The dependences of the front advance rate during polymerisation of $Co(AAm)_4(H_2O)_2(NO_3)_2$ on time from the moment of ignition for various ignition temperatures are plotted in Fig. 10. It is clear that the kinetic functions consist of two parts corresponding to the nonequilibrium and steady-stage regimes of polymerisation front advance. Depending on the ignition temperature, the rate before equilibrium is reached can be higher or lower than the steady-state rate w_{fr}.

Addition of radical inhibitors has a significant influence on frontal polymerisation. Addition of 2,2,4,4-tetramethylpiperidine-1-oxyl to the polymerising system practically linearly decreases w_{fr}. At inhibitor concentrations $\geqslant$ 0.1 mass%, the frontal process is completely stopped. The effective inhibition is consistent with a radical mechanism for thermally initiated frontal polymerisation. An estimate of the number of active centres gives a value less than 3.0×10^{-3} mol per mol of MCM.

A study of the influence of the nature of the metal on the rate of frontal polymerisation of $M(AAm)_4(H_2O)_2(NO_3)_2$ demonstrated that w_{fr} decreases in the order $Co^{II} > Ni^{II} > Mn^{II} > Zn^{II}$.

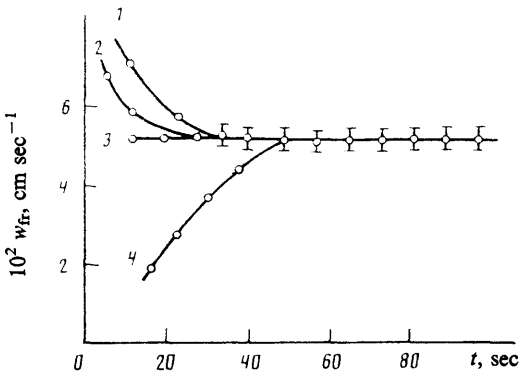


Figure 10. Dependence of front advance rate during polymerisation of $Co(AAm)_4(H_2O)_2(NO_3)_2$ on ignition temperature and process time. Diameter of sample container d = 4 mm, p = 1.02 g cm^{-3}. Ignition temperature, °C: *1*, 300; *2*, 250; *3*, 180; *4*, 120.

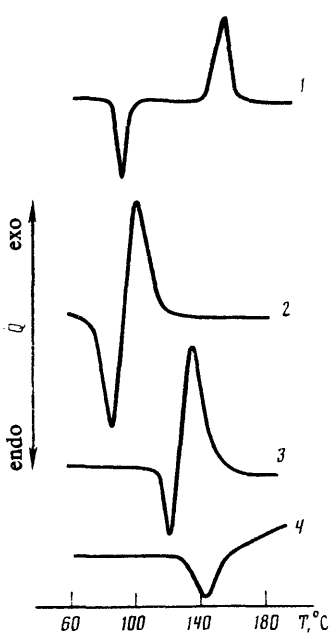


Figure 11. DSC curves of acrylamide and its complexes: *1*, AAm; *2*, $Co(AAm)_4(H_2O)_2(NO_3)_2$; *3*, $Cu(AAm)_4(NO_3)_2$; *4*, $Ni(AAm)_4Cl_2$.

It should be emphasised that frontal polymerisation has been detected only for AAm complexes of Mn^{II}, Co^{II}, Ni^{II} and Zn^{II}. Uncoordinated AAm, AAm complexes of Cu^{II} and Fe^{III} nitrates and transition metal chlorides, bromides and perchlorates, and the complex of 4-vinylpyridine with Co^{II} under analogous conditions do not polymerise in spite of a wide variation of the process parameters. Therefore, this is a unique property of the AAm complexes of Mn^{II}, Co^{II}, Ni^{II} and Zn^{II} nitrates, analogues of which have not yet been found.

Thermal polymerisation of these MCM was investigated by differential scanning calorimetry (DSC). The process was demonstrated to proceed at a high rate with participation of all four unsaturated AAm ligands. The yield of polymer reaches 100%.[32] The reaction occurs at unexpectedly low temperatures (80–100 °C). It characteristically occurs close to the melting point of the complex (Fig. 11, curve *2*). However, heating $Cu(AAm)_4(NO_3)_2$ and $Fe(AAm)_4(NO_3)_3$ effectively oxidises the organic part of the AAm complex. This is apparently initiated by nitrate decomposition (Fig. 11, curve *3*).

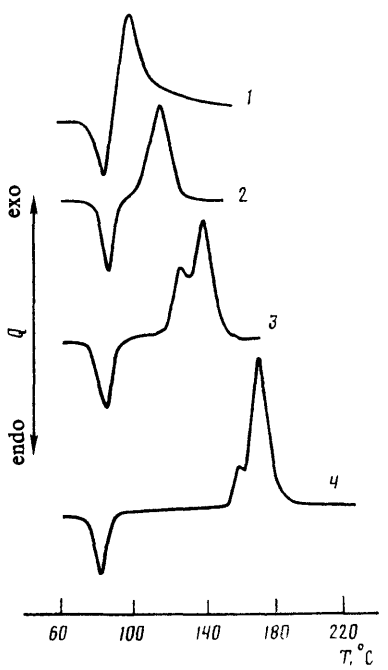


Figure 12. DSC curves of $Ni(AAm)_4(H_2O)_2(NO_3)_2$ with various amounts of 2,2,4,4-tetramethylpiperidine-1-oxyl, mass%: *1*, 0 (no inhibitor); *2*, 0.35; *3*, 0.9; *4*, 8.5.

Addition of radical inhibitors to $Ni(AAm)_4(H_2O)_2(NO_3)_2$ prevents polymerisation close to the melting point of the MCM (Fig. 12). However, extensive nitrate decomposition occurs at certain inhibitor concentrations ($\geqslant$0.9 mass%) with oxidation of the organic part of the complex. The two exotherms (Fig. 12, curves *3* and *4*) can probably be explained by two processes, partial polymerisation (the low-temperature peak) and nitrate decomposition with oxidation of the organic part of the complex (high-temperature peak).

It was concluded that Mn^{II}, Co^{II}, Ni^{II}, Zn^{II}, Cu^{II} and Fe^{III} nitrates in monomeric AAm complexes are thermally unstable at

temperatures above 130 °C. However, these complexes, which are incorporated into the polymer matrix during polymerisation, remain stable up to 200 °C, i.e. the polymer matrix to a large extent prevents their decomposition.

It is interesting that AAm complexes of Mn^{II}, Co^{II}, Ni^{II} and Zn^{II} nitrates can undergo thermal copolymerisation with other monomers. Thus, AAm complexes effectively copolymerise with uncoordinated AAm (Fig. 13). At ratios [AAm]:[MCM] < 4, thermal copolymerisation is seen in the thermogram as a single peak (Fig. 13, curve *2*), like for the starting complex (Fig. 13, curve *1*). At [AAm]:[MCM] > 4, the polymerisation region in the thermograms appears as a high-temperature shoulder apparently owing to polymerisation of uncoordinated AAm (Fig. 13, curve *4*).

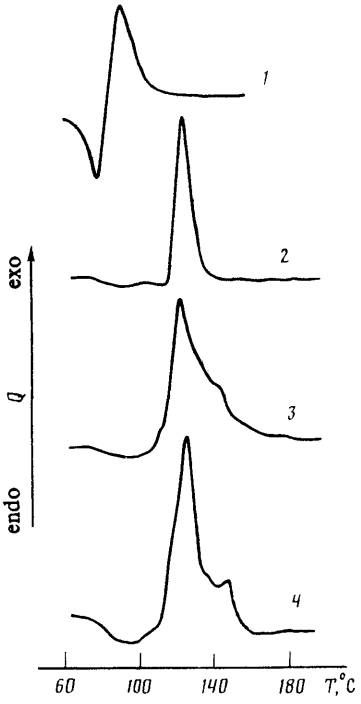


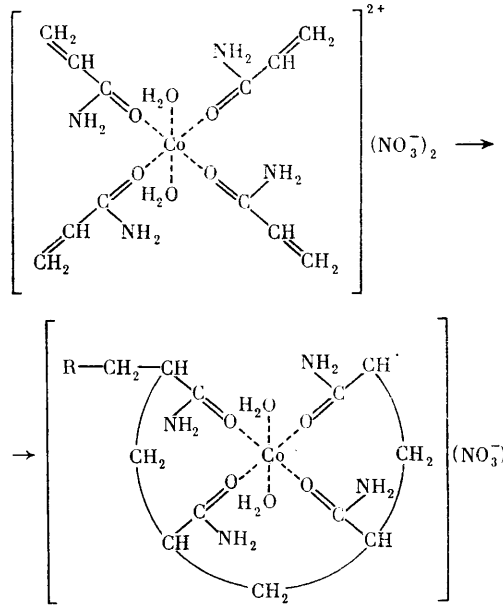
Figure 13. DSC curves of $Ni(AAm)_4(H_2O)_2(NO_3)_2$ and AAm mixtures. [AAm]:[MCM] ratio: *1*, 0; *2*, 2.0; *3*, 4.0; *4*, 7.1.

Elemental analysis of the frontal polymerisation products showed that the polymers produced were practically identical to the starting MCM. The average relative molecular mass of the polyacrylamide isolated from polymeric AAm complexes of Co^{II} and Ni^{II} nitrates after removal of metal compounds was 9.88×10^5 and 4.14×10^5, respectively. This is 100 and 200 times greater than the relative molecular mass of the polymer obtained by radical-initiated polymerisation of $Co(AAm)_4(H_2O)_2(NO_3)_2$ in water.

The following scheme involving nitrate decomposition products was proposed for initiation of the process:

$$Co^{2+}(AAm)_4(H_2O)_2(NO_3^-)_2 \rightleftharpoons$$
$$\rightleftharpoons Co^{3+}O(AAm)_4(H_2O)_2(NO_3^-) \ldots (NO_2).$$

The high rate constant for polymerisation of AAm complexes of these metal nitrates is probably attained owing to a favourable steric position of the AAm molecules in the metal complex. Growth of the polymeric chain can be represented as follows:[33]



The polymeric chain seemingly twists around the four AAm groups of the complex. The chain is then apparently transferred to the next precursor.

VIII. Spontaneous polymerisation

The properties of AAm complexes of metal nitrates are not limited to the ability to undergo thermal polymerisation. Complexes of AAm with such metal nitrates as Cr^{III}, Bi^{III}, Pb^{II}, Ca^{II}, Er^{III} and Nd^{III} spontaneously polymerise in concentrated aqueous solutions even at room temperature during synthesis and cannot be isolated as monomers.[34,35] The water in the starting mixture is retained in the polymer formed. This enables the polymerisation process to be investigated using measurements of the relative permittivity of the system. As seen in Fig. 14, the relative permittivity of reaction mixtures based on AAm and Cr^{III} and Bi^{III} nitrates sharply decreases in the first 10–30 min after complex formation. After this both ε' (real part of the relative permittivity) and ε'' (imaginary part) change slowly.

The kinetics of spontaneous polymerisation were investigated by calorimetry.[36] The composition of the reaction mixture was found to have a substantial influence on the reaction. The kinetic curves plotted in Fig. 15 describe polymerisation of AAm in the presence of $Cr(NO_3)_3.9H_2O$ at various ratios [AAm]:[$Cr(NO_3)_3.9H_2O$]. In the majority of instances, they are analogous, with the exception of 5:1. Here the process occurs at a significantly higher initial rate and a more rapid decrease. A similar path of the curves (although less clearly evident) is observed on addition of a small amount of water (Fig. 15*b*). It can be proposed that the composition of the polymerising complex in this instance has the ratio [AAm]:[$Cr(NO_3)_3.9H_2O$] = 5:1.

It is interesting that the amount of heat released by polymerisation at 20 °C for 3–6 h after the start is only 20–25% of

the calculated value. This may indicate that a comparatively small fraction of the AAm molecules are activated at the start of the reaction. The process is finally finished only after 1–2 days at room temperature. The mixture is already solid. Therefore, its second step cannot be recorded but does become detectable at elevated temperatures where the rate of the process increases (Fig. 16). Thus, the reaction is practically completely finished after 2 h at 60 °C. Increasing the temperature further to 70 °C causes the nitrate to decompose with subsequent oxidation of the organic part of the complex.

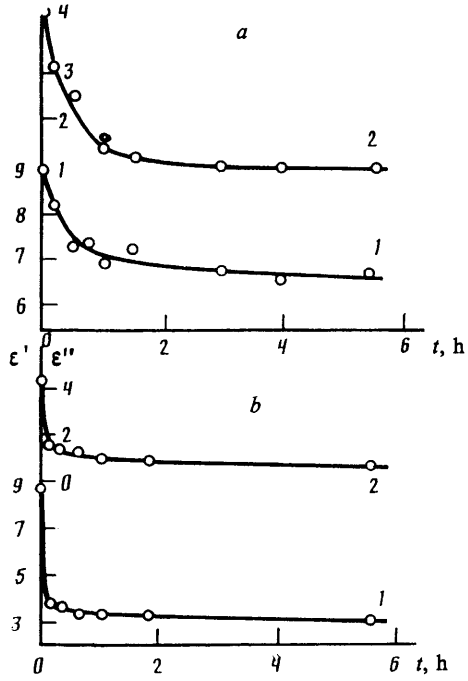


Figure 14. Dependence of change of relative permittivity ε′ (curve *1*) and ε″ (curve *2*) on time during spontaneous polymerisation in the systems [AAm]–[$Cr(NO_3)_3.9H_2O$] (*a*) and [AAm]–[$Bi(NO_3)_3.5H_2O$] (*b*). T = 20 °C. Mole ratio [AAm]:[$M(NO_3)_3.nH_2O$] = 5:1.

Investigation of the spontaneous polymerisation of AAm complexes of Cr^{III} nitrate in the presence of 2,2,4,4-tetramethylpiperidine-1-oxyl demonstrated that this process is radical in nature. The data were used to estimate the rate of initiation of the reaction, equal to 4×10^{-9} mol sec^{-1}. The dependence of the rate on the amount of water added to the system is rather unexpected. Practically the same effects are observed as adding an inhibitor to the system. The start of the reaction shifts. Its initial rate falls. The steric proximity of the polymerising complexes obviously is important for occurrence of spontaneous polymerisation.

Investigation of the properties of the product formed during spontaneous polymerisation of AAm–$Cr(NO_3)_3.9H_2O$ revealed that it contains two fractions. One of these dissolves in water at room temperature, the other does not. The insoluble part is practically pure (without metal compounds) polyacrylamide. It can be assumed that a gigantic molecular polymer forms during spontaneous polymerisation.

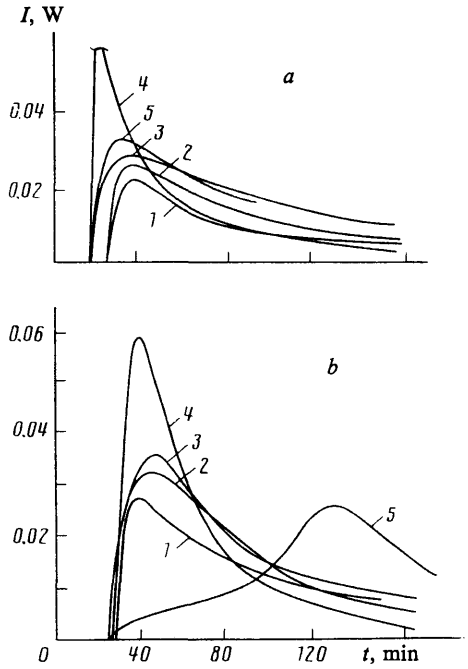


Figure 15. Dependence of rate of heat release on time of spontaneous polymerisation of AAm in the presence of $Cr(NO_3)_3.9H_2O$ with reaction mixtures of various composition: *a*) 20 °C, 0.516 g AAm; [AAm]:[$Cr(NO_3)_3.9H_2O$] ratio: *1*, 2.0; *2*, 3.0; *3*, 4.0; *4*, 5.0; *5*, 6.0. *b*) 20 °C, 0.516 g AAm, 0.10 dm^3 H_2O; [AAm]:[$Cr(NO_3)_3.9H_2O$] ratio: *1*, 3.0; *2*, 4.0; *3*, 5.0; *4*, 6.0; *5*, 8.0.

Addition of other comonomers opens broad possibilities for regulating the properties of the product formed during spontaneous polymerisation of coordinated AAm. This ability was demonstrated using AAm–$Cr(NO_3)_3.9H_2O$–CH_2=CH–CO_2H as an example. Spontaneous polymerisation is slower than homopolymerisation. The reaction is finished only after 5–7 days. However, the product is stronger. The ability to prepare copolymers of the AAm complex of metal nitrates with *N,N*-methylene-*bis*-acrylamide, methacrylic acid and *N*-vinylpyrrolidone has also been demonstrated.

The mechanism of spontaneous polymerisation of AAm complexed with metal nitrates is still largely unclear. However, the fact that the reaction occurs only using the nitrate salts suggests that nitrate is involved in the initiation.

In contrast with the example examined above, spontaneous polymerisation in DMF of vinylazoles complexed with $MnCl_2$, Mn(vinylbenzimidazole)$_2Cl_2$ and Mn(vinylbenztriazole)$_2Cl_2$, stopped after 15% conversion of MCM.[37] The reaction was inhibited by *p*-benzoquinone. Its occurrence depended strongly on the presence in the system of oxygen from air. The reaction rate increased significantly on saturation of the reaction mixture with oxygen. In

the absence of oxygen spontaneous polymerisation was not observed. It was proposed that the reaction is initiated by Mn^{3+} formed by partial oxidation of Mn^{2+}. Manganese(III) coordianted to DMF can probably be reduced by vinylazole to generate radicals that initiate spontaneous polymerisation.

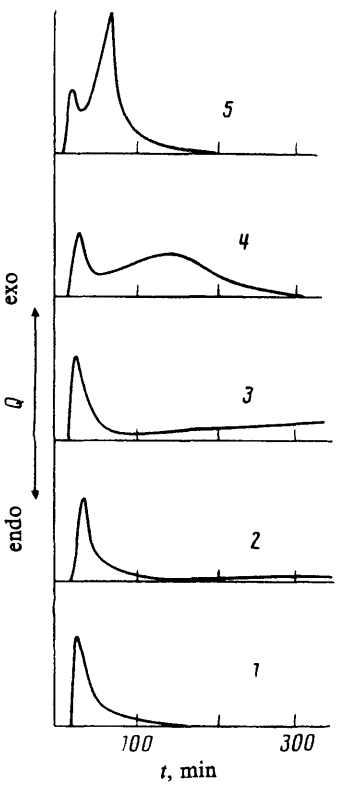


Figure 16. Dependence of rate of heat release on time of spontaneous polymerisation of AAm in the presence of $Cr(NO_3)_3.9H_2O$ at various reaction temperatures, °C: *1*, 20; *2*, 30; *3*, 40; *4*, 50; *5*, 60. m_{AAm} = 0.516 g, $m_{Cr(NO_3)_3.9H_2O}$ = 0.574, [AAm]:[$Cr(NO_3)_3.9H_2O$]= 5:1.

IX. Photopolymerisation with an applied magnetic field

A recent patent[38] claiming photopolymerisation of uranyl acrylate in alcohol with simultaneous application of a high-intensity magnetic field (10 kG) is extremely interesting. As it turned out, the process occurred at a disproportionately greater rate for ^{235}U than for ^{238}U. The insoluble polymer obtained in this way contained up to 50% of the former isotope (natural abundance ^{238}U, 99.3%; ^{235}U, 0.7%). Photopolymerisation typically did not occur without the magnetic field. This was related to the magnetic properties of the U isotopes, including the magnetic dipole of ^{235}U. Therefore, polymerisation of uranyl acrylate can be used to separate U isotopes. It should be noted that this is still the only example where the isotopic composition of the metal in the monomer affects the polymerisation properties of the MCM.

X. Conclusion

A large variety of nontraditional methods have been used to polymerise ionic and donor–acceptor MCM. It is noteworthy that the polymerisation properties of metal (meth)acrylates have been studied rather well. Nevertheless, involvement of such monomers in polymerisation by nontraditional methods enables their polymerisation properties to be more fully described. With respect to acrylamide complexes of metal nitrates, they have been practically ignored until recently. A recent surge of interest in polymerisation of complexes of traditional vinyl monomers with metal nitrates has been noted. This class of MCM is very interesting since the metal cation, the nitrate anion and the reactive double bond coexist in one molecule. Such symbiosis can lead to very unexpected effects, as evident from the material presented above. Hence, MCM based exclusively on metal nitrates participate in frontal and spontaneous polymerisation. It should also be noted that $M(NO_3)_3L_3$, where M = Fe^{III}, Cr^{III} and Co^{III} and L = vinylsulphoxide, can spontaneously explode during synthesis, storage or polymerisation to form oxides of N, S and metals and carbon-containing products.[39] The thermal explosion is caused by spontaneous polymerisation of spatially organised monomeric precursors formed by self-association of MCM through van der Waals and coordinative interactions.

Non-traditional approaches to synthesising metal-containing polymers recently have been extensively developed. This is due primarily to the desire to reduce the influence of extraneous factors that occur with traditional initiation. However, it should be remembered that a differentiated approach to the choice of MCM polymerisation method must be taken in order to account for the specific structures and properties.

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Advances in the chemistry of metal chelate monomers

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ABSTRACT. This review covers the chemistry of metal chelate monomers. Depending on the bonding of the metal to the chelating group, all metal chelate monomers are divided into three main types: molecular chelates, inner-sphere compounds, and macrocyclic complexes. The data are systematised according to methods of preparing similar compounds. Special attention is paid to the specifics of homo- and co-polymerisation of metal chelate monomers. The principal applications of metal chelate monomers and polymers based on them are considered.

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I. Introduction

Problems on the chemistry of macromolecular metal chelates (MMC) have attracted increasing attention over the last few years.[1–8] Polymeric chains and chelating rings are characteristic of MMC. The interest in such compounds is primarily due to their wide use as catalysts,[1–5,9–12] antifriction materials,[13–15] biologically active substances,[16,17] electrically conductive coatings,[18–22] etc. A large number of MMC have already been synthesised (MMC of practically all metals are known). Quantitative characteristics of chelate-formation processes involving polymeric ligands have been defined. Their principal structure features have been revealed.

However, the chelating systems are constructed, as a rule, in many steps including a whole series of successive conversions: the synthesis of the polymeric support, its functionalisation, creation of the chelating groups, synthesis and chelation of the metal complex, and separation of the chemically unbound components. Moreover, chelation in metal–polymer systems is significantly more complicated compared with low molecular weight analogues since both reagents can undergo a variety of reactions. The most important reactions of the transition metal during chelation are redox reactions, dissociation of dimeric complexes, cluster formation, etc. Destruction of the polymer, its conformational transitions, a change in the nature of the functional groups, etc. are also important. It is noteworthy that the compositional inhomogeneity of the MMC, a non-uniform distribution of metal ions on the polymeric support, different valence states, and the modes of coordination of the transition metals significantly affect the properties of the MMC.

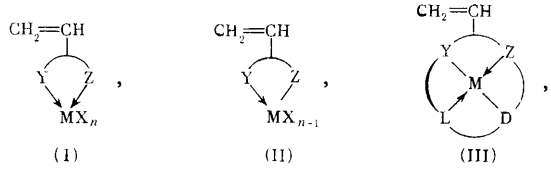
In this respect, much of the attention of the last two decades has been directed toward the development of new methods for synthesising MMC. The most promising of these are polymerisation and copolymerisation of metal chelates of monomers (MCM) containing a metal chelate ring and a multiple bond. This enables preparation of MMC in one step. In such MMC each chelating group contains a metal ion and in most instances has a definite spatial configuration in the metal chelate ring.

Chelation is an effective method of stabilising monomer–metal pairs (MMP). Thus, allyltrichlorotitanium is barely stable whereas its complex with 2,2′-bipyridine (bipy) decomposes only at 180 °C.[23] Unsaturated organocobalt compounds are stable only if they contain bulky chelating ligands, in particular, dimethylglyoxime (DH_2).[24,25] Moreover, MCM are independently interesting owing to the influence of the double bond on the stereochemistry of the coordination sphere and the electronic properties of the metal on the one hand and to the influence of the metal on the reactivity of the multiple bond on the other.

In this review, data for the synthesis, homopolymerisation, copolymerisation and graft polymerisation of MCM are summarised. Routes for the most rational development of this area are outlined.

II. Synthesis

Metal chelate monomers include complexes containing a metal chelate ring and a multiple bond capable of undergoing addition. Depending on the type of metal–chelate bonding, MCM can be classified into the following three types: molecular metal chelates (I), inner-sphere compounds (II) and macrocyclic complexes (III).



(I) (II) (III)

where M is the metal, n is the metal valence, X is a ligand, and Y, Z, L and D are the corresponding functional groups.

Type (I) MCM have only coordinate bonds between the metal and the donors of the chelate. Such MCM are formed if the groups have donors positioned to form a metallocycle or are conformationally non-rigid with two or more donors. In type (II) MCM, at least one group forms both a coordinate and covalent bond to the metal. These compounds can be neutral, cationic or anionic and can contain monodentate and chelating ligands. The metal ion in type (III) MCM is bonded to a macrocycle. These three

types of MCM can be further divided into groups depending on the nature of the donors (O,O-; N,N-; N,O-; and P,P-chelates, etc.).

In the modern synthetic chemistry of MCM, general methods and principles for synthesising complexes are widely used.[26,27]

1. Molecular metal chelates

The traditional route for synthesising type (I) MCM is based on reaction of metal compounds (MX_n) with chelating monomers. This method has been used, in particular, to prepare the complex of Cu^{II} chloride with the vinyl ether of monoethanolamine;[28] Ru^{II}, Co^{II} and Fe^{II} complexes with 4-vinyl-, 6-vinyl-, or 4′-vinylterpyridyls;[29] Ru^{II}, Zn^{II} and Ir^{III} complexes with 4-vinyl-4′-methyl-2,2′-bipyridyl;[30–33] the Ru^{II} complex with 6-vinyl-2,2′-bipyridyl;[33] Ni^{II}, Co^{II}, Cd^{II}, Bi^{III}, Hg^{II} and Pd^{II} complexes with 1-allyl-3-(2′-pyridyl)-2-thiourea;[34] Cu^{II}, Ni^{II}, Co^{II}, Mn^{II} and Zn^{II} complexes with 1-vinyl-2-hydroxymethylimidazole and 1-vinyl-2-vinyloxymethylimidazole;[35,36] etc.

A method based on interaction of monofunctional monomers with metal chelates has also been widely employed. For example, chelates of monomers have been prepared for Ru^{II} and Os^{II} with chelates of the type bipy or phen (1,10-phenanthroline) and monofunctional 4-vinylpyridine (4-VP), bis-(4-pyridyl)ethylene, *trans*-4-stilbazole, *N*-(4-pyridyl)-acrylamide, etc.[18–20,37,38]

Molecular metal chelates can be obtained through reaction of metal-containing monomers with chelates. An example of this reaction is the interaction of bipy and phen with transition metal acrylates to give type (IV) MCM:[13,39,40]

$$M(CH_2{=}CHCOO)_n \cdot mH_2O + L \rightarrow M(CH_2{=}CHCOO)_n \cdot L \cdot pH_2O \quad (IV)$$

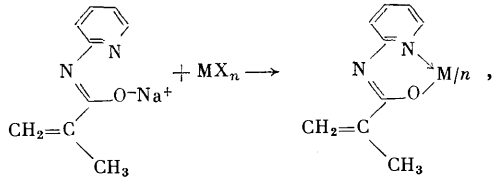
where M = Cu^{II}, Ni^{II}, Co^{II}, Cr^{III}, L = bipy or phen, n = 2, 3; and m and p = 0–2.

2. Inner-sphere compounds

Various methods of synthesising type (II) MCM have been developed. The following examples are typical:

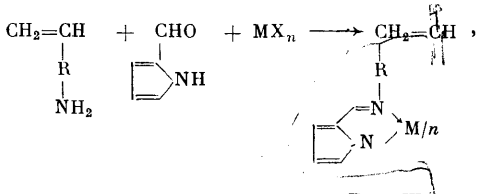
1. direct reaction of MX_n with monomers containing chelating groups. For example, this method was used to prepare Cu^{II} complexes of *N*-vinylsalicylaldimines,[41] complexes of transition[42–44] and rare earth[45] metals with vinyl-β-diketones, chelates of Cu^{II}, Ni^{II}, Co^{II}, Zn^{II} and Cd^{II} with 3-allyl-1-[2-mercapto-4-oxo-3(4*H*)-quinazolinyl]-2-thiopseudourea[46] or 1-isonicotinoyl-4-allyl-3-thiosemicarbazide,[47] a palladiated monomer based on *N*-allylsalicylaldimine,[48] complexes of Cu^{II}, Ni^{II} and Cd^{II} with 5-hydroxyl-5-hydroxy-3-vinyl-3-vinyl-1*H*-benz[*f*]indazole-4,9-dione,[49] etc.

2. Exchange of an alkali or alkaline earth metal in the chelate monomer for a transition metal:[50]



where M = Cu^{II}, Ni^{II}, Co^{II}, Fe^{III}, Cr^{III}; n = 2, 3.

3. Template synthesis of MCM, for example, according to the scheme:[51,52]



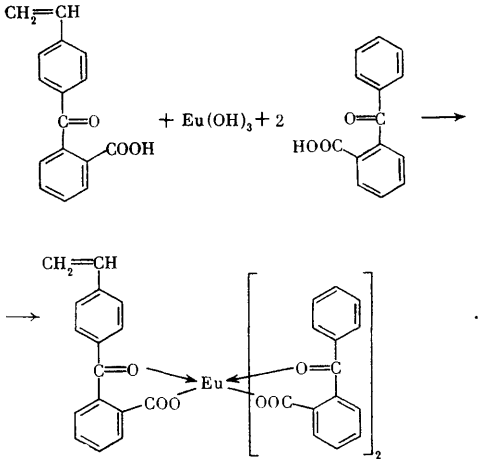
where R = $-C_6H_4-$ or $-CH_2-$; M = Cu^{II}, Co^{III}; n = 2, 3.

4. Addition of acetylenic monomers to metal chelates, in particular, phenylacetylene to dimethylglyoxime complexes of Co:[24,25]

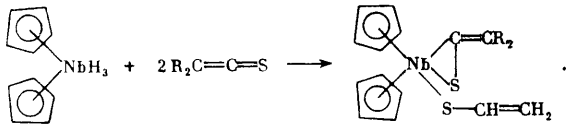
$$HCo(DH)_2 + CH{\equiv}CPh \rightarrow CH_2{=}C(Ph)Co(DH)_2 \ .$$

5. Covalent bonding of metal chelates to monomers. An example is the reaction of Co chelates with *p*-chloromethylstyrene to give cobalt chelate monomers with a cobalt–carbon bond.[4]

6. Neutralisation reactions. Thus, the chelate monomer of Eu^{III} was synthesised by neutralisation of $Eu(OH)_3$ by a mixture of 4-vinylbenzoyl-2′-benzoic and 2-benzoylbenzoic acids in a 1:2 mole ratio:[53]



7. Reaction of metal hydrides with thioketenes:[54,55]

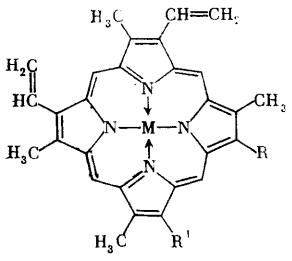


3. Macrocyclic complexes

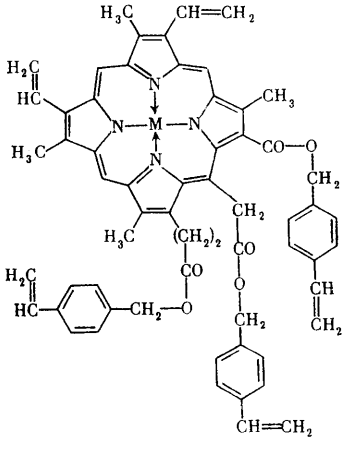
The macrocyclic type of MCM have been synthesised using a whole range of methods. One of these consists of direct reaction of MX_n with unsaturated macrocycles, for example, reaction of nickel acetate with vinylporphyrin.[56] Other metalloporphyrins, in particular, Co^{II}, Fe^{III}, Fe^{II}, Mg^{II}, Zn^{II}, Cu^{II}, etc. containing one or

two vinyl substituents were prepared analogously.[57–59] Typical representatives of these are shown in Scheme 1.

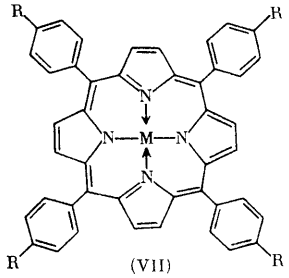
Scheme 1



(V)



(VI)

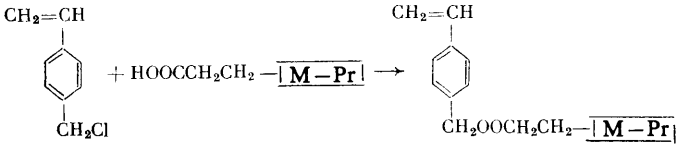


(VII)

where (V) are metal complexes of protoporphyrin-IX [R = R′ = $(CH_2)_2CO_2H$], the dimethyl ester of protoporphyrin-IX [R = R′ = $(CH_2)_2CO_2CH_3$], the vinylbenzyl ester of protoporphyrin-IX [R = R′ = $(CH_2)_2CO_2CH_2C_6H_4CH{=}CH_2$], *N*-(*p*-vinylbenzyl)-*N*′-(imidazolylpropyl)dipropylamidoprotoporphyrin-IX {R = $(CH_2)_2CONHCH_2C_6H_4CH{=}CH_2$, R′ = 1-[$(CH_2)_2CONH.(CH_2)_3$]pyrrole}, and the dimer of protoporphyrin-IX [R = $(CH_2)_2.CONHCH_2-$, R′ = $(CH_2)_2CO_2CH_2C_6H_4CH{=}CH_2$]; (VI) are metal complexes of the porphyrin chlorine; and VII are metal complexes of tetra(*p*-styryl)porphyrin (R = $CH_2{=}CH-$) or acrylamidotetraphenylporphyrin (R = $NHCOCH{=}CH_2$).

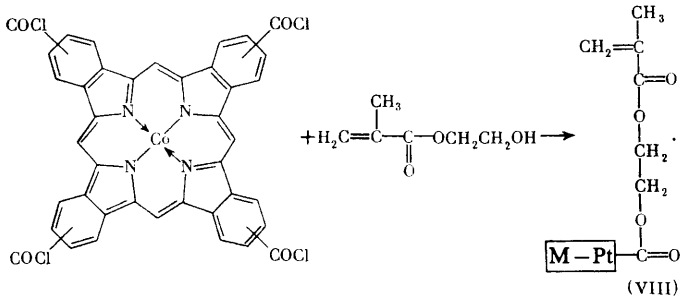
Another method is based on the well known ability of planar metalloporphyrins and -phthalocyanines to accept another ligand owing to coordinative unsaturation of the metal. The additional ligands occupy the fifth and sixth sites in the inner sphere of the transition metal.[60] Such ligands can be vinylpyridines, vinylimidazoles, etc.

However, the method used most widely to synthesise metalloporphyrin monomers consists of interaction of reactive peripheral groups of transition metal porphyrinates (for example, metal complexes of chlorophyll, chlorine, etc.) with monomers:[58,59,61]



where the symbol M–Pr denotes the metalloporphyrin. The most frequently used peripheral groups are carboxyls, sulpho and amino groups. Analogous MCM can be synthesised by reaction of acryloyl chloride with M^{II} tetra-*p*-aminophenylporphyrinate acetate.[61]

These approaches were also used to synthesise metallophthalocyanine monomers. Thus, synthesis of Co phthalocyaninate (VIII) has been described.[62]



(VIII)

Here the symbol M–Pt denotes the metallophthalocyanine. This can also be accomplished using the reaction of acryloyl or methacryloyl chlorides with metal tetra-*p*-carboxyphenylphthalocyaninates.[63]

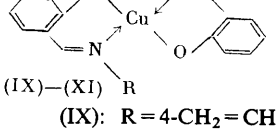
Therefore, analysis of the existing data indicates that the synthesis of MCM is rather well developed and continues to be improved. There appear at present to be no significant synthetic difficulties in synthesising MCM of practically any metals in various valence states. However, as for other types of MCM,[64] aspects of homo- and copolymerisation of MCM are largely unstudied.

III. Homopolymerisation

The kinetics of homopolymerisation of MCM and the properties of the MMC formed have begun to be studied only recently. Thus, the first radical polymerisation of haemin dimethyl ester was effected in 1977.[65] The possibility was demonstrated[18] of polymerising 4-VP complexed to Ru^{II} {complexes *cis*-$[Ru(bipy)_2(4\text{-VP})X]^{n+}$, where n = 1, X = Cl, n = 2, X = CO or 4-VP}. However, the properties of the polymers obtained were not described.

Radical polymerisation of the appropriate monomers produces Er^{III} and vanadyl(II) poly(*p*-acryloyloxyphenyltriphenylporphyrinates). The elemental analyses are consistent with 100% occupancy of the coordination sites by metal.[66] In contrast, the usual method (polymerisation of the corresponding chelate monomer with subsequent binding of metal by the macroligand obtained) gives only 50% metal incorporation. It is interesting that, in contrast with the starting chelate monomer of vanadyl with a weak antiferromagnetic exchange interaction (the Curie–Weiss θ value is −25 K), the polymer obtained that is based on it exhibits strong antiferromagnetic interaction (θ = −170 K). This indicates that the polymer chains play an important role in the magnetic interaction.

Salicylaldimine (Salim) chelates of Cu^{II}, CuL_2



(IX)–(XI)

(IX): R = 4-$CH_2{=}CH-C_6H_4-$ (L = Salim′),
(X): R = 4-$CH_2{=}C(CH_3)-CO_2C_6H_4-$ (L = Salim″),
(XI): R = $CH_2{=}C(CH_3)-CO_2-(CH_2)_2-$ (L = Salim‴),

were polymerised in the presence of azobisisobutyronitrile (AIBN) in the ratio AIBN:MCM = 0.12:1.[41] The rate of polymerisation was much less than that for the corresponding salicylaldimines (Table 1). Moreover, homopolymerisation of MCM of Cu^{II} was entirely impossible in a number of other attempts. For example, polymerisation of Cu^{II} methacryloylacetonate in the presence of very different initiators was unsuccessful.[42] Their ineffective homopolymerisation may be due to intramolecular chain termination:

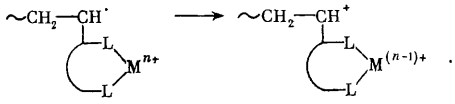


Table 1. Rate of polymerisation of type (IX)–(XI) MCM and the corresponding salicylaldimines.

L	CuL_2	W_{tot}, 10^5 mol dm^3 sec^{-1}		W_{sp}, 10^5 (dm^3)^2 sec^{-1}	
		L	CuL_2	L	CuL_2
Salim′	(IX)	2.59	0.23	5.28	2.10
Salim″	(X)	9.26	1.95	18.89	17.73
Salim‴	(XI)	0.34	0.0079	0.69	0.0718

It should be noted that allyl derivatives of metal β-diketonates do not undergo radical homopolymerisation.[44]

The mechanism of reductive electrochemical polymerisation of Ru^{II}, Os^{II} and Fe^{II} perchlorate and hexafluorophosphate mixed-ligand chelates of monomers has been studied in more detail.[19,20,38,67–69] Such complexes contain a chelating group of the type bipy, phen or terpyridyl (terpy) and a monofunctional monomer of the type 4-VP, *trans*-4-stilbazole, etc. Polymerisation occurs by repeated cycling of the electrode potential (Pt, vitreous carbon, etc.) near values corresponding to ligand reduction. This causes the electrode surface to be covered with an even film of polymer. The MCM in which the vinyl group is bonded to the chelating group polymerise in a similar way (for example, Zn^{II}, Ru^{II} and Ir^{III} complexes of 4-vinyl-4′-methyl-2,2′-bipyridyl).[31] In this instance the film forms much more effectively (the number of moles of polymer per mole of starting MCM).

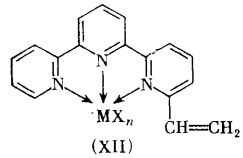
The mechanism of the electrochemical polymerisation includes formation of an anion–radical, for example, by the following reaction:

$$[Ru(bipy)_2(L)_2]^{2+} + \bar{e} \rightarrow [Ru(bipy)(bipy^{-})(L)_2] + \bar{e} \rightarrow [Ru(bipy^{-})_2(L)_2]^0,$$

where L is a monofunctional monomer. However, polymerisation is initiated by one-electron reduction based on an intramolecular redox equilibrium involving the thermodynamically less stable isomer in which the electron is localised on L;

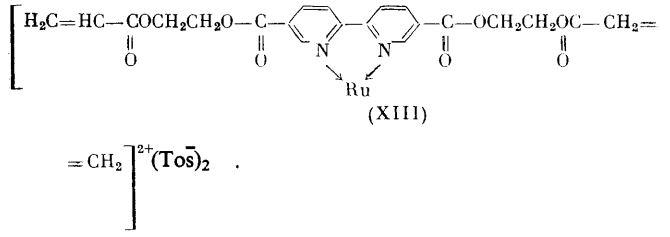
$$[Ru(bipy)(bipy^{-})(L)_2]^+ \rightleftarrows [Ru(bipy)(bipy^0)(L)(L^{-})]^+.$$

The dependence of polymerisation rate on the number of vinyl groups in the MCM and their position relative to the coordinated nitrogen atoms was studied for the example of Co, Fe and Ru complexes of various vinyl derivatives of terpy.[29] In particular, it was found that increasing the number of vinyl groups in the complex leads to significantly increased polymerisation. This was noted in a number of other instances.[64] Also, introduction of a vinyl group in the α-position relative to the nitrogen of the pyridine ring [complex (XII)] inhibits polymerisation of the MCM.



(XII)

Similar metal polymer coatings can be prepared by another method, deposition of MCM solution on the electrode surface with subsequent thermal polymerisation. The effectiveness of such an approach was demonstrated for polymerisation of 5,5′-bis-[(3-acryloyl-1-propoxy)carbonyl]-2,2′-bipyridylruthenium(II) toluenesulphonate (Tos) (XIII).[70–73]

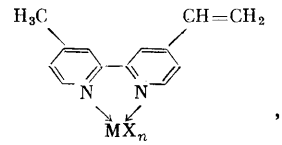


(XIII)

The thickness of the coating is regulated by the polymerisation conditions.

IV. Copolymerisation

Copolymerisation of MCM with traditional monomers is more common than their homopolymerisation. Thus, copolymers containing complexed rare earths (Eu^{III} and Tb^{III}) were prepared by copolymerisation of MCM of type (XIV)–(XIX) with methylmethacrylate (MMA) in a block or methanol.[45]

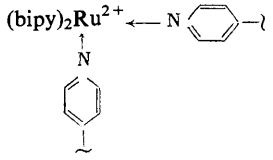


M = Tb^{III}, X = bipy(XIV), phen(XV), terpy(XVI);
M = Eu^{III}, X = bipy(XVII), 1-furyl-4-trifluoroacetylacetone(XVIII), dibenzoylmethane(XIX).

As it turns out the nature of the ligand X had a considerable influence on the fluorescence intensity of the copolymers obtained. In particular, the fluorescence intensity of the Tb complexes decreased in the order: (XVI) > (XIV) > (XV). That for the Eu complexes followed the order: (XIX) > (XVIII) > (XVII). Moreover the fluorescence intensity of the copolymers was much greater than a mixture of the starting monomers. This is consistent with fluorescence quenching by the double bond in the MCM.

Radical copolymerisation of *cis*-$[Ru(bipy)_2(4\text{-}VP)Cl]ClO_4$ and *cis*-$[Ru(bipy)_2(4\text{-}VP)_2](ClO_4)_2$ with styrene (St), MMA and 4-VP has also been achieved.[18] The copolymers based on Ru^{II} complexes

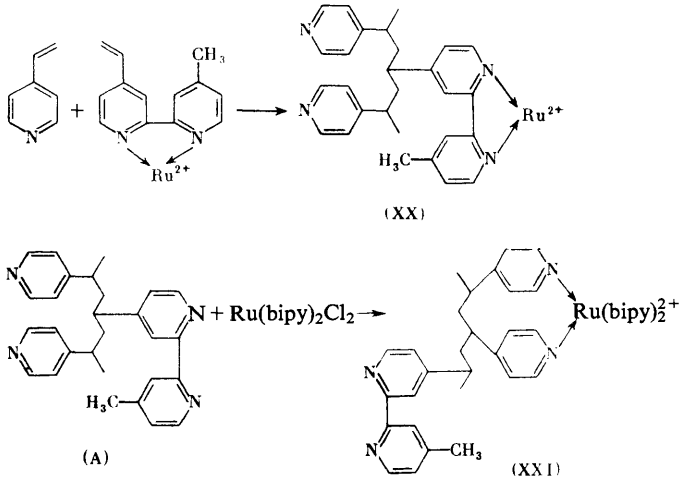
containing one 4-VP molecule were soluble in CH_2Cl_2 and methanol whereas the product of $[Ru(bipy)_2(4\text{-VP})_2](ClO_4)_2$ copolymerisation (comonomer of 4-VP, starting ratio [4-VP]:[MCM] = 20) were insoluble in organic solvents owing to crosslinking through metal atoms:[18]



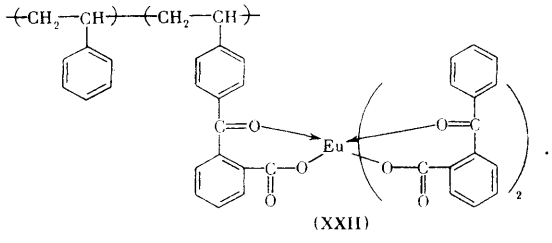
It was demonstrated that MX_n has much less influence if the ratio [4-VP]:[MCM] is increased to 200, for which a soluble product is formed.

It is interesting that copolymerisation of MCM can produce MMC of different structure from those formed by reaction of MX_n with analogous chelating macroligands prepared in advance. For example, copolymerisation of 4-VP with the Ru complex based on 4-vinyl-4′-methyl-2,2′-bipyridyl produces the polymer (XX) (Scheme 2),[31] whereas reaction of the chelating macroligand (A) with $Ru(bipy)_2Cl_2$ gives polymer (XXI).

Scheme 2



Unfortunately, kinetic aspects of the copolymerisation are not treated in the majority of studies of MCM copolymerisation. The mechanism of copolymerisation also is not described in detail for such MCM as Eu[2-(4′-vinylbenzoyl)benzoate]-di(2-benzoylbenzoate) with St to form (XXII).



This MMC characteristically has a high fluorescence intensity proportional to metal content, in contrast with complexes prepared by reaction of $EuCl_3$ with macroligands containing 2-carboxybenzoyl (XXIII) or 2-carboxynaphthoyl (XXIV) groups (Fig. 1).[53] The Eu^{III} complex of 1-(*p*-vinylphenyl)-3-phenylpropane-1,3-dione was copolymerised with MMA in an analogous manner.[45]

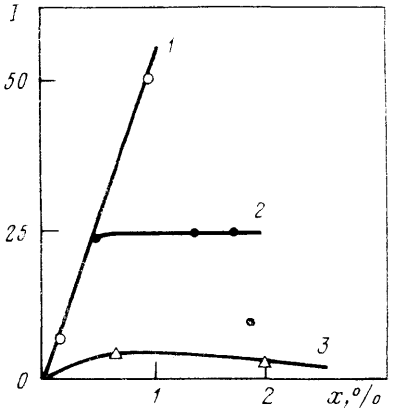
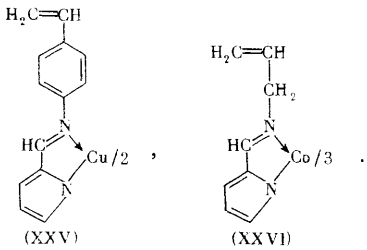


Figure 1. Dependence of fluorescence intensity (*I*) on Eu content (*x*) in complexes (XXII) (curve *1*), (XXIII) (*2*), and (XXIV) (*3*).

Radical copolymerisation of the Co^{II} complex of *N,N′*-bis-[4′-(*p*-vinylbenzyloxy)salicylaldehyde]-1,2-diaminocyclohexane with St and divinylbenzene (DVB) led to ternary copolymerisation in which 20 St and DVB molecules were added for each MCM.[74]

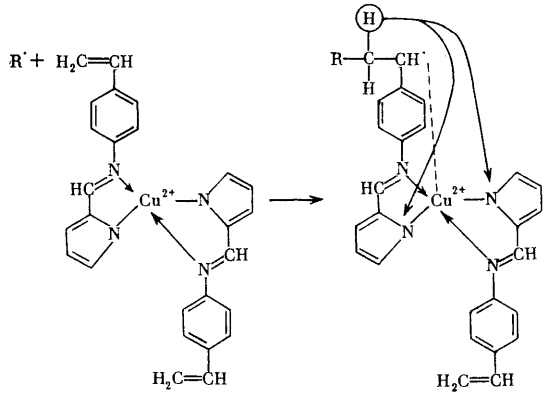
In contrast with the qualitative work mentioned above, the mechanism of copolymerisation of St, MMA, acrylonitrile (AN) or acrylic acid (monomer M_1) with MCM (monomer M_2), represented by the Cu^{II} complex with pyrrolylmethyleneiminostyrene (PIS) of type (XXV) or the Co^{III} complex with pyrrolylmethyleneiminopropene (PIP) or type (XXVI), has been studied.[51]



As seen from Fig. 2, the mole fraction of monomer M_2 in the copolymers formed is greater for MCM than for its metal-free analogue. The reactivity of the comonomer increases on adding metal (Table 2). This is comparatively rare in the polymerisation and copolymerisation of MCM.[64] Furthermore, only one or two out of the three multiple bonds in the Co^{III} chelate of type (XXVI) are involved in the copolymerisation of MCM. The third multiple bond is incorporated into the copolymer. For the Cu chelate, all vinyl groups are involved in the process. However, the polymerisation of this MCM is initiated along a complicated path (Scheme 3). The primary radical first attacks the vinyl group of the monomer. The free electron then transfers from this group to the central metal ion. This process is enhanced by conjugation (a long coplanar π-electron

system). The chain does not propagate until Cu^{II} is completely reduced to Cu^{I}. β-Elimination of a proton from the vinyl group attacked by the primary radical and addition of the proton to the pyrrole nitrogen atom occur simultaneously.

Scheme 3



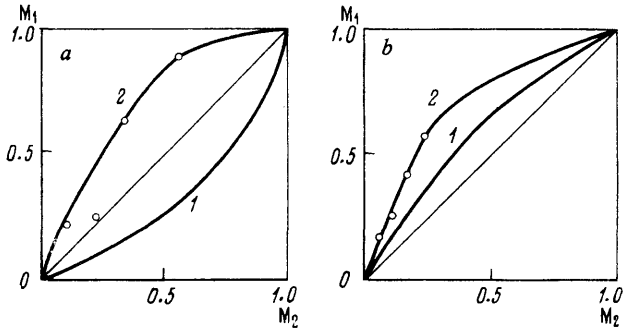


Figure 2. Composition diagram of copolymerisation of MCM (*2*) and their metal-free analogues (*1*) with AN (*a*) and St (*b*). *a* is copolymerisation of complex (XXVI); *b*, complex (XXV).

Copolymerisation of macrocyclic MCM is less well studied. The comonomers used for this are classified according to the *Q* parameter (resonance stabilisation of the monomer during copolymerisation). Monomers with high *Q* values (St, MMA, π-conjugated monomers) copolymerise with haemin and its dimethyl ester. During the copolymerisation Fe^{III} is reduced to Fe^{II}.[75,76] The haemin content in the copolymer with St is basically the same as that in the mixture of monomers (Table 3). As the ratio [MCM]:[St] increases, the yield, relative molecular mass, and viscosity of the polymer decrease owing to the influence of the metalloporphyrin on chain propagation (the coefficient of chain propagation C_s = 2.3).

However, copolymerisation of non-conjugated monomers (with a low *Q* value) does not occur as a result of addition of a radical to haemin to form stable adducts. Therefore, attempts to copolymerise haemin with vinylpyrrolidone (VPr) and vinylimidazole (VIA) were unsuccessful.[75] It is interesting that non-conjugated monomers can be copolymerised with haemin in the presence of a third conjugated comonomer, for example, to form the ternary copolymer haemin–VIA–St.[65,75,76] Copolymerisation of haemin with VPr under the influence of γ-irradiation from ^{60}Co or with 2-hydroxyethylmethacrylate in a buffer (Na_2CO_3–$NaHCO_3$, pH 10) has been described.[77] The MCM obtained through reaction of Mn tetra-*p*-aminophenylporphyrinate-acetate with acryloyl chloride readily copolymerises with MMA or 4-VP to form soluble MMC.[61] Tetra(*p*-vinyl)benzyl esters of the dinuclear Mg^{II} complex with chlorophyll copolymerise through a cationic mechanism (BF_3 etherate) with α-methylstyrene.[78] A three-dimensional structure with the metal monomer immobilised in the bulk of the polymeric gel is formed as a result of copolymerisation of the vinylporphyrin monomers of Co^{II}, Fe^{II} and Ni^{II} containing one or two vinyl substituents with acrylamide or *N*,*N*′-methyl-bis-acrylamide.[57] The parameters of such a networked structure are easily regulated by the ratio of comonomers.

Table 2. Copolymerisation activity of metal chelate monomers (XXVI) and (XXV) and their corresponding free ligands.

M_1	M_2	Copolymerisation constant	
		r_1	r_2
АН	ПИП	2.30	0.40
АН	(XXVI)	0.86	8.60
Ст	ПИС	0.50	1.80
Ст	(XXV)	0.45	6.90

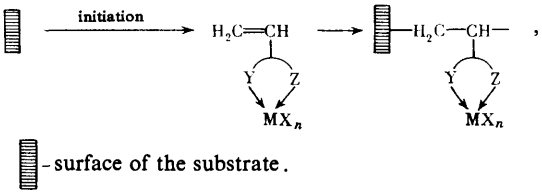
Table 3. Radical polymerisation of styrene with haemin[76] and its dimethyl ester.[75]

Porphyrin	Amount of porphyrin, mol%		Polymer yield, %	$\bar{M}_\eta \cdot 10^{-4}$	[η], 10^2 dm^3 g^{-1}
	in the monomer mixture	in the polymer			
Haemin dimethyl ester*	0	0		12.3	
	0.025	0.1		8.3	
	0.05	0.12		5.9	
	0.125	0.31		3.0	
Haemin**	0.49	0.53	75.6		9.96
	1.95	1.94	60.7		8.66
	3.44	3.31	41.7		7.65

* Copolymerisation in pyridine with AIBN at 358 K.
** Block polymerisation with AIBN at 333 K.

Copolymerisation of a type (VIII) monomer with 9-vinylcarbazole is an example of copolymerisation of metallophthalocyanine monomers.[62]

A special type of MCM copolymerisation is graft polymerisation, where the initiators are fixed to a polymeric or other kind of substrate.



Unfortunately, data on graft polymerisation of MCM are very limited, the majority of them being recently obtained.[13,40,79–85] Nevertheless, it is noteworthy that a distinguishing feature of the grafting of these MCM is the nearly complete absence of the homopolymer. The kinetic dependences of polymerisation are similar to those found for other types of MCM.[64,86,87] In particular, the kinetic dependences exhibit an identical nature for all chelates studied (Fig. 3). The rate is maximal during the first 0.5 h and then quickly drops. Moreover, the nature of the transition metal has a substantial effect on the grafting. Absorption bands of the C=C bond at 1640 cm^{-1} in the IR spectra of grated polymers containing metals are consistent with a certain amount of unpolymerised vinyl groups. In other words, only part of the vinyl groups polymerise during grafting of the MCM. The similarity of the spectral and magnetic properties of the monomers and polymers based on them (Table 4) indicates that the valence state and the coordination sphere of the metal do not change during grafting. However, the splitting parameter (Dq) decreases and the Racah interelectron repulsion parameter (B') increases on going from MCM to their polymers. Considering[88] that $Dq \approx d^{-6}$, it can be assumed that the decrease of the splitting parameter indicates an increase of the metal–ligand distance (d) in the indicated order. Moreover, the nephelauxetic parameter β increases in this same order. This indicates a decrease of the covalency of the metal–ligand bond.

V. Applications

Metal chelate monomers and polymers based on them find very diverse applications stimulating the direction of investigations in this area of chemistry.

1. Improvement of operating and physicomechanical properties of polymers

As a rule, polymers based on MCM are stable up to 473–523 K. Introduction of even a small amount of these monomers to copolymers of common monomers leads to crosslinked polymers with increased thermoplasticity and stability toward organic solvents. In particular, bis-(aminoethyleneamido-maleate-tetrahydrate)zinc prepared from zinc maleate and ethylenediamine was used to crosslink polyethylene in order to increase its resistance to thermal ageing and cracking.[89,90]

The reduced products of electrochemical polymerisation of vinyl derivatives of Fe^{II}, Ru^{II} and Os^{II} containing bipy are photoconductive (λ_{max} = 420–520 nm).[91] It should be noted that the metal ions in MMC, as a rule, have the same photophysical properties as in the corresponding MCM. Thus, monomeric Eu^{III} and Tb^{III} complexes with 4-vinyl-4′-methyl-2,2′-bipyridyl, like their copolymers with MMA, are excited at λ_{max} = 335 and λ_{max} = 500–600 nm, respectively. This is characteristic of these ions.[45] It is interesting that the polymeric products exhibit more intense fluorescence than the MCM. These substances may have utility in lasers.

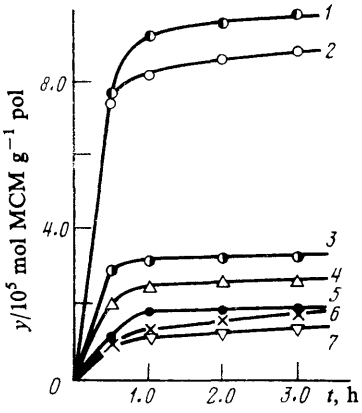


Figure 3. Kinetic curves of yield of grafted MCM polymers based on methacryloylacetophenone: Co^{II} (*1*), Ni^{II} (*2*), Pd^{II} (*3*), Mn^{II} (*4*), Cu^{II} (*5*), Fe^{III} (*6*), Cr^{III} (*7*) (ethylacetate, [MCM] = 0.04 and dm^{-3}, 70 °C, D = 200 kJ kg^{-1}).

Table 4. IR, electron-spectroscopic, and magnetochemical data for type (IV) MCM and their grafted polymers.

Complex	M	L	IR spectrum (principal frequencies), cm^{-1}			Dq, cm^{-1}	B', cm^{-1}	β	μ_{eff}, μ_B
			ν(C=C)	ν (heterocycle)	ν(COO–)				
Monomer	Ni	bipy	1635	1605	1565	1134	773	0.743	3.16
Polymer	Ni	bipy	1639	1606	1560	1028	837	0.804	2.96
Monomer	Co	bipy	1637	1610	1560	1152	834	0.859	4.53
Polymer	Co	bipy	1638	1608	1560	1018	883	0.909	4.75
Monomer	Ni	phen	1637	1600	1565	1166	830	0.797	3.17
Polymer	Ni	phen	1640	1600	1560	990	857	0.823	2.95
Monomer	Co	phen	1635	1605	1565	1163	849	0.874	4.75
Polymer	Co	phen	1639	1608	1565	1016	884	0.911	4.87

Macromolecular metal chelates based on $[Ru(bipy)_2(4\text{-}VP)_2]^{2+}$ and $[Ru(bipy)_2(4\text{-}VP)Cl]^+$ exhibit luminescence in methanol or dilute acids at room temperature.[18] Thus, absorption of the metal ions in poly-$[Ru(bipy)_2(4\text{-}VP)Cl]_n^+$ in methanol at 455 nm leads to a broad emission with a maximum at 615 nm.

Electroactive polymeric coatings are prepared by reductive electrochemical polymerisation of MCM consisting of vinylpyridine derivatives of Fe^{II}, Ru^{II} and Os^{II} complexes with chelates.[19] They are unique in that the redox centres are localised on each monomeric nucleus.

It also seems interesting to use grateful metal chelate polymers as antiwear and anticorrosion additives to lubricants.[15,40] In particular, addition to TsIATIM-201 lubricant of the type (IV) Cu acrylate

complex of bipy grafted to the surface of polytetrafluoroethylene (PTFE) improves its tribiological characteristics (corrosion index, seizing load and weld load) (Fig. 4). Whereas this MMC is more effective than grafted Cu acrylate,[92] this is apparently related to the involvement of the chelating ligand (bipy) in the transfer of Cu from one contacting surface to another. A very thin film of Cu metal (protective film) can be seen on the frictional surface after the tests. This is consistent with a "wearless" regime in these systems.[93,94]

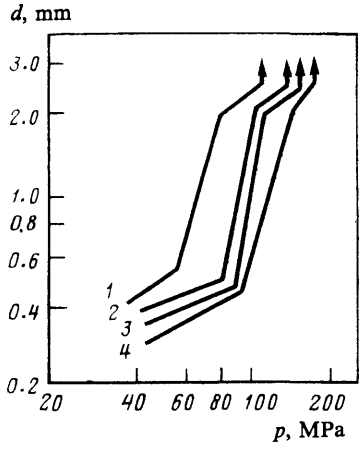


Figure 4. Dependence of average wear-spot diameter (d) of a four-ball machine on applied axial loading (P) for TsIATIM-201 lubricant: without PTFE additive (*1*), with PTFE additive (*2*), with PTFE additive and grafted Cu acrylate (*3*), with PTFE additive and grafted Cu acrylate complex with bipy (*4*).

2. Catalytic activity

Macromolecular metal chelates based on chelate monomers include immobilised catalysts[9,10] that combine the high activity and selectivity of homogeneous systems with the technology of heterogeneous ones. Chelation is one of the simplest methods of surmounting the principal drawback of immobilised catalysts, the relatively unstable metal–polymer bond during the catalysed reaction.[12] Moreover, such MMC can be prepared in one step. This is important in planning practical applications of these catalytic systems. Finally, an important advantage of such catalysts is the possibility of rather simple determination of the metal complex structure (the valence and electronic state of the metal, its ligand environment, the geometric structure of the metal chelate group, etc.) in addition to the controlled distribution of metal complexes along the polymer chain. This is due to the ease of separating intermediates at any step of the catalysed reaction.

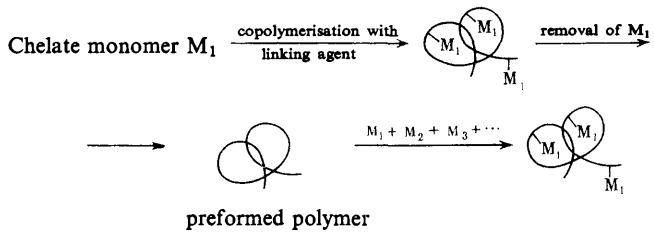
Examples of the use of MMC based on MCM are numerous. Therefore, let us point out the most typical ones. Soluble metalloporphrin polymers prepared by copolymerisation of MMA or 4-VP with macrocyclic MCM, represented by the product of reacting Mn tetra-*p*-aminophenylporphyrinate-acetate and acryloyl chloride, were capable of catalysing oxidation of olefins by molecular oxygen.[61] The copolymer of acrylamide and *N,N'*-methylene-bis-acrylamide with the Ni^{II} vinylporphyrin complex (in combination with H_2O_2) has been used to create effective redox systems for initiating polymerisation of acrylamide in aqueous medium.[57] Effective catalysts for ethylene dimerisation have been prepared by radical polymerisation of type (IV) Ni^{II} acrylate complexes with bipy and phen.[95]

As expected, more active catalysts are obtained by graft polymerisation of MCM since in this instance the catalytically active centres are localised on the support surface. For example, the grafted Pd^{II} chelate of a diketone ligand showed high activity for hydrogenating isomers of chloronitrobenzene.[82] This catalyst remains active for 15 cycles.

3. Template effect in macromolecular metal chelates

As applied to metal polymer systems, the template effect refers to the "recognition" and binding of those metal ions that were used as templates for synthesis of metal polymer complexes.[94,96–99] Ordinary chelate polymers do not selectively bind particular metal ions. As a rule, the selectivity is determined by the formation constants of the corresponding complexes and reaction conditions such as pH, solvent, temperature, etc.[7,8] Also, MMC prepared by copolymerisation of MCM with crosslinking agents exhibit "superstructure". The sorption capacity, sorption rate and selectivity of superstructured polymers increases dramatically after metal ions are removed. The mechanism of this effect is depicted in Scheme 4. The bond length and angle between the central metal ion and the coordinated ligand are strictly determined by their nature. When the chelating groups of the MMC are somehow immobilised and the metal ion is then removed geometrically, i.e., with retention of the preformed structure, the remaining polymeric ligand can have "pockets" specifically disposed to the same metal ions (templates) that were removed from the polymeric matrix.

Scheme 4



Thus, although the copolymer of 4-vinyl-4'-methyl-2,2'-bipyridyl, St and DVB from solutions of Ni^{II} and Cu^{II} salts of identical concentrations to a large extent binds Cu^{II} (as a result of the large binding constant of this complex), this same polymer preformed in the presence of Ni^{II} exhibits a template effect for Ni (Fig. 5).[100]

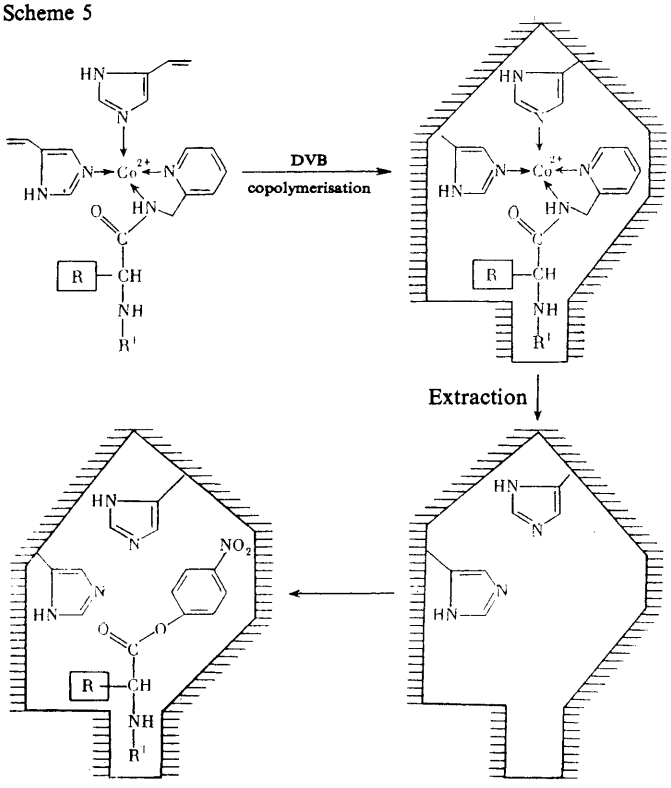
Polymeric chelates prepared by copolymerisation of dithiophosphate complexes, for example bis-[di(4-vinylphenyl)dithiophosphato].Ni^{II} or -Co^{II} and -Cr^{III}, with St and ethyleneglycolmethacrylate exhibit selectivity for the particular ion after removal of the metal. The enrichment factor (ratio of metal bound by the structured and unstructured polymers) for Ni^{II} is 1.4; for Co^{II}, 2.4.[101]

It should be noted that template syntheses can be effected using MMC. For example, it is possible to separate the racemate of D- and L-phenylalanine.[74] In this instance the separation is carried out as follows. The chelate monomer of Co^{II} with the Schiff base is initially synthesised. Then D-phenylalanine is added. Copolymerisation with St and DVB is carried out. The D-phenylalanine is extracted using HCl. The polymer obtained, structured for the

D-isomer, exhibits a template effect relative to the D-isomer of the racemic mixture (with optical purity 74 ± 1%).

New types of structured polymers that model active group histidine have been synthesised.[102] Complexes of Co^{II} with 4(5)-vinylimidazole and leucine-2-picolinimide or with leucine are copolymerised with DVB in a mixture of water, alcohol and butanol. The polymer particles (200–500 nm) are subjected to extraction with methanol for 12 h. The template molecules are then removed using bipy. The structured polymer formed is used as a catalyst for hydrolysis of *p*-nitrophenyl esters to amino acids (Scheme 5). The hydrolysis rate in the presence of polymers structured for the corresponding methionine or leucine derivatives is significantly greater than in the presence of unstructured ones. This is explained by the creation in the structured polymers of discrete voids with imidazole groups. The effect is retained after repeated use of the structured polymers. This is indicative of the catalytic nature of such action.

Scheme 5



IV. Conclusion

Analysis of existing data on the synthesis, homopolymerisation and copolymerisation of MCM indicates that significant progress has been made in solving several problems on the chemistry of MCM and that extensive investigations are being carried out in this area. Among the most important questions, the solutions of which would reveal general principles of the chemistry of MCM, we note the following:

1) development of new methods for preparing MCM;
2) establishment of the activation pathways of the multiple bonds of MCM, a detailed analysis of the influence of the metal on the separate polymerisation steps, discovery of new methods of initiating polymerisation;
3. investigation of the reactivity of the multiple bonds of MCM in other reactions (hydrogenation, isomerisation, oxidation, ozonolysis, hydroformylation, etc);
4) study of the copolymerisation of MCM with each other and with common monomers;
5) determination of the structures of metal polymer chains, investigation of the changes experienced by the metal ion during polymerisation, and the study of cooperative effects in MMC and their topochemistry;
6) study of the stereoregulation and supermolecular organisation in MMC;
7) discovery of new applications of MCM and polymers based on them, including their industrial use.

The final resolution of these problems requires joint efforts of specialists on the chemistry of polymers, coordination compounds, organic synthesis, catalysis, etc.

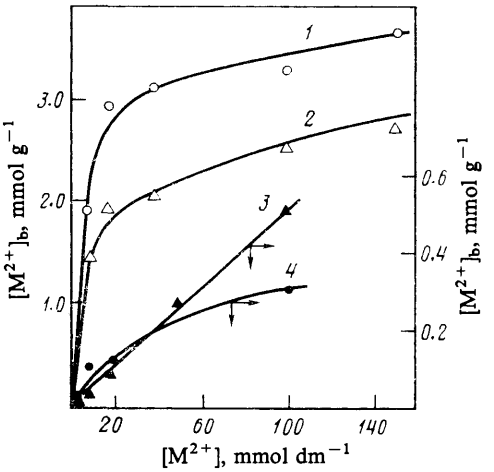


Figure 5. Binding of Cu (curves *1* and *3*) and Ni (curves *2* and *3*) by the copolymer of 4-vinyl-4′-methyl-2,2′-bipyridyl, styrene and divinylbenzene (*1*, *4*) and this same copolymer synthesised with a Ni template (*2*, *3*).

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Translated from *Uspekhi Khimii* **60** 1553–1569 (1991) U.D.C. 541.64;541.128;546.732.547.1/13

From sandwich and triple-decker to organometallic polymers

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ABSTRACT. Several types of organometallic polymers with different backbones are known. Our approach for the construction of metal-containing polymers uses the ability of Lewis-acidic boron heterocycles to interact antifacially with metals. The boron heterocycle 2,3-dihydro-1,3-diborole (*10*) not only allows the formation of sandwich and triple-decker complexes but also the stacking of metal complex fragments to oligodecker and polydecker compounds. This account reviews sandwich and triple-decker complexes as potential building blocks for polymers, and reports on the nickel- and rhodium-2,3-dihydro-1,3-diborolyl polymers *79* and *80*.

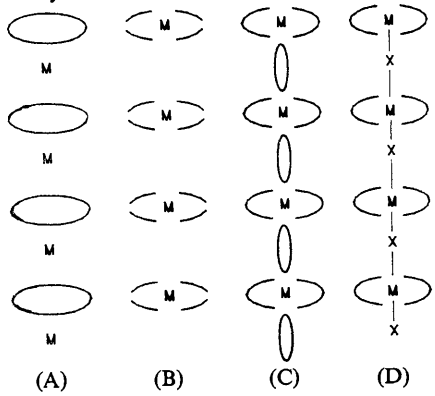
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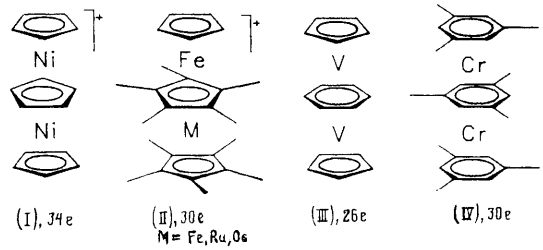
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I. Introduction

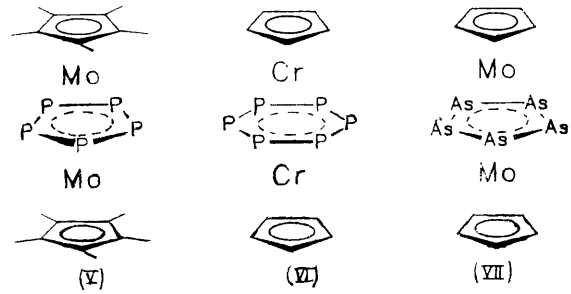
Organometallic polymers may be divided into several classes, depending on the backbone of the polymers. In coordination polymers of type *B*, e.g. in tetracyanoplatinate complexes $M_2Pt(CN)_4$ [1] and in porphyrinmetal complexes[2] the metals have direct contact via the d_{z^2} orbitals. Other polymers may contain heterocycles (type *C*) or chalcogen and halogen atoms (type *D*) as bridging ligands between the metal atoms.[3] Our approach for the construction of organometallic polymers uses electron-poor boron heterocycles in bridging positions (type *A*). They allow antifacial coordination with strong metal-ligand interactions in oligodecker and polydecker sandwich complexes.[4,5] A theoretical study of stacking complex fragments to one-dimensional arrangements has been published by Böhm.[6]



The idea of synthesising polydecker sandwich compounds (stacked cyclic ligands with metal atoms in between) is as old as metallocene chemistry. Early information on triple-decker sandwich species came from mass-spectroscopic studies of ferrocene and nickelocene. Parent ions like $Cp_3Ni_2^+$, Cp_3NiFe^+ and $Cp_3Fe_2^+$ have been detected.[7] It was two decades after the mile-stone discovery of ferrocene when Werner and Salzer[8] obtained the first triple-decker sandwich $Cp_3Ni_2^+BF_4^-$ (*1*) from Cp_2Ni and HBF_4. Only recently the long-sought complexes *2* with M = Fe, Ru, Os; M′ = Fe, Os were synthesised by Rybinskaya, Kudinov, et al.[9] Dinuclear complexes of the types *3* and *4* with arenes in bridging position have been reported by Jonas[10] and Lamanna.[11]



The chemistry of triple-deckers with homocyclic bridging ligands experienced a most interesting addition when Scherer, et al.[12] prepared the first dinuclear compounds *5* and *6* with μ-P_5 and μ-P_6 rings. Another example is the triple-decker *7* with an asymmetric As_5-ring.[13]



Until now all attempts to obtain larger molecules with carbocyclic ligands in bridging positions have failed. In contrast to these findings organoboron heterocycles have not only allowed the construction of a large number of triple-decker complexes, but also the first tetra-, penta- and hexadecker, as well as polydecker sandwich complexes.[4,5] Several reviews have summarised the extensive chemistry of boron heterocycles as ligands in transition metal complexes.[14–16]

In order to outline the principles for the construction of oligo- and polydecker complexes it is necessary to refer to the electronic situation (HOMO/LUMO) of triple-decker complexes as published by Hoffmann, et al.[17] and by Chesky and Hall.[18] *1* has 34 valence

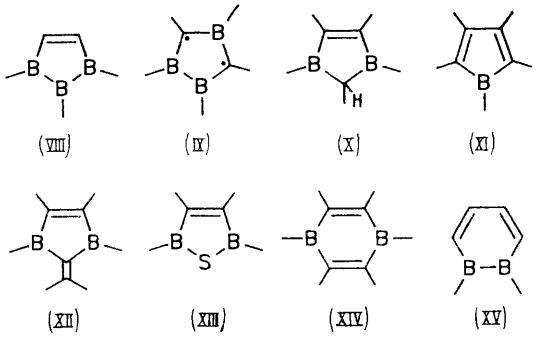
electrons (Ve, closed shell). In *2*, 30 VE (closed shell) are present. The diamagnetic triple-decker cations *2* are the electronic analogues of ferrocene (18 VE), while *1* is that of nickelocene (20 VE). They are formed when the sandwich complexes are stacked with a CpM^+ moiety. Applying the electron-counting for triple-decker to oligodecker complexes, we proposed that the optimum number of valence electrons is given by $12n + 6$, where n is the number of stacking units, each composed of a cyclic ligand and a metal (ferrocene, $n = 1$, 18 VE; *2*, $n = 2$, 30 VE), for $n = 3$ and 4 the optimum numbers are 42 and 54 VE. The maximum VE number should be given by $14n + 6$; examples are Cp_2Ni ($n = 1$, 20 VE) and *1* ($n = 2$, 34 VE). However, 48 VE for tetradecker ($n = 3$) has not yet been verified.

To date the smallest VE number for a triple-decker is observed in *3* (26 VE) belonging to the series with $10n + 6$ VE. On this basis we expect 36 VE as a minimum number for tetradecker complexes ($n = 3$).

For the design of oligodecker complexes one should focus the synthetic efforts at or near $12n + 6$ VE species, since chances for the realisation of such species are greatest. If we assume that $12n + 6$ species have a closed shell arrangement, then $11n + 6$ VE species have a hole (11 VE), and $13n + 6$ VE have an extra electron (13 VE) per stacking unit. Both should lead to a half filled band in a polydecker arrangement.

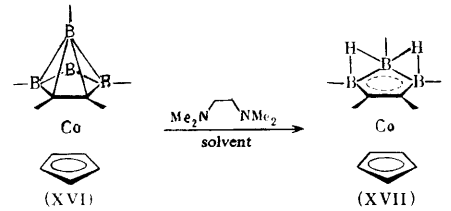
II. Boron heterocycles as ligands[14–16,19,20]

The organic ligands C_5H_5 and C_6H_6 in bridging positions yield complexes with weak interactions between metals and the μ-ligands. This is well documented by the high reactivities of *1–4*. Replacements of CH groups in carbocyclic ligands by BH or BR increase the acceptor properties of the μ-ligands, and thereby strengthen the antifacial interactions to the neighbouring metals. The following boron heterocycles *8–15*, formally derived from cyclopentadiene, fulvene, thiophene, and benzene, have been incorporated as bridging units in various types of complexes.



The ligands *8–10* and *15* have no independent stability. They are formed during complexation via activation of B–H or C–H bonds by the metal centre leading to the elimination of hydrogen. *8* and *9* function as 2e donors, *10* as a 3e donor and *11–15* supply 4e for bonding to one or two metal moieties.

Because of its low donor potential, *8* cannot be stabilised in sandwich complexes unless two more hydrogens are incorporated into the C_2B_3 framework. An example is *17*, obtained by the "decapitation" of the sandwich *16* (alternatively described as a *closo* metallo-carborane) with tetramethylethylenediamine. In *17* the two bridging hydrogens function as 2e donors, as does the apex BH group in *16*.[14,20]

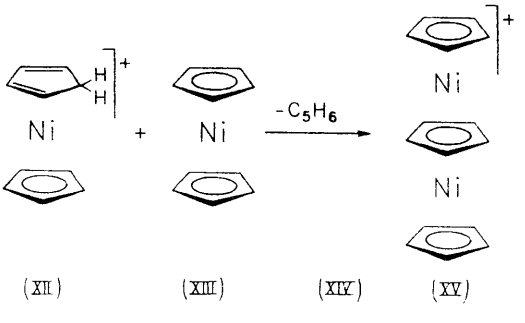


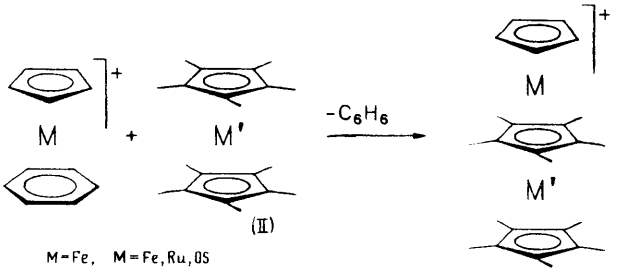
The ligands *10–14* have been used to synthesise various sandwich compounds having good acceptor functions to allow the formation of triple-decker complexes.

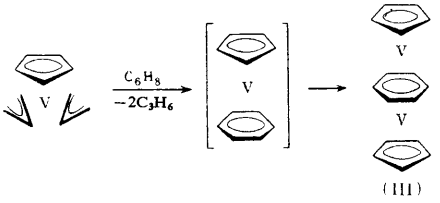
III. Triple-decker complexes

1. Homocyclic ligands in triple-decker complexes

Protonation of nickelocene, with HBF_4 at low temperature occurs at the C_5H_5 ring to give the 18 VE species. This then loses C_5H_6 and the resulting $(C_5H_5)Ni^+$ quantitatively stacks nickelocene to give *1*.[8] A related approach has been used to obtain the diamagnetic species *2* by replacing benzene in $[(C_6H_6)M(C_5H_5)]^+$ complexes with a sandwich molecule.[9] The formation of *3* occurs when $(C_3H_5)V(C_3H_5)_2$ reacts with cyclohexadiene, leading to the $(C_5H_5)V(C_6H_6)$ intermediate, which is stacked to yield *3*.[10]





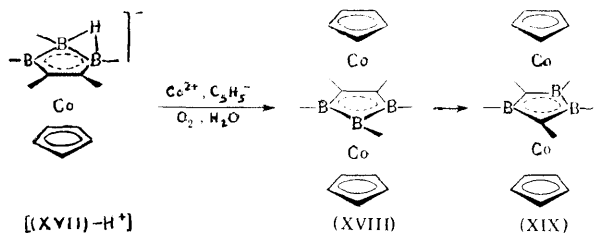


The formation of *4* via co-condensation of mesitylene and chromium atoms also occurs via stacking of the bis(mesitylene)-chromium with a $Cr(C_6H_3Me_3)$ moiety.[11]

In contrast the triple-deckers *5* and *7* are built from dinuclear species and P_4 molecules, which requires the formation of the P_n ring at the metal centres. A detailed study of *6* has been published.[12]

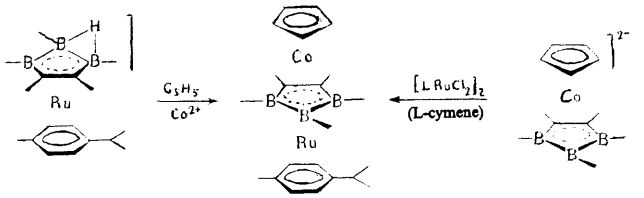
2. The isomeric μ-$R_2C_2B_3H_3$ ligands *8* and *9*

The synthesis of the first neutral triple-decker sandwich complex *18* has been achieved by Grimes et al.[21] via a three-component reaction of $R_2C_2B_4H_5^-$, Co^{2+} and $C_5H_5^-$, followed by treatment of the reaction mixture with oxygen and water. The sandwich *17* plays the key-role in the stacking reaction leading to *18* in a low yield. A designed synthesis involves a deprotonation of *17* to give [*17*−H^+], which is then reacted with $Co^{2+}/C_5H_5^-$.



[(XVII)−H^+] (XVIII) (XIX)

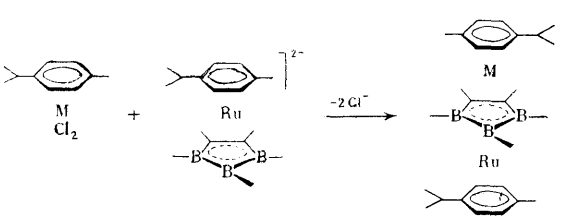
The red complex *18* (30 VE) quantitative isomerises at 400 °C to give the green 2,4-isomer *19*. Replacing one cobalt atom in *18* by iron leads to a paramagnetic 29 VE species. It is obtained in 20% yield by deprotonation of $(Et_2C_2B_3H_5)Fe(C_8H_{10})$ with NaH followed by reaction with $CoCl_2$ and $C_5H_5Na^+$.[22] For the synthesis of *20* a similar strategy has been applied. *20* is obtained in 40% yield by reacting the Ru sandwich anion [*21*−H^+] with Co^{2+} and $C_5H^-_5$ or by reacting the dianion [*17*−$2H^+$] with $[(cymene)RuCl_2]_2$. In addition the analogous compound *20* with Co and Os has been prepared.



[(XX1)−H^+] (XX) [(XVII)−$2H^+$]

$[(Cymene)MCl_2]_2$ (*22*) and the dianion [*21*−$2H^+$] form the dark orange *23* and yellow *24* in 30−45% yield, respectively. Both complexes have 30 VE.

The results described above prove that for the construction of triple-decker sandwich complexes the sandwich *17* and its anions [*17*−H^+] and [*17*−$2H^+$] as well as *21* and [*21*−H^+] are the best choices to obtain dinuclear species.

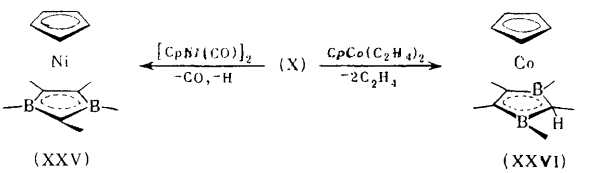


(XXII) [(XX1)−$2H^+$] (XXIII), (XXIV)

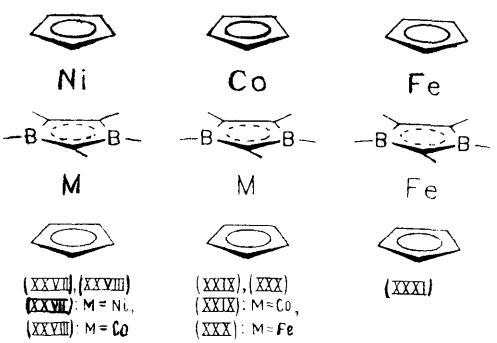
(XXIII): M=Ru,
(XXIV): M=Os

3. 2,3-Dihydro-1,3-diborole complexes.[4,5,15,19,23]

2,3-Dihydro-1,3-diboroles *10* can function as 3e or 4e donors, depending on the electronic requirement of the $(C_5H_5)M$ moiety. During the formation of yellow-orange *25* a hydrogen atom is lost, whereas in the orange-red cobalt complexes *26* the ligand *10* remains intact and functions as a 4e donor through its C=C and axial C−H group. Both sandwich complexes possess high acceptor properties and they are easily stacked in high yields to give the first complete series of triple-decker sandwich complexes *27*−*31*.[25]



(XXV) (XXVI)

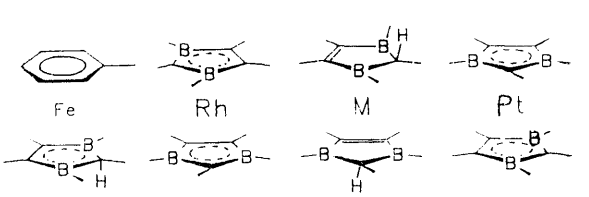


(XXVII), (XXVIII)
(XXVII): M = Ni,
(XXVIII): M = Co

(XXIX), (XXX)
(XXIX): M=Co,
(XXX): M=Fe

(XXXI)

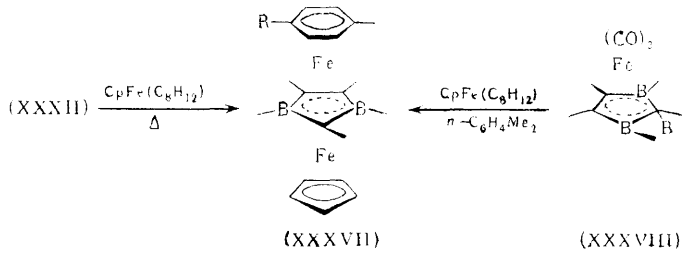
1,3-Dihydro-1,3-diborafulvene derivatives *12*[24] react with Cp_2Ni to give derivatives to *27* with C_5H_5 at the exocyclic C_6 atom. The mixed-valence blue triple-decker *31* is obtained from *10* and $[CpFe(CO)_2]_2$. A three-component reaction between *10*, $CpCo(CO)_2$ and $[CpFe(CO)_2]_2$ only leads in small yields to *30*. Deprotonation of *26* with potassium affords the anion [*26*−H^+], which on reaction with $CpFe(CO)_2I$ gives only a low yield of *30*, since a redox reaction with formation of $[CpFe(CO)_2]_2$ is favoured over the substitution of CO. The magnetic properties of *27*−*31* are in agreement with the number of unpaired electrons as derived from the MO scheme. *27*$^-$ and *30*, are diamagnetic closed-shell species.[25] The former is obtained by reduction of *27* with potassium. Several other sandwich complexes such as *32*−*36* with the 2,3-dihydro-1,3-diborole ligand have been prepared and used as precursors for triple-deckers.[5] *32* is stacked with $CpFe(C_8H_{12})$ to give the 30 VE species *37* (R=H). Another derivative of *37* ($R=CH_3$) is obtained when *38* reacts with $CpFe(C_8H_{12})$ in *p*-xylene.



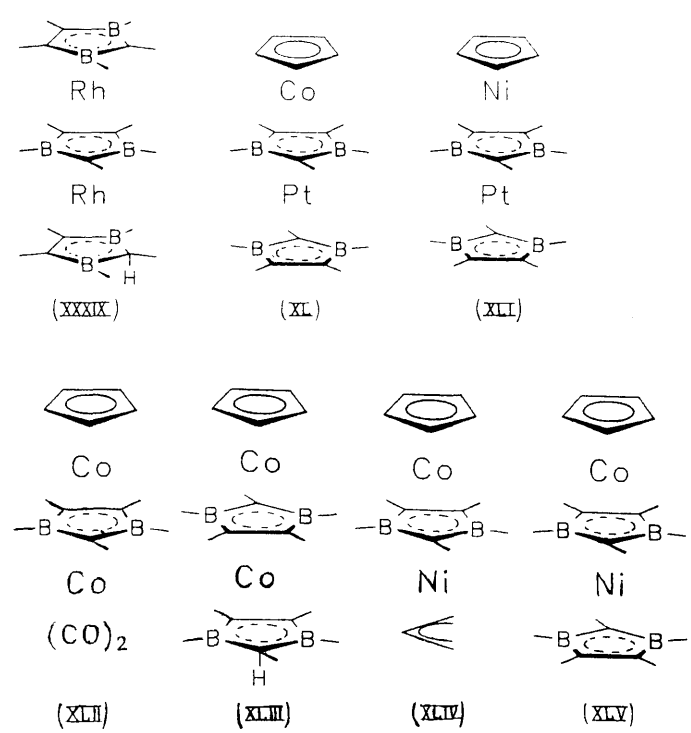
(XXXII) (XXXIII) (XXXIV), (XXXV) (XXXVI)

(XXXIV): M=Ni;
(XXXV): M=Pt

On heating the 16 VE sandwich *33* above its melting point, an unusual condensation reaction occurs with elimination of one 2,3-dihydro-1,3-diborole ligand. Red *33* turns into green *39*, a diamagnetic 28 VE triple-decker sandwich.[26] As observed in the sandwich compounds *26*, *32*, *34*, and *35* the axial hydrogen at C2 of the dihydro-diborole ligand of *39* exhibits a high-field ^{1}H NMR signal (δ = 10.1).

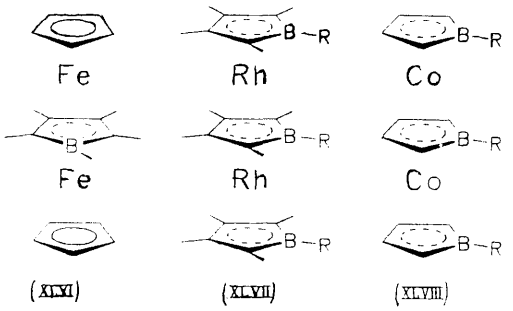


The platinum sandwich *36*, which is formed from *35* by thermal elimination of hydrogen, reacts with $CpCo(C_2H_4)_2$ and $[CpNi(CO)]_2$ to yield the unsymmetrical triple-decker sandwich complexes *40* and *41*, respectively.[27] Two further complexes of this type are obtained when *42* and *44* react with *10* to give *43* and *45*, respectively. Both are 30 VE diamagnetic species which have been used for the construction of penta- and hexadecker sandwich complexes.[29,29]



4. Triple-decker complexes with borole ligands[16]

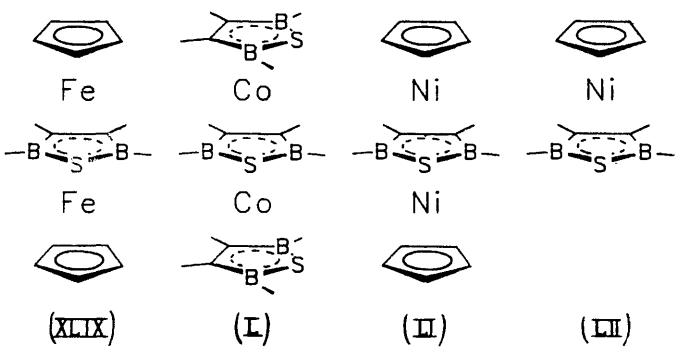
The borole ligand *11* functions as a 4e donor and a 2e acceptor to complete a η^6-system. A number of 18 VE metal complexes of *11* are known, and stacking of sandwich complexes analogous to that of *25* have been reported. Reaction of $[CpFe(CO)_2]_2$ with *11* leads to *46*, a diamagnetic 30 VE complex.



Dehydrogenative complexation of borolenes C_4H_6BR (R = Me, Ph) with $[Rh(C_2H_4)_2Cl]_2$ gives the 30 VE triple-decker *47*.[30] Its reaction with C_5H_5.Na leads to $(C_5H_5)Rh(C_4H_4BR)$ and $[(C_4H_4BR)_2Rh^+]Na^+$. $Co_2(CO)_8$ and the borole ligand form the dinuclear complex $[(C_4H_4BR)Co(CO)_2]_2$, which on thermal treatment results in the formation of *48* (R = Me). The borole rings in *48* are nearly coplanar with torsional angles of 59.8° and 72.2°.

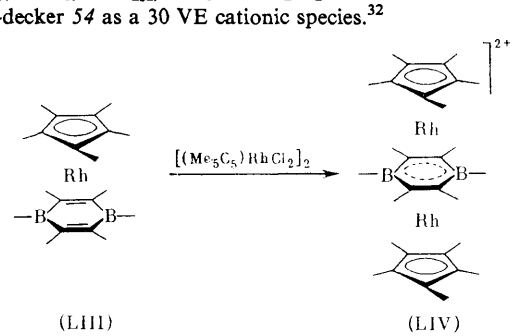
5. Triple-decker complexes with 2.5-dihydro-1,2,5-thiadiborole ligands[15]

The heterocycle *13* [31] allows the formation of various complexes, however none of the mononuclear species could be stacked to a triple-decker. *13* reacts with $[CpFe(CO)_2]_2$ and $Co_2(CO)_8$ to give the triple-decker sandwich complexes *49* and *50*. Attempts to obtain the 34 VE complex *51* only led to the paramagnetic sandwich *52*, which decomposes at 100 °C to Cp_2Ni and $(13)_2Ni$.

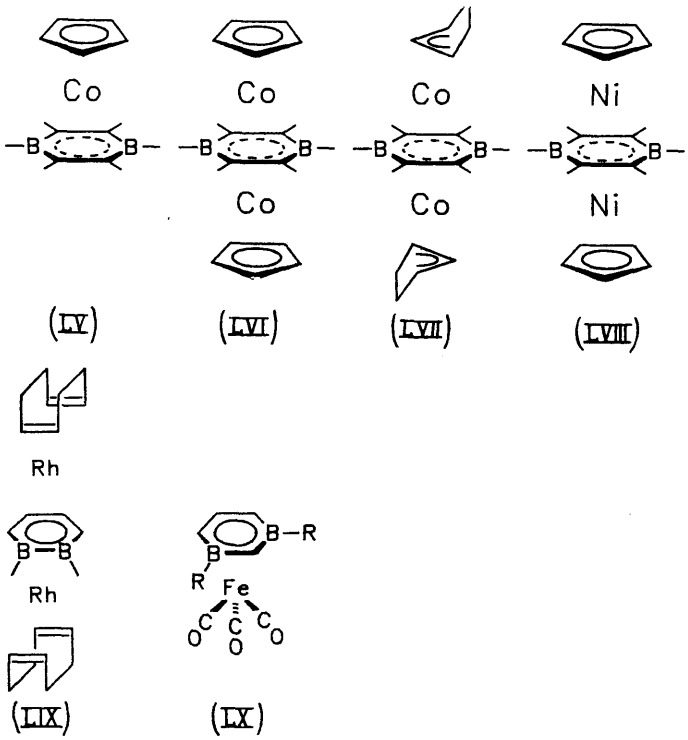


6. 1,4-Diboracyclohexadiene triple-decker complexes[16]

The 1,4-diboracyclohexadiene ligand *14* is related to the borole ligand *11* in its donor properties, and to the 2,3-dihydro-1,3-diborolyl in its acceptor properties. Treating the sandwich *53* with $[(Me_5C_5)RhCl_2]_2/AlCl_3$ in CH_2Cl_2 leads to the formation of the triple-decker *54* as a 30 VE cationic species.[32]



For the construction of the triple-deckers *56*–*58* alkyl derivatives of the 1,4-diboracyclohexene ring have been used. Dehydrogenative complexations of $C_4B_2R_4H_4$ with $(C_5H_5)Co(C_2H_4)_2$ and $[(C_5H_5)Ni(CO)]_2$ lead to the complexes *55*–*58*.[5,33,34]



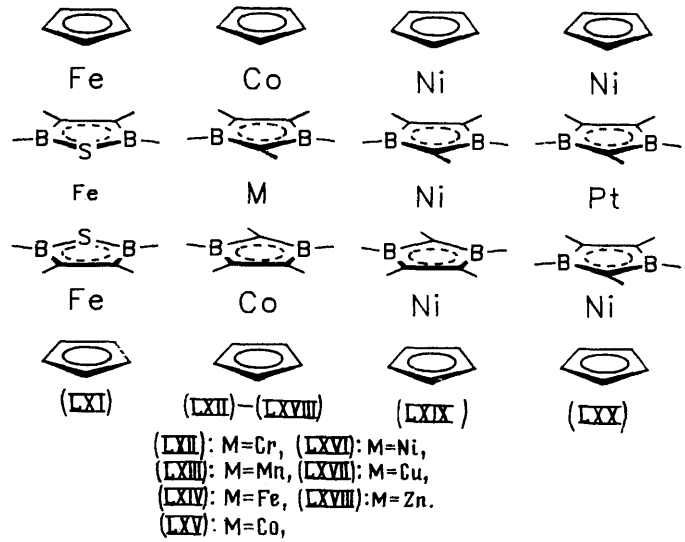
56 and *58* have 32 and 34 VE, respectively. *57* is a remarkable case, as the hydrogen atoms of $C_4B_2R_4H_6$ are transferred to the cyclopentadienyl groups to form the cyclopentenyl ligands. The constitutions of *57* and *58* have been studied by X-ray structure analyses.

7. 1-2-$B_2C_4R_6$ and 1,3-$B_2C_4R_6$ ligands

Herberich, et al.[35,36] have obtained the first examples of the title ligands stabilised in metal complexes such as *59* and *60*.

Both boron ligands in *59* and *60* should be capable of bridging two $(CH)_nM$ moieties to yield triple-decker sandwich complexes.

reaction between $[(C_5H_5Fe(COD)]_2Zn$ [38] and *13* leads to the 46 VE tetradecker $[(C_5H_5)Fe(13)]_2Zn$, which after reductive cleavage and reaction with Fe^{2+} yields the 42 VE tetradecker sandwich *61*.



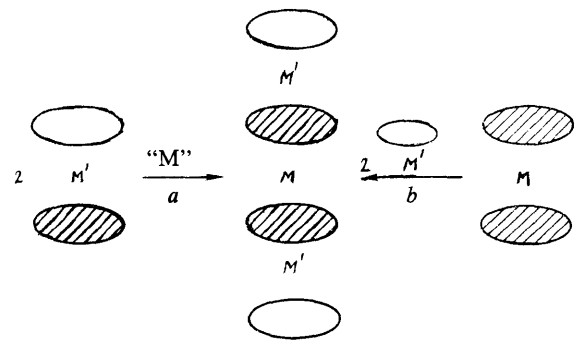


Figure 1. Routes of formation for oligodecker compounds.

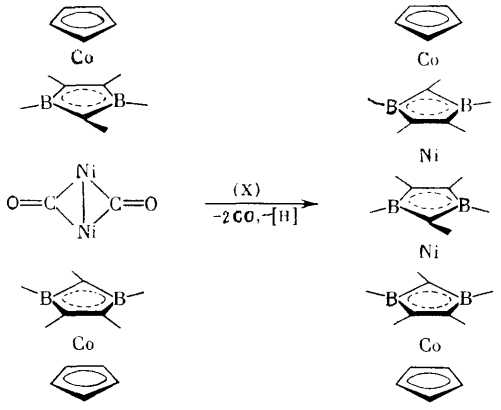
IV. Oligodecker complexes[4,5]

As outlined above the formation of triple-decker compounds can be achieved via several routes. For the construction of oligodecker complexes two reaction principles have been applied: a) reaction of two sandwich anions with a metal cation and b) stacking of a Lewis-acidic sandwich with two $(C_5H_5)M^+$ complex fragments (Fig. 1).

We synthesised and structurally characterised the first example of a tetradecker complex with the 1,2,5-thiadiborole ligand *13* in the bridging position. The diamagnetic, 42 VE hexacarbonyl dimanganese-iron complex $[(CO)_3Mn(C_2H_2B_2R_2S)]_2Fe$ was obtained in low yield by cleaving the triple-decker $[(CO)_3Mn]_2(13)$ with $C_5H_5^-$ and reacting the formed anion $[(CO)_3Mn(13)]^-$ with Fe^{2+}.[37] The

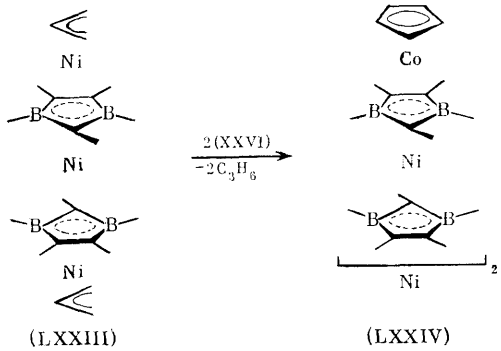
The first series of tetradecker complexes has been obtained from the deprotonated cobalt sandwich $[26-H^+]$ and the metal dications Cr(*62*), Mn(*63*), Fe(*64*), Co(*65*), Ni(*66*), Cu(*67*), and Zn(*68*).[39,40] With the exception of *68* (M = Zn) the highly coloured trinuclear species are paramagnetic; the compounds *62*–*65* have a high-spin configuration. All complexes are structurally characterised: the 2,3-dihydro-1,3-diborolyl rings adopt an antiperiplanar arrangement, and the central metal to ring distances correlate well with the Shannon–Prewitt ionic radii for octahedrally coordinated M^{2+} ions. Considerable deviations from the ideal tetradecker sandwich structure are observed due to a slip of the central metal away from the position above the centroid of the heterocycle towards the C2 carbon (between the two boron atoms). In contrast to the antiperiplanar arrangement of the boron heterocycles in the

diamagnetic 46 VE tetradecker *69*,[4] the isoelectronic platinum complex *70*,[27] obtained via reaction type *b*) in Fig. 1, exhibits a synclinal conformation.



(LXXI) (LXXII)

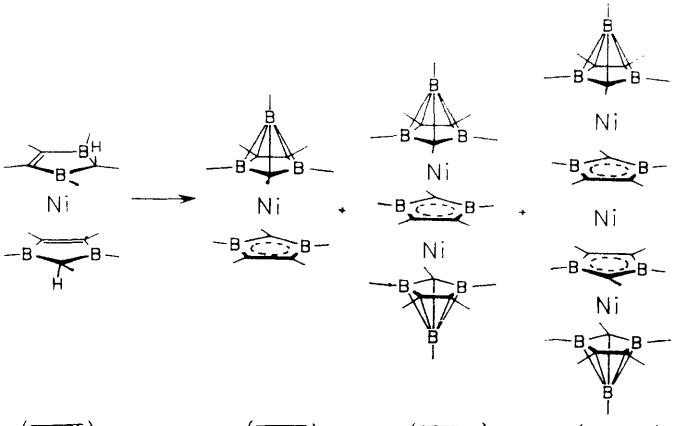
To extend the number of stacks, we have explored routes to pentadecker and hexadecker complexes. The pentadecker *72* was first obtained upon reaction of the tetranuclear complex *71* with the ligand *10*, which replaces the two CO groups of the diamagnetic, 58 VE *71* to yield the paramagnetic, 57 VE *72*. Alternatively, *72* is formed when the allyl groups in the triple-decker *44* is susbtituted for *10* to give the unsymmetrical triple-decker sandwich *45*. Its reaction with *44* leads to the pentadecker *72*.[41] This compound has been studied by X-ray, ESR, paramagnetic NMR and cyclic voltammetry. It was shown that paramagnetic *72* can be reduced to the diamagnetic, 58 VE anion and to the paramagnetic, 59 VE dianion. The next step led us to the synthesis of the first hexadecker sandwich complex via the reaction of the bis(allyl)tetradecker *73* with two sandwich molecules *26* in refluxing mesitylene. Besides the diamagnetic 70 VE hexadecker *74* paramagnetic triple-decker and tetra-decker were also formed.[42] The second route leading to *74* involves stacking at both ends of the bis(2,3-dihydro-1,3-diborole)nickel sandwich *34* with the allyl-triple-decker *44* at 160 °C. Again several by-products are formed, which can be separated by column chromatography. Due to the poor quality of the crystals structural determination of the red-violet *74* was unsuccessful.



(LXXIII) (LXXIV)

V. Carboranyl sandwich complexes

The bis(2,3-dihydro-1,3-diborole)nickel sandwich *34* exhibits an unusual reactivity: at room temperature it is slowly transformed into *75* and a series of carboranyl nickel oligodecker complexes *76*, *77* and higher molecular species (determined by FAB mass spectra up to the decadecker complex).[43]



(XXXIV) (LXXV) (LXXVI) (LXXVII)

Its formation occurs via capping of the diborolyl ring with a boranediyl fragment (R−B:) to give *75* after elimination of the two axial hydrogen atoms from *34*. Besides capping, a stacking to oligodecker takes place, which leads to *76*, *77* and higher oligodeckers. Several of the new carboranylnickel complexes have been structurally characterised.[43,44] This unusual finding of capping and stacking at room temperature clearly indicated a route to polydecker formation. The problem was to prevent the capping reaction, because it stops the one-dimensional system from growing.

VI. Polydecker sandwich complexes

For the synthesis of polydecker compounds reactive monomers and/or dimers are required. Reactions of sandwich complex dianions with metal dications shoud lead to polymers. However, the only complex dianion $[(C_3H_3B_2)_2Pt]^{2-}$ [*36*]$^{2-}$ was oxidised by Fe^{2+} to neutral *36* in an attempt to build a mixed-metal polymer, *78*−*79*.

The unusual reaction sequence of capping and stacking when the nickel sandwich *34* is heated to 80 °C for one hour in benzene to give *75*−*77* and higher oligomers indicated that the combination of Ni(d^{10}) and the 2,3-dihydro-1,3-diborolyl [*10*−H] leads to stacked products. This "self-organisation" of stacks (which also occurs slowly at room temperature) has the disadvantage of the capping reaction (tricarbahexaboranyl formation) and therefore prevents the oligomers from growing to polymers. Therefore we have studied polycondensation reactions of tris(allyl)dinickel-(μ-2,3-dihydro-1,3-diborolyl) complexes *78*, which on heating slowly to 200 °C *in vacuo* yield black polymeric products *79*, bis(allyl)nickel and hexadiene.[5,45] The material is readily attacked by oxygen at ambient temperature. It does not dissolve in toluene, tetrahydrofuran or methylene chloride. A TGA study of three polymeric products with different substituents at the 1,3-diborolyl ring showed that on heating from 200 to 450 °C the polymers lose weight (almost linearly with increasing temperature). Above 450 °C the loss of mass is

reduced (Fig. 2, heating was carried out under an atmosphere of nitrogen, 10 °C/min, up to 600 °C). The absolute mass losses of three polymers (in the range 200–600 °C) amount to 26–27%.

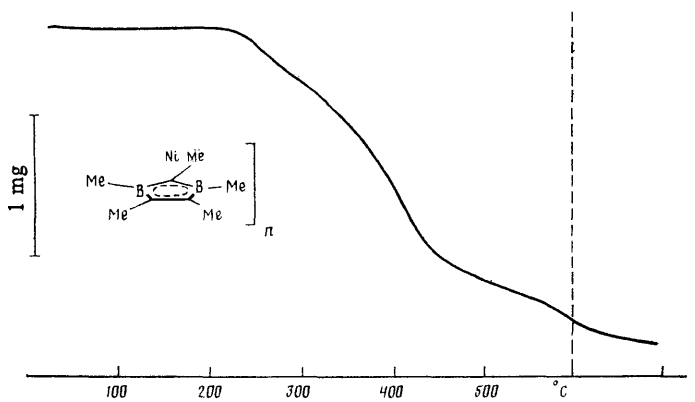
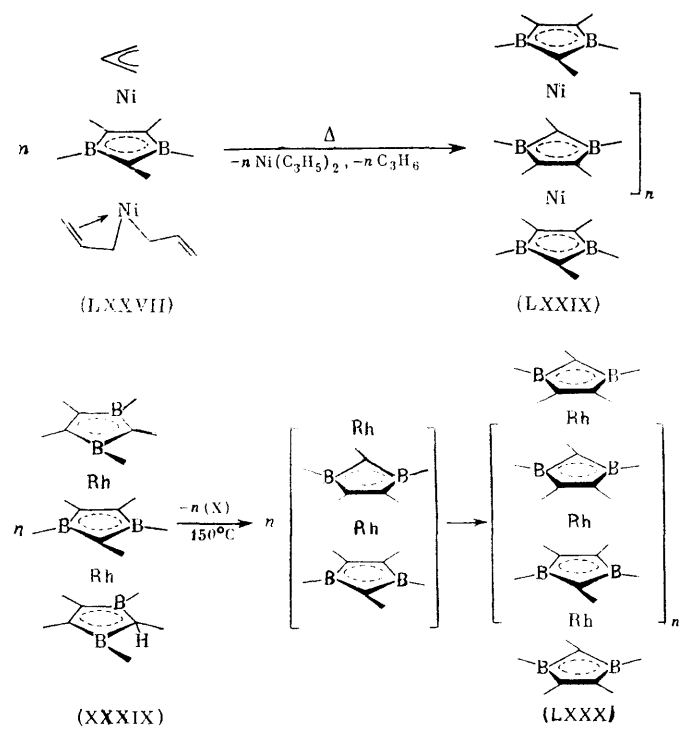


Figure 2. TGA study of compound (LXXIX).

The second polymer was formed by heating the red sandwich *33* to give the green rhodium triple-decker *39*. Elimination of the terminal 2,3-dihydro-1,3-diborole ligand *10* occurs, leaving the reactive double stack behind, which undergoes stacking to the black polymer. *12a* is less sensitive to oxygen than *79*.



The nickel and rhodium polydeckers are amoprhous and insoluble in organic solvents. Therefore a determination of the average molecular weight is not possible. EXAFS studies of *79* at 120, 300 and 340 K confirm the polydecker sandwich structure.[45,46] A 1:1 ratio of Ni to ligand and a Ni...Ni distance of 3.35 Å was observed. Preliminary results of an EXAFS study of the rhodium polymer *80* indicate a Rh...Rh distance of 3.6 Å.

Conductivity measurement on the nickel polymer gave results which are characteristic for a semiconductor (hopping mechanism). The four-probe measurements at room temperature yielded a conductivity of 10^{-2} Scm^{-1} which is similar to that of germanium. In contrast the rhodium polymer is an insulator, the conductivity is 10^{-10} Scm^{-1}. The high sensitivity toward oxygen results in a drop of the conductivity when the sample is exposed to air or doped with iodine. However, chemical alteration of the ligand and the switch to less electronic-rich metals (e.g. iron) may have stabilising effects.

Acknowledgements

I wish to thank my co-workers for their valuable contributions in developing this field of oligodecker and polydecker sandwich complexes. Our research reported here was generously supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the State of Baden-Württemberg and the BASF AG.

[Ed. of Translation: this paper was typeset from an English manuscript supplied by the Author.]

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Translated from *Uspekhi Khimii* **60** 1570–1595 (1991) U.D.C. 541.64:541.69

Equilibria in interpolyelectrolyte reactions and the phenomenon of molecular "recognition" in solutions of interpolyelectrolyte complexes

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ABSTRACT. The results of studies on the equilibria in interpolyelectrolyte reactions occurring in homogeneous aqueous solutions of linear synthetic polyelectrolytes bearing unlike charges and accompanied by the transfer of polyions are described. The influence of the chemical nature of low-molecular-weight ions and also of the chemical nature, linear charge density, and the degree of polymerisation of polyelectrolytes on equilibria in interpolyelectrolyte exchange and substitution is analysed. The phenomenon of the molecular "recognition" of one set of polyions by others is described and the factors leading to the selective binding of polyelectrolytes are indicated.

The bibliography includes 93 references.

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I. Introduction

The study of the reactions betweem chemically complementary linear macromolecules and also the structures and properties of the interpolymer complexes (IPC) formed constitute one of the most interesting and promising aspects of the development of the physical chemistry of macromolecular compounds. The knowledge of the main features of the occurrence of such interpolymer reactions (IPR) is essential for the creation and further development of a general theory of interpolymer reactions and interpolymer complexes. This refers fully also to interpolyelectrolyte reactions involving polyelectrolyte complexes (PEC). Cooperative interpolymer reactions are convenient models for the study of the processes in which biopolymers participate, for example, the self-assembly of complex structures such as viruses, for a deeper understanding of the mechanism of the self-regulation of enzyme systems, and for the elucidation of the principles of the action of artificial antigens and the creation of fundamentally new vaccines based on synthetic polyelectrolytes.

The study of the equilibria in interpolyelectrolyte reactions is also essential for the specific synthesis and the optimisation of the application of polyelectrolyte complexes in various branches of the national economy, for example as highly effective flocculants, stabilisers of colloidal dispersions, ion-exchange materials, membranes, binders, sorbents, structure-forming agents, physiologically active compounds, etc. This task is of particularly great current interest in connection with the prospects of using water-soluble polyelectrolyte complexes as carriers of biologically active substances, in particular enzymes, and their use in this state in biotechnology and medicine.

This review gives an account of the results of our systematic studies of the equilibria in interpolymer reactions accompanied by the transfer of polyions. The most important factors determining the direction of these reactions and the high selectivity of the interpolyelectrolyte interaction are specified and discussed.

II. Reactions involving interpolymer complexes

The reactions between chemically complementary polymers, i.e. polymers whose functional groups have an affinity for one another and whose geometrical structure does not hinder the formation of a fairly large number of intermolecular bonds per chain, have now been investigated in fair detail.[1–3] The reactive groups can be located both in the main chain and in the side groups and also on the surfaces of globular or other particles. The products of such reactions have come to be referred to as interpolymer complexes.

The nature of the forces by virtue of which interpolymer complexes exist can be various: hydrogen bonds [complexes of polycarboxylic acids with polyvinylpyrrolidinone, poly(vinyl alcohol), and poly(ethylene glycol);[4–9] complexes of biopolymers—for example, the native form of DNA [10]], electrostatic interactions (polyelectrolyte complexes[2,11,12]), van der Waals interactions [stereocomplexes of iso- and syndiotactic poly(methyl methacrylates)[13–15]], and donor–acceptor interactions (charge-transfer complexes[16]). Hydrophobic interactions may play a significant role in the stabilisation of interpolymer complexes in aqueous solutions.[17,18] The reason for the stability of such complexes is the cooperative nature of the interaction of the polymers with one another. The formation of interpolymer complexes is accompanied by an appreciable entropy gain compared with the analogous reactions involving low-molecular-weight reactants (for equal degrees of reaction) because after the formation of one bond between the units of the reacting macromolecules, the formation of all the subsequent bonds no longer entails the loss of additional translational degrees of freedom.

The physicochemical, mechanical, and other properties of interpolymer complexes differ significantly from those of their constituent components.[19] These polymeric compounds exist both in dilute solutions and in block and can be obtained either by mixing

the solutions of macromolecular reactants or as a result of matrix polymer reactions.[20–23]

One of the important properties of interpolymer complexes is their ability to enter into interpolymer exchange and substitution reactions in aqueous solutions. The essential feature of these reactions is the transfer of macromolecules from one interpolymer complex species to another. Interpolymer reactions involving interpolymer complexes stabilised by a system of hydrogen bonds were discovered and investigated systematically in the 1970s.[1,3,4–9,17–19,23–32]

The selectivity of the polymer–polymer interactions in systems containing more than two types of polymer molecules is also directly related to the interpolymer reactions. Such selectivity is a characteristic evolution-dependent property of the components of living organisms.[33,34] The selectivity of interactions is characteristic also of simpler polymer systems.[3,24,25]

III. Intermacromolecular reactions in solutions of polyelectrolytes bearing unlike charges

The formation of complexes between ionogenic polymers, manifested by a phase separation of the liquid–liquid type in their solutions, was discovered as early as the 1890s.[35] Such phase separation in solutions of polyelectrolytes, incorporating in their composition hydrophilic non-ionogenic groups for a low content of ionogenic groups, has been called complex coacervation.[36,37] According to modern ideas, coacervation is none other than the formation of polyelectrolyte complexes. The thermodynamic description of the phase separation process in the formation of a coacervate complex has been achieved, the composition and concentration of the complex have been predicted, and the influence of salts and various low-molecular-weight substances on its stability has been investigated.[38–41] The importance of the study of these questions arises from the fact that the coacervation phenomenon is used in various technological processes, for example in microencapsulation[42] or in the creation of medicinal preparations. Complex coacervation has been considered as a possible mechanism of the prebiological compartmentalisation, which constitutes an important stage in the prebiological evolution of organic compounds.[43] It therefore became necessary to investigate the interaction of such coacervate complexes with polyelectrolytes.[44–46]

The attempts to investigate complex formation in solutions of polyions bearing unlike charges with a high linear charge density were undertaken as early as the 1960s.[47–49] It was established that the precipitate of the polymeric complex formed as a result of the macromolecular reaction contains virtually equimolar amounts of polymeric components, while the precipitate itself is insoluble in any of the known individual solvents. Admittedly it is possible to dissolve it in ternary systems of the acetone–water–NaBr type, but this process takes place as a result of the decomposition of the complex — the polyelectrolytes in such systems hardly interact with one another. The combination of insolubility in familiar simple solvents with a high swellability in water, selectivity in the sorption of ions, and high biological compatibility have led to the application of such complexes as materials for medical-biological purposes.[50] However, the insolubility of stoichiometric complexes, formed by strong polyelectrolytes, as well as the insolubility of the coacervate complexes hinder the study of the structure of such species and also of the interpolymer reactions involving them.

The study of the cooperative interpolymer reactions in solutions of synthetic polyelectrolytes became possible after the discovery of non-stoichiometric polyelectrolyte complexes (NPEC) formed by polyions with a high charge density. Notable properties of non-stoichiometric polyelectrolyte complexes are their ability to dissolve in water and to participate in interpolyelectrolyte reactions occurring in homogeneous aqueous solutions. This factor gave rise to the possibility of using various physicochemical methods for the study of polymer solutions in order to investigate such reactions (light scattering, high-speed sedimentation in the analytical version, viscometry, etc.) and made it possible to avoid many complications which arise in the study of colloidal dispersions of insoluble stoichiometric polyelectrolyte complexes (SPEC).

IV. Water-soluble non-stoichiometric polyelectrolyte complexes

The procedure used to obtain water-soluble non-stoichiomdtric polyelectrolyte complexes was first described in detail by Tsuchida et al.[51] It consisted in mixing aqueous solutions of aromatic ionenes and sodium polystyrenesulphonate (NaPSS) in non-equivalent proportions. The complete dissolution of the polyelectrolyte complex is observed in the presence of a three-fold excess of the charged units of sodium polystyrenesulphonate relative to the charged units of ionene. After the introduction of excess amounts of ionene into a solution of sodium polystyrenesulphonate, an insoluble stoichiometric polyelectrolyte complex is obtained instead of the non-stoichiometric one, while the excess ionene remains in solution. These observations led the authors[51] to the conclusion that polymers of the ionene series have a special capacity for the formation of soluble non-stoichiometric polyelectrolyte complexes, which is in their view associated with the location of the charged groups in the ridge of the macromolecules. This conclusion was confirmed by the failure of the attempt to obtain water-soluble non-stoichiometric polyelectrolyte complexes from sodium polystyrenesulphonate and polytrimethylbenzylvinylammonium chloride, i.e. from a pair of electrolytes in which the ionogenic groups are located in the lateral substituents. It was soon shown for the reaction between sodium polyacrylate and 5,6-ionene bromide that aliphatic ionenes are also capable of forming water-soluble non-stoichiometric polyelectrolyte complexes.[52] This finding was also seemingly consistent with the hypothesis of the exceptional properties of ionenes, which, if one agreed with the conclusions of Gulyaeva et al.,[52] are due to the steric "accessibility" of the positively charged quaternary nitrogen atoms.

It was shown later that water-soluble non-stoichiometric polyelectrolyte complexes can be obtained, whilst maintaining certain conditions, from polyelectrolytes bearing unlike charges and having a wide variety of chemical structures.[53–55] It has been established[53] in relation to the sodium polymethacrylate (NaPMA)–poly-*N*-ethyl-4-vinylpyridinium bromide (PEVP) system that water-soluble non-stoichiometric polyelectrolyte complexes can be obtained for polyions each of which contains charged groups in their lateral substituents. In this case, i.e. when at least one weak polyelectrolyte (sodium polymethacrylate) is incorporated in the composition of the non-stoichiometric polyelectrolyte complex, there is a possibility of the formation of non-stoichiometric polyelectrolyte complexes under conditions where the interpolymer reaction is still far from completion. Such non-stoichiometric polyelectrolyte complexes, formed in acid media in the reaction of polymethacrylic acid

(PMAA) with poly-*N*-ethyl-4-vinylpyridinium bromide, are insoluble in water. The addition of alkali leads to the ionisation of the free carboxy-groups of the polymethacrylic acid, incorporated in the non-stoichiometric polyelectrolyte complex in excess, and to the dissolution of the non-stoichiometric polyelectrolyte complex.

In conformity with the terminology adopted nowadays,[2] the non-stoichiometric polyelectrolyte complex species contains a lyophilising polyelectrolyte (LPE) and the oppositely charged blocking polyelectrolyte (BPE). The units of the lyophilising polyelectrolyte are incorporated in the non-stoichiometric polyelectrolyte complex species in excess relative to the units of the blocking polyelectrolyte, i.e. the composition of the non-stoichiometric polyelectrolyte complex is φ = [BPE]/[LPE] and φ is less than unity. The fragments of the lyophilising polyelectrolyte chains and of the blocking polyelectrolyte chain, linked by interpolymer salt bonds, form relatively hydrophobic double-stranded sequences, which tend to segregate in aqueous solutions. The tails and loops of the lyophilising polyelectrolyte (see the left-hand side of Scheme 1) ensure the solubility of the non-stoichiometric polyelectrolyte species as a whole.

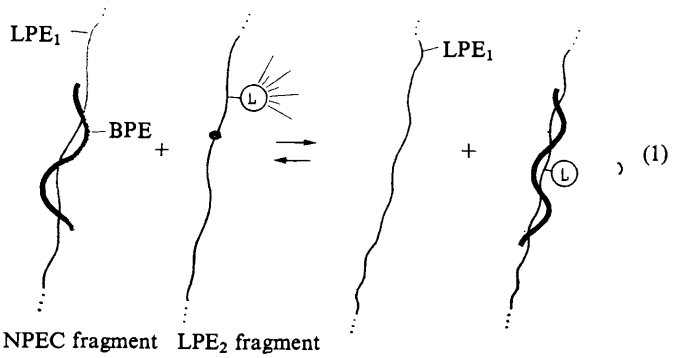
A simple and universal method of preparation of non-stoichiometric polyelectrolyte complexes consists in the direct mixing of aqueous solutions of polyelectrolytes bearing unlike charges taken in non-equivalent proportions in the pH range where they are both fully charged and in the presence of small amounts of a low-molecular-weight electrolyte.

Clearly in this synthetic method polymeric complexes of different composition, including complexes insoluble in water, should be formed as a consequence of inevitable local supersaturation. However, the final product—a water-soluble non-stoichiometric polyelectrolyte—is homogeneous as regards composition. The study of aqueous salt solutions of various non-stoichiometric polyelectrolytes by light scattering[55] showed that the macromolecular characteristics of the non-stoichiometric polyelectrolyte species are independent of the method of preparation, i.e. such complexes are equilibrium compounds. These findings show that interpolyelectrolyte reactions accompanied by the transfer of polyions do indeed take place in aqueous solutions.

Evidently, the observed[51] dissolution of the suspension of a stoichiometric polyelectrolyte complex incorporating sodium polystyrenesulphonate and ionene, which occurred after the addition of an excess of sodium polystyrenesulphonate, is also caused by the transfer of ionene chains from the stoichiometric polyelectrolyte complex species to the sodium polystyrenesulphonate chains introduced and by the appearance of new water-soluble non-stoichiometric polyelectrolyte species. However, the transfer of polyions, which occurs in this system also in salt-free media, is not due to structural-chemical characteristics[51] but is caused by the low linear charge density of ionene. The breakdown of the electrostatic complementarity of the interacting chains, as a result of both a change in the linear charge density and the introduction of low-molecular-weight ions capable of being bound specifically to the charged units of the macromolecules incorporated in the non-stoichiometric polyelectrolyte complex, accelerates the interpolyelectrolyte exchange.[56] In dilute salt-free solutions of electrostatically complementary polyelectrolytes, for example, in mixtures of sodium polymethacrylate and poly-*N*-ethyl-4-vinylpyridinium bromide,[57] the transfer of polyions hardly occurs, but, after the addition of low-molecular-weight electrolytes its rate increases sharply. The formation of soluble non-stoichiometric polyelectrolyte complexes is not observed in mixtures of salt-free solutions of electrostatically complementary polyions apparently for the same reason.[51]

V. Interpolyelectrolyte reactions

Cooperative interpolyelectrolyte reactions of various types, occurring in solutions of linear synthetic polyelectrolytes bearing unlike charges, are presented below in a generalised schematic form:



NPEC fragment LPE_2 fragment

where LPE_1 and LPE_2 are lyophilising polyelectrolytes competing for binding with the blocking polyelectrolyte. Predominantly the literature has reported interpolyelectrolyte reactions in solutions of non-stoichiometric polyelectrolyte complexes, where polyanions play the role of the lyophilising polyelectrolyte, while the blocking polyelectrolyte consists of polycations.

The transfer of the blocking polyelectrolyte to the lyophilising polyelectrolyte of the same chemical nature as that incorporated in the composition of the initial non-stoichiometric polyelectrolyte (in this case the initial and resulting non-stoichiometric polyelectrolytes are stabilised by interpolyelectrolyte salt bonds of the same kind) is referred to as the interpolyelectrolyte exchange reaction. Otherwise, if LPE_1 and LPE_2 have different chemical structures, then the transfer of the blocking polyelectrolyte to LPE_2 is called an interpolyelectrolyte substitution reaction. Apart from these two main types of interpolyelectrolyte reactions, the reaction involving the coupling of polyions bearing unlike charges has been investigated. The interpolyelectrolyte reactions described in this review take place in homogeneous aqueous solutions.

The occurrence of interpolyelectrolyte reactions involving a wide range of polyions has been established by various methods. The formation of products was detected on the sedimentograms for solutions of reaction mixtures in both the normal and scanning versions.[54,58–61] The molecular characteristics of the non-stoichiometric polyelectrolyte species—the products of the interpolyelectrolyte exchange—were measured by the light scattering method.[55,62–64] The interpolyelectrolyte substitution reaction was accompanied in individual instances by a change in viscosity or by the phase separation of the reaction mixtures, which made it possible to use viscometric and turbidimetric titration for their detection and investigation.[58,61] The rate of formation and decomposition of polymer–polymer complexes was recorded directly by the luminescence quenching method.[65] The advantages of this method include high sensitivity, which makes it possible to work with highly dilute polymer solutions, the possibility of studying opalescent solutions, the absence of a need for the introduction of a supporting low-molecular-weight electrolyte into the system, as happens, for example when light scattering and the high-speed sedimentation

method are used, and the possibility of continuous recording of rapid processes and hence the possibility of studying their kinetics.

The essential feature of the luminescence quenching method as applied to the study of interpolyelectrolyte reactions is as follows. A luminescent label L (see Scheme 1) is introduced into one of the polyelectrolytes, for example LPE_2. A blocking polyelectrolyte whose units are luminescence quenching agents, is selected. The formation (or decomposition) of the lyophilising polyelectrolyte LPE* carrying a luminescent label on reaction with the blocking polyelectrolyte is accompanied by a decrease (or increase) in the relative intensity of the luminescence of the solution I/I_0 (I_0 is the intensity of the luminescence of the LPE* solution). The degree of quenching is determined by the composition of the complex φ. By recording the change in I/I_0 in the reaction mixture containing all three polyelectrolytes, it is possible to follow the interpolyelectrolyte reaction.

The change in the quenching of the luminescence observed in the experiments constitutes direct evidence for the replacement of the LPE_1-BPE contacts by LPE_2-BPE contacts as a result of the interpolyelectrolyte reaction (1).

Salts of polycarboxylic acids — polymethacrylic and polyacrylic — bearing a luminescent label were used as the LPE*. The introduction of luminescent anthracene or pyrene groups into their chains was achieved by the interaction of fractions of the polyacids with anthryl- or pyrenyl-diazomethane by the method of Krakovyak et al.[66] In contrast to the copolymerisation method,[67] this procedure makes it possible to obtain specimens of labelled and unlabelled polyacids with the same molecular weight distribution (MWD). Polymeric amines played the role of blocking polycationic quenching agents. Polycations with pyridinium groups, which effectively quench luminescence, have been most widely used:[68] poly-*N*-ethyl-4-vinylpyridinium bromide together with its statistical copolymers and poly-4-vinylpyridine (PEVP-β).[69]

The question of the validity of the application of the luminescence quenching method in the study of interpolyelectrolyte reactions with selected polyelectrolytes is important. The kinetics of the quenching of luminescence in solutions of complexes of lyophilising polyelectrolytes bearing a luminescent label and polycationic quenching agents were investigated with the aid of a pulsed fluorimeter using single photon counting. The identity of the kinetics of the quenching of the luminescence of the NPEC* and the initial NaPMA* with the simultaneous decrease in luminescence intensity shows that the static quenching mechanism predominates in NPEC* solutions.[70]

This picture has been observed in solutions of various NPEC*, regardless of the composition of the latter, at different concentrations of the low-molecular-weight electrolytes introduced into the system and for different linear charge densities and degrees of polymerisation of the polyions. This means that in all the systems investigated the quenching mechanism is static, i.e. the lifetime of the contacts between the units of the polyions forming the NPEC* under the conditions investigated is significantly greater than the lifetime of the excited state of the label.[71]

VI. Equilibria in interpolyelectrolyte reactions

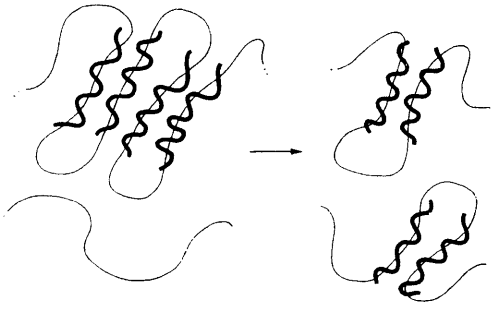
Before proceeding to the description of the results of the study of equilibria in interpolyelectrolyte exchange and substitution reactions, it is necessary to make the following comments. Low-molecular-weight electrolytes are known to exert an enormous influence on the behaviour and state of the polyelectrolyte complex species in solutions. At a high ionic strength of the solution, at which extensive decomposition of the cooperative system of interpolyelectrolyte salt bonds takes place, the uniform distribution of the blocking polyelectrolyte with respect to the lyophilising polyelectrolyte breaks down (the so called disproportionation is observed[63]), while in concentrated solutions of simple salts polyelectrolyte complexes are fully dissociated into the constituent polyions.[65] The results described below refer to interpolyelectrolyte reactions occurring under conditions far from such far-reaching action on polyelectrolyte complex species. In the dilute solutions of low-molecular-weight electrolytes investigated, the cooperative system of interpolyelectrolyte salt bonds in the initial polyelectrolyte complexes is still entirely stable as are those formed subsequently.

1. The equilibrium in an interpolyelectrolyte exchange reaction

(a) The uniform distribution of the blocking polyelectrolyte among the non-stoichiometric polyelectrolyte species

It follows from the results of the study of aqueous salt solutions of non-stoichiometric polyelectrolyte complexes by the light scattering method[55] that the molecular characteristic of the species of such complexes are independent of the method of synthesis, i.e. the non-stoichiometric polyelectrolyte complexes are equilibrium interpolymer compounds. The determination of the equilibrium distribution of the blocking polyelectrolyte among the polymeric complex species presupposes the transfer of blocking polyelectrolyte chains from one set of lyophilising polyelectrolyte chains to another, i.e. the occurrence of reaction (1) in the $LPE_1 = LPE_2$ version. We investigated the equilibrium in such an exchange reaction between a non-stoichiometric polyelectrolyte complex and a free lyophilising polyelectrolyte and also between non-stoichiometric polyelectrolyte complexes of different composition.

We shall consider initially the case where the degrees of polymerisation of the lyophilising and blocking polyelectrolytes $\overline{P}$ satisfy the condition $\overline{P}_{LPE} > \overline{P}_{BPE}$ and each non-stoichiometric polyelectrolyte complex species incorporates a considerable number of relatively short blocking polyelectrolyte chains. At the present time, this is the situation most frequently encountered in practice. The properties of such non-stoichiometric polyelectrolytes have been studied in detail and such complexes have in fact been used for the solution of many important problems, in particular for the creation of reversibly soluble immobilised enzymes.[72] The results of sedimentation studies[59] have shown that the transfer of blocking polyelectrolyte macromolecules from the non-stoichiometric polyelectrolyte complex to the free polyions of the lyophilising polyelectrolyte does indeed occur and results in the formation of a new non-stoichiometric polyelectrolyte whose composition is identical with that of the mixture of polyelectrolytes [reaction (2)]:



(2)

It follows from the comparison of the sedimentograms that in the solution of a mixture of a non-stoichiometric polyelectrolyte and a lyophilising polyelectrolyte a single component NPEC* is observed, its sedimentation coefficient not differing from that of a specially prepared non-stoichiometric polyelectrolyte complex having the same composition as the reaction mixture. The areas of the peaks on both sedimentograms also agree. The latter fact demonstrates convincingly that the interpolyelectrolyte exchange reaction (2) reaches completion during the experiment.

The results of the study of the same system by the luminescence quenching method using labelled NaPMA* (containing on average one anthrylmethyl methacrylate unit per 900 chain units) agree with the above conclusion. The relative luminescence intensity of aqueous salt solution of a mixture of NPEC* (NaPMA*–PEVP) having the composition $\varphi = 0.45$ and NaPMA with [NaPMA*] = [NaPMA] agrees with the value of I/I_0 for the solution of a non-stoichiometric polyelectrolyte (NaPMA*–PEVP) having the composition $\varphi = 0.23$ and incorporating half the amount of the polycationic quenching agent. The addition of an aqueous solution of the labelled NaPMA* to the solution of the non-stoichiometric polyelectrolyte complex (NaPMA–PEVP) leads to the same result.

Similar phenomena have been observed also on mixing solutions of non-stoichiometric polyelectrolyte complexes formed by a pair of the same polyelectrolytes but in different proportions.[59]

Thus interpolyelectrolyte exchange reactions lead to the appearance of non-stoichiometric polyelectrolyte complexes characterised by a uniform distribution of the blocking polyelectrolyte chains among the non-stoichiometric polyelectrolyte complex species, whose composition is identical to that of the mixture of polyelectrolytes formed ultimately. This has been explained[59] by the fact that, for a constant total number of interchain salt bonds and with retention of solubility, a higher entropy corresponds to a uniform distribution of the blocking polyelectrolyte among the non-stoichiometric polyelectrolyte complex species, i.e. the driving force of the transfer of polyions is the increase in the entropy of the systems. This constitutes a significant difference between the reactions investigated and those between linear polyelectrolytes and globular proteins[73–75] and also the reactions between polymethacrylic acid and poly(ethylene glycol) or poly-*N*-vinylpyrrolidinone[76] in which disproportionation is clearly manifested, i.e. there is a significantly non-uniform distribution of one of the macromolecular components among the species of the corresponding polymeric complexes.

The important question of the state and behaviour of the products of the interpolymer reactions—non-stoichiometric polyelectrolyte complexes whose composition is identical with that of the reaction mixture—remains obscure in the study of the exchange reaction. In particular, it is not clear whether the exchange of chains of the blocking polyelectrolyte between the non-stoichiometric polyelectrolyte complex species of the same composition, which are illustrated on the right-hand side of scheme (2), does occur. Evidently, this problem cannot be solved solely by studying the system examined above in the $\overline{P}_{LPE} \gg \overline{P}_{BPE}$ version. Even if such mutual exchange of the blocking polyelectrolyte chains between the non-stoichiometric polyelectrolyte complex species does occur, it is not accompanied by a change in the properties of the species themselves; in particular, it should not lead to an alteration of the luminescence intensity because it is not accompanied by a change in the number of label–quenching agent contacts.

However, it was found that such reactions are characteristic of non-stoichiometric polyelectrolyte complexes formed by pairs of polyelectrolytes with not unduly different degrees of polymerisation of the lyophilising and blocking polyelectrolytes. The ratio of the degrees of polymerisation of the lyophilising and blocking polyelectrolytes can be specified in such a way that it coincides with the ratio of the numbers of units [BPE]/[LPE] incorporated in the non-stoichiometric polyelectrolyte complex, i.e. $\overline{P}_{BPE}/\overline{P}_{LPE}$ = [BPE]/[LPE]. In a non-stoichiometric polyelectrolyte complex of this composition, there is on average only one blocking polyelectrolyte chain per lyophilising polyelectrolyte chain. If a free lyophilising polyelectrolyte is added to the solution of the given non-stoichiometric polyelectrolyte, then the "migration" of the blocking polyelectrolyte chains from the non-stoichiometric polyelectrolyte complex species to the chains introduced will naturally not be accompanied by a change in composition and such a process would correspond entirely to the conditions formulated above for the reaction involving the mutual exchange of blocking polyelectrolyte chains between the non-stoichiometric polyelectrolyte complex species.

We investigated the behaviour of the system obtained on mixing aqueous solutions of a free lyophilising polyelectrolyte and a non-stoichiometric polyelectrolyte complex formed by sodium polymethacrylate ($\overline{P}_{LPE} = 3000$) and poly-*N*-ethyl-4-vinylpyridinium bromide ($\overline{P}_{BPE} = 1300$) for which $\overline{P}_{BPE}/\overline{P}_{LPE} = 0.4$.[77] It follows from the results of high-speed sedimentation that free lyophilising polyelectrolyte polyions and non-stoichiometric polyelectrolyte complex species, whose composition is identical with that of the initial non-stoichiometric polyelectrolyte complex, do indeed coexist in the mixtures obtained.

The "migration" of the blocking polyelectrolyte chains derived from the species of the initial non-stoichiometric polyelectrolyte to the chain of the free lyophilising polyelectrolyte has been established also for the above system. The luminescent-labelled NaPMA* chain with the same degree of polymerisation as the sodium polymethyacrylate incorporated in the initial non-stoichiometric polyelectrolyte was used as the free lyophilising polyelectrolyte. The results of the study of this system by the high-speed sedimentation method indicate unambiguously the occurrence of reaction (2). Scanning at the wavelength corresponding to the absorption by the luminescent (anthryl) label make it possible to detect the LPE* in both fractions. The results presented demonstrate unambiguously that the interpolyelectrolyte exchange is completed before the end of the experiment, the latter requiring 3 h. It might be thought that similar exchange reactions occur also in solutions of a non-stoichiometric polyelectrolyte complex whose species contain more than one blocking polyelectrolyte chain; an example may be provided by the mutual exchange reactions between non-stoichiometric polyelectrolyte complex species illustrated on the right-hand side of scheme (2).

A similar picture has been observed also in mixtures of non-stoichiometric polyelectrolyte complexes formed by the same lyophilising high-molecular-weight sodium polymethacrylate and different blocking polycations—5,6-ionene bromide and poly-*N*-ethyl-4-vinylpyridinium bromide.[78] High speed sedimentation data show that a solution of a mixture of these two non-stoichiometric polyelectrolyte complexes contains one component which has a rate of sedimentation intermediate between the rates of sedimentation of the initial non-stoichiometric polyelectrolyte complexes. The occurrence of interpolyelectrolyte exchange is also confirmed by the behaviour of the mixture of non-stoichiometric polyelectrolyte complexes in solutions of low-molecular-weight electrolytes. The curve for the turbidimetric titration of a mixture of

non-stoichiometric polyelectrolytes does not coincide with the titration curves for either non-stoichiometric polyelectrolyte complex and occupies an intermediate position on the ionic strength scale for the solution. There is a single distinct jump on the turbidimetric titration curve. Mixtures of such polyelectrolyte complexes having other compositions behave similarly.

Thus the species of different non-stoichiometric polyelectrolyte complexes exchange in solution the blocking polyelectrolyte chains incorporated in their composition and the equilibrium in the exchange reaction shifts under the experimental conditions, i.e. at pH 7.5 and [NaCl] = 0.06 M, towards the formation of the final reaction product—a new soluble non-stoichiometric polyelectrolyte complex which incorporates both BPE_1 and BPE_2.

The variation of the degree of exchange can be followed by the luminescence quenching method because the introduction of ionene into the test solutions is accompanied by only a slight decrease in the luminescence intensity, whereas poly-*N*-ethyl-4-vinylpyridinium bromide effectively quenches the labels on the polyanion in the NPEC* species. The relative luminescence intensities I/I_0 of a solution of the mixture of non-stoichiometric polyelectrolyte complexes, which does not coincide with the values of I/I_0 for solutions of the individual non-stoichiometric polyelectrolyte complexes, occupies an intermediate position on the NaCl concentration scale, which agrees with the formation of mixed non-stoichiometric polyelectrolyte complexes in which some of the LPE* units are blocked by ionene, which is not a luminescence quenching agent.

The results show that the mutual exchange reactions investigated take place continuously, i.e. that the species of the non-stoichiometric polyelectrolyte complexes whose composition coincides with that of the reaction mixture exchange continuously the blocking polyelectrolyte chains with one another, the rate of exchange being controlled by the ionic strength of the solution. The reactions observed are none other than a form of thermal motion in polyelectrolyte complexes which are the products of reversible ionic reactions between polyelectrolytes.

(b) The influence of the degree of polymerisation of the lyophilising polyelectrolyte on the equilibrium in the interpolyelectrolyte exchange reaction

The influence of the length of the lyophilising polyelectrolyte chains on the equilibrium in the interpolyelectrolyte exchange reaction was investigated in solutions of non-stoichiometric polyelectrolyte complexes formed by sodium polymethacrylate and poly-*N*-ethyl-4-vinylpyridinium bromide fractions with different molecular weights.[79] We shall consider the results obtained when the three most characteristic conditions are fulfilled:

$$\overline{P}_{LPE} \gg \overline{P}_{BPE}, \quad \overline{P}_{LPE} \simeq P_{BPE}, \quad \text{and } \overline{P}_{LPE} \ll \overline{P}_{BPE}.$$

Sodium polymethacrylate (NaPMA*) specimens with $\overline{P}_W$ = 4100 and 500 and $\overline{P}_n$ = 50, which will henceforth be referred to as long, moderately long, and short polyanions respectively, and the poly-*N*-ethyl-4-vinylpyridinium bromide specimen with $\overline{P}_W$ = 500 satisfy these conditions. It is important to note that the labelled polymers NaPMA* were obtained by the reaction of chemically activated derivatives of the labels with sodium polymethacrylate fractions. This eliminates the question of the inconsistency between the $\overline{M}_W$ and the MWD for the labelled and unlabelled specimens.

The influence of the chain length of the lyophilising polyelectrolyte on the equilibrium in the exchange reaction

$$\text{NPEC(NaPMA}-\text{PEVP)} + \text{NaPMA*} \Leftrightarrow \text{NPEC*(NaPMA*}-\text{PEVP)} + \text{NaPMA}, \quad (3)$$

is manifested particularly strikingly in systems containing lyophilising polyelectrolyte chains of different length. This follows from the results of the study by the luminescence quenching method of mixtures of polyions, prepared in different ways and containing long and short polyanions (Fig. 1). As can be seen from Figs. 2 and 3, reaction (3) does not occur in the absence of a low-molecular-weight electrolyte. The introduction of even insignificant amounts of a simple salt leads to the complete displacement of the short chains into the solution from their complexes with poly-*N*-ethyl-4-vinylpyridinium bromide (curves *2* and *3*). The reverse reaction, i.e. the insertion of short chains in the non-stoichiometric polyelectrolyte species with long lyophilising polyelectrolytes, does not occur under these conditions (curve *1*).

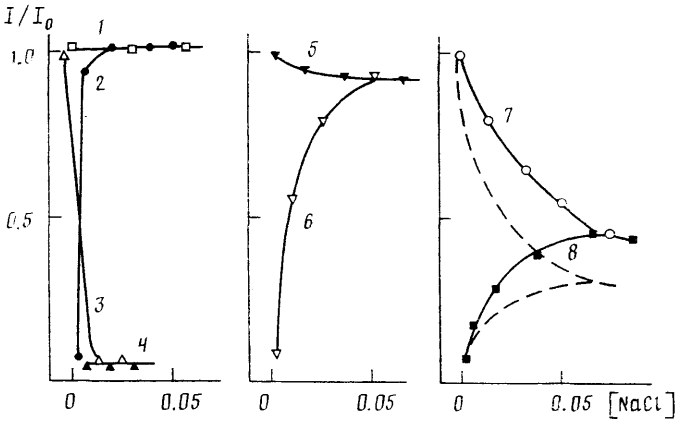


Figure 1. Dependence of I/I_0 on the NaCl concentration in mixtures of solutions of polyions containing polyanions polymerised to different extents: *1*, NPEC(P = 4100) and NaPMA*(P = 50); *2*, NPEC*(P = 50) and NaPMA (P = 4100); *3*, NPEC(P = 50) and NaPMA*(P = 4100); *4*, NPEC*(P = 4100); *5*, NPEC(P = 500) and NaPMA*(P = 50); *6*, NPEC*(P = 500) and NaPMA(P = 500); *7*, NPEC(P = 4100) and NaPMA*(P = 500); *8*, NPEC*(P = 500) and NaPMA(P = 4100).[79]

This result shows that in systems containing lyophilising polyelectrolytes of the same chemical nature, interpolyelectrolyte substitution of one set of chains by another can in essence occur. The displacement of short chains into the solution is accompanied by an entropy gain as a consequence of the liberation of a large number of short lyophilising polyelectrolyte chains previously immobilised in the NPEC or NPEC* species, which is apparently the reason for the virtual completion of reaction (3).

Very similar results were obtained in the study of mixtures containing moderately long and short polyanions (Fig. 1, curves *5* and *6*). In the absence of a salt, reaction (3) does not occur in this styrene either, while in aqueous salt solutions the displacement of short chains into the solution is observed. However, the differences

between the chain lengths and hence also the amounts of the chains in the non-stoichiometric polyelectrolyte species are insufficient to ensure such a high entropy gain when short lyophilising polyelectrolyte chains are displaced from the non-stoichiometric polyelectrolyte into the solution, so that a proportion of them, albeit extremely small, remains bound in the initial non-stoichiometric polyelectrolyte complex; $I/I_0 \neq 1$ at [NaCl] = 0.03 M.

This trend is manifested distinctly also in systems containing long and moderately long polyanions (Fig. 1, curves *7* and *8*). On attainment of equlibrium, which occurs at [NaCl] = 0.05 M, an appreciable proportion of the moderately long lyophilising polyelectrolyte chains remain in the non-stoichiometric polyelectrolyte complex. However, in this case too an appreciable amount of them pass into the solution. This is indicated by a higher value of I/I_0 corresponding to the state of equilibrium at [NaCl] = 0.05 M compared with I/I_0 for the NaPMA ($\overline{P}_W$ = 500)–PEVP–NaPMA* ($\overline{P}_W$ = 500) mixture at equilibrium (dashed curves).

Thus the ratio of the chain lengths of the competing lyophilising polyelectrolytes determines the direction of the interpolyelectrolyte exchange reaction in aqueous salt solutions.

(c) The influence of groups capable of stabilising additionally the polyelectrolyte complex on the exchange reaction equilibrium

It has been shown[80] that the presence in the polyanion of a small number of groups (one per hundreds of chain units) capable of interacting specifically with the polycation units in the non-stoichiometric polyelectrolyte complex formed can ensure the "recognition" by the polycation of such modified chains among unmodified polyanions.

Aqueous salt solutions of the non-stoichiometric polyelectrolyte complex formed by sodium polymethacrylate having $\overline{P}_W$ = 4100 and poly-*N*-ethyl-4-vinylpyridinium bromide having $\overline{P}_W$ = 600 were studied. Modified sodium polymethacrylate (NaPMA*) containing anthrylmethylmethacrylate (Ant-NA) groups or pyrenylmethyl methacrylate (Pyr-MA) units was used as the competing polyanion. The presence of the luminescent Ant-MA or Pyr-MA groups in the NaPMA* chains makes it possible to record the interpolyelectrolyte reaction by the luminescence quenching method:

$$\text{NPEC(NaPMA – PEVP)} + \text{NaPMA*} \overset{K_e}{\Leftrightarrow} \Leftrightarrow \text{NPEC*(NaPMA* – PEVP)} + \text{NaPMA}. \quad (4)$$

The experiments were carried out as follows. A solution of the non-stoichiometric polyelectrolyte complex (NaPMA–PEVP), in which there is on average one polycation chain per polyanion chain, was prepared initially. The non-stoichiometric polyelectrolyte complex having the composition

$$\varphi = [\text{PEVP}]/[\text{NaPMA}] = \overline{P}_{\text{PEVP}}/\overline{P}_{\text{NaPMA}} = 0.147$$

corresponds to this condition. An aqueous salt solution of NaPMA was then added to the resulting solution so that the amounts of NaPMA and NaPMA* in the reaction mixture were identical and the time variation of I was recorded. The degree of completion of the reaction was judged from the value of I/I_0, where I_0 is the intensity of the luminescence of the aqueous solutions of NaPMA* at the same concentration as in the initial mixture. In the study of the reverse reaction, a solution of a labelled non-stoichiometric polyelectrolyte complex NPEC* (NaPMA*–PEVP), having the composition φ = 0.147, was prepared by a similar procedure and was treated with an aqueous salt solution of sodium polymethacrylate.

It was found that that presence in the NaPMA* chain on average of only three Pyr-MA units per 4100 methacrylate (MA) units already leads to the predominant binding of the polycation to the labelled polyanion, i.e. to an appreciable shift of the equilibrium in the exchange reaction (4) to the right. The equilibrium value of I/I_0, obtained in both the forward (Fig. 2, curve *1*) and reverse (curve *2*) reactions, is lower than expected on the assumption of a uniform distribution of poly-*N*-ethyl-4-vinylpyridinium bromide between the labelled and unlabelled polyanions (the dashed arrow in Fig. 2 indicates the value of I/I_0 for the NPEC* having the composition $\varphi = 0.5 \times 0.147 = 0.073$). With increase in the average number of Pyr-Ma units to 12 per 4100 MA units (Fig. 2, curves *3* and *4*), a virtually complete selectivity of the binding is attained: the vast majority of the sodium polymethacrylate polyanions in the non-stoichiometric polyelectrolyte complex are substituted by the NaPMA* polyanions and I/I_0 at equilibrium is identical with I/I_0 for the NPEC* solution having the composition φ = 0.147 (Fig. 2, continuous arrow).

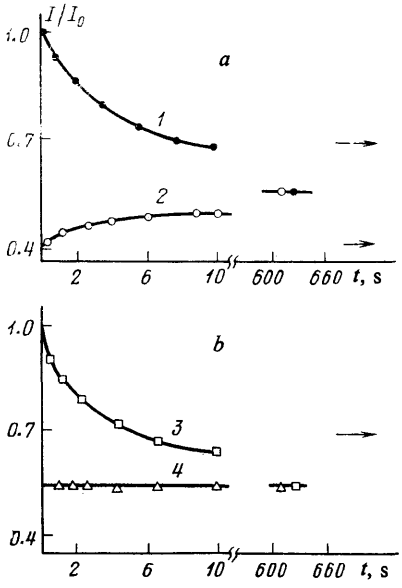


Figure 2. Kinetic curves for reaction (*4*); *1* and *3*, mixtures of the non-stoichiometric polyelectrolyte complexes NaPMA–PEVP and NaPMA*; *2* and *4*, mixtures of labelled non-stoichiometric polyelectrolyte complexes (NPEC*) NaPMA*–PEVP and NaPMA; [NaPMA*] = [NaPMA] = 1.3×10^{-4} M (curves *1* and *2*) and 3.2×10^{-5} M (curves *3* and *4*); [NaCl] = 0.08 M.[80]

The equilibrium constant of reaction (4) under the experimental conditions, involving the transfer of one polycation chain, i.e. [NaPMA] = [NaPMA*], is given by

$$K_e = X^2/(1-X)^2, \quad (5)$$

where X is the fraction of the NPEC* (NaPMA*–PEVP) species formed as a result of reaction (4). If preferential binding of the polycation by the modified polyanion is observed (Fig. 2), X varies in the range $0.5 < X < 1$, which corresponds to the variation of the

equilibrium constant in the range $1 < K_e < \infty$. In the range $0.5 < X < 1$ in which we are interested, the relative luminescence intensity I/I_0 decreases linearly with increase in X. This makes it possible to determine X experimentally using the equation

$$X=0.5+0.5(I_l-I)/(I_l-I_\infty), \quad (6)$$

where I_l and I_∞ are the intensities of the luminescence of solutions of poly-*N*-ethyl-4-vinylpyridinium bromide and NaPMA* having the composition $\varphi = 0.073$ and $\varphi = 0.147$ respectively. Thus the determination of the equilibrium constant of reaction (4) reduces to the measurement of the quantities I, I_l, and I_∞, the calculation of X by Eqn. (6), and the calculation of K_e by Eqn. (5).

The equilibrium constants K_e of the interpolyelectrolyte reaction (4) involving NaPMA* with $\overline{P}_W = 4100$, differing in the number of Ant-MA and Pyr-MA units, are presented in Table 1.

Table 1. The quantities $\overline{M}_k$ and K_e for the exchange reaction (4) involving NaPMA* modified by different numbers of pyrenyl or anthryl groups {$\overline{P}_{NaPMA} = \overline{P}_{NaPMA^*} = 4100$, $\overline{P}_{PEVP} = 600$, [NaCl] = 0.08 M}.

No. of groups in NaPMA*	5	9	3	12
Chemical nature of groups	Ant-MA	Ant-MA	Pyr-MA	Pyr-MA
$\overline{M}_k$	2.5	3.5	1.5	5.5
K_e*	≃1	10	10	>200

* The accuracy of the determination of K_e is to within 10–15%.

The average number of labelled units $\overline{M}_k$ in contact with the units of the polycationic quenching agent in the NPEC* formed was calculated from the experimental values of I/I_0 for solutions of NPEC* having the composition $\varphi = 0.147$ by the formula

$$\overline{M}_k=\overline{M}(1-I/I_0), \quad (7)$$

where $\overline{M}$ is the average number of labelled units in the NaPMA* chain and the expression in brackets corresponds to the fraction of quenched labels.

Table 1 shows that the experimental values of $\overline{M}_k$ in the NPEC* with the composition $\varphi = 0.14$ are greater than the calculated values $\overline{M}_k = \overline{M}\varphi$, i.e. the average number of labels in the NaPMA* chains per contour length of the poly-*N*-ethyl-4-vinylpyridinium bromide chains bound electrostatically to them. It follows also from Table 1 that the equilibrium constant of reaction (4) is determined by the number of labels in the polyanion chain and their chemical nature. For example, the presence of five anthryl groups per 4100 MA units in the NaPMA* chains hardly disturbs the uniform distribution of poly-*N*-ethyl-4-vinylpyridinium bromide among all the polyanions present in solution ($K_e \simeq 1$) and does not therefore introduce perturbations into the occurrence of the corresponding interpolyelectrolyte reactions.[57,60,65,77] An increase in the number of anthryl labels to nine already displaces the equilibrium of reaction (4) appreciably to the right. Other conditions being equal, the pyrenyl labels influence K_e much more strongly than the anthryl labels. The "recognition" of the labelled polyanions by the polycations is probably determined by the decrease in free energy which is attained after the immersion of hydrophobic anthryl (pyrenyl) groups in the hydrophobic clusters formed by sections of the oppositely charged chains of the polymeric complex bound to one another. The free energy changes on transfer of anthracene and pyrene from octanol to water are respectively 24.9 and 29.0 kJ mol^{-1}.[82] This difference is apparently responsible for the better "recognition" of the pyrenyl groups compared with the anthryl groups. The stabilisation of the NPEC* (NaPMA*–PEVP) probably promotes also the formation of charge-transfer complexes (CTC) between the anthryl or pyrenyl groups (donors) and the pyridinium units (acceptors). Such charge-transfer complexes can be detected directly in the absorption spectra of the corresponding solutions.[81]

The higher experimental values of $\overline{M}_k$ compared with the calculated values can probably be accounted for by the same factors.

Thus a small number of molecular "anchors" with energies of the order of several kT is apparently sufficient to ensure a decided advantage for the labelled polyanion, whose length is greater by a factor of several hundreds than the length of the "anchor", in the competition with its unlabelled analogue for the binding of the polycation. In our view, this result is of fundamental importance for the understanding of the mechanisms of the selective biological action *in vivo* of functionalised polyelectrolytes (in particular, artificial immunogens—conjugates of high-molecular-weight linear polyions with a small number of antigens or antigen determinants[83]).

(d) The influence of the linear charge density of the blocking polyelectrolytes on the equilibrium in the interpolyelectrolyte exchange reaction

The influence of the linear charge density of the blocking polyelectrolyte on the equilibrium in the exchange reaction was investigated in solutions of non-stoichiometric polyelectrolyte complexes formed by sodium polymethacrylate and partly quaternised poly-4-vinylpyridines (PEVP-β).[84] The PEVP-β specimens, obtained by alkylating poly-4-vinylpyridine with ethyl bromide, were alkylated to different extents, the degree of alkylation being $\beta(\%) = 100n/(n + m)$, where n and m are respectively the mole fractions of the alkylated and non-alkylated units.

Under the experimental conditions, the non-alkylated units, distributed statistically along the polycation chain, are uncharged. The molar extinction coefficient at $\lambda = 257$ nm is $\varepsilon = 1800$ litre mol^{-1} cm^{-1} for the above pyridine units and $\varepsilon = 3600$ litre mol^{-1} cm^{-1} for the charged pyridinium units. Comparison of the UV spectra of solutions of the non-stoichiometric polyelectrolyte complex and PEVP-β at identical concentrations showed that the optical densities at $\lambda = 257$ nm are identical, i.e. under experimental conditions at pH 10 the charge on the PEVP-β chains is determined solely by the alkylated units, while the pyridine units of PEVP-β, incorporated in the non-stoichiometric polyelectrolyte complex species, disturb the continuity of the sequence of the charged quaternised unit. The study of the alkylation of poly-4-vinylpyridine by ethyl bromide showed that the reaction proceeds without the "neighbour effect", all three alkylation rate constants, calculated from the kinetic curve, being virtually identical.† This means that,

† The constants were calculated by L B Stroganov and A N Olonovskii—members of the Department of Macromolecular Compounds in the Faculty of Chemistry of Moscow State University.

up to the attainment of high degrees of quaternisation, the non-alkylated units are arranged along the chain in accordance with the statistical law.

The equilibrium constant of the exchange reaction

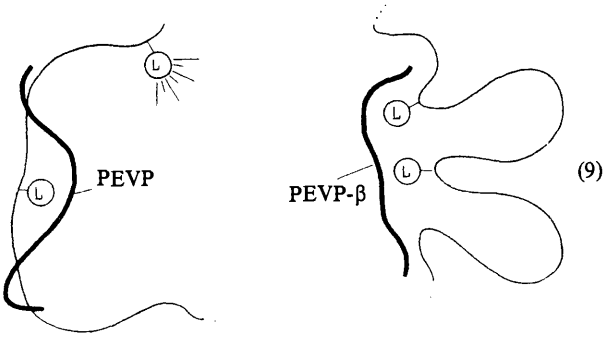
$$\text{NPEC(NaPMA} - \text{PEVP} - \beta) + \text{NaPMA}^* \overset{K_e}{\Leftrightarrow}$$
$$\Leftrightarrow \text{NPEC}^*(\text{NaPMA}^* - \text{PEVP} - \beta) + \text{NaPMA} \quad (8)$$

increases with decrease in the degree of quaternisation β. This follows from the results of the study of solutions of mixtures of polyelectrolyte by the luminescence quenching method[84] (Table 2). The quantities K_e were determined as described above for non-stoichiometric polyelectrolyte complexes incorporating the exhaustively alkylated poly-*N*-ethyl-4-vinylpyridinium bromide.

The sharp increase in K_e with decrease in the degree of alkylation of the polycation is accompanied by an increase in the number of labels covered by a single chain of the blocking polyelectrolyte in the NPEC*, which follows from the increase in $1 - I/I_0$ with decrease in β (Table 2).

An increase in the number of labels quenched by the blocking polyelectrolyte chain is accompanied by a decrease in the size of the non-stoichiometric polyelectrolyte complex species. This follows from the measurements by the quasi-elastic light scattering method of the effective sizes of the non-stoichiometric polyelectrolyte complex species incorporating PEVP-β alkylated to different extents.[84] It is important to note that the values of $\overline{M}_W$ measured by the light scattering method for all the test specimens proved to be constant and amounted to 445 000, which indicates the absence of associated species in the solutions.

Thus the increase in the number of defects in the structure of the non-stoichiometric polyelectrolyte complex with decrease in β, caused by the disturbance of the continuity of the sequence of quaternised blocking polyelectrolyte units, promotes the compaction of the non-stoichiometric polyelectrolyte complex and an increase in the number of labels covered by the polycationic quenching agent [Scheme (9)]. The appreciable decrease in the free energy of the system when an additional number of labels are immersed in the hydrophobic region of the NPEC* species is in fact the cause of the increase in K_e for reaction (8) with decrease in the degree of alkylation of the polycation.



(9)

Similar conformational transformations of the non-stoichiometric polyelectrolyte species have been observed on rupture of a proportion of the interpolymer salt linkages, stabilising the non-stoichiometric polyelectrolyte complex, under the influence of the low-molecular-weight electrolyte.[85] According to the authors,[85] the driving force of this process is the increase in the combinatorial entropy caused by the contribution of structures of the type illustrated on the right-hand side of Scheme (9). Evidently, the endeavour of the labels located on the LPE* to become immersed in the hydrophobic regions of the NPEC* species should promote still further such compaction. This is also indicated by the sharp decrease in the luminescence intensity of NPEC* solution when low-molecular-weight electrolytes are introduced into them.[71]

Table 2. The values of $1 - I/I_0$ and K_e for the exchange reaction (8) involving PEVP-β for different degrees of alkylation β:[84] $\overline{P}_{NaPMA} = \overline{P}_{NaPMA^*} = 4400$, $\overline{P}_{PEVP} = 500$, [NaCl] = 0.10 M; pH 10; in NaPMA* there is on average one Pyr-MA unit per 1400 methacrylate (MA) units.

β, %	40	55	80	90
$1-I/I_0$	0.74	0.78	0.62	0.59
K_e*	>200	160	60	7

* The accuracy of the determination of K_e is to within 10–15%.

Thus non-stoichiometric polyelectrolyte complexes should be regarded as compounds which are extremely resistant to the disrupting effect of low-molecular-weight electrolytes and which are capable of exchanging their constituent polyions in aqueous salt media. Such exchange results in a uniform distribution of relatively short blocking polyelectrolyte chains among all the long lyophilising polyelectrolyte chains present in the solution. However, highly selective interaction of the polyions with the oppositely charged chains can be achieved, for example, by changing the degree of polymerisation or by slight chemical modification of the polyions. Thus in mixtures of relatively long and short sodium polymethacrylate chains the poly-*N*-ethyl-4-vinylpyridinium polycation is bound preferentially to the long sodium polymethacrylate chains. When the degrees of polymerisation of sodium polymethacrylate are significantly different, this competing interaction can lead to the complete displacement of short chains from the polyelectrolyte complex by long sodium polymethacrylate chains. The cation selects from the mixture of modified and unmodified polyanions macromolecules containing groups capable of additional stabilisation of the polyelectrolyte complex and binds them preferentially. This is manifested even in the presence of only one hydrophobic pyrene group per hundreds of sodium polymethacrylate chain units, whereupon such labelled chains are selected for incorporation in the polyelectrolyte complex almost without error.

2. Equilibrium in the interpolyelectrolyte substitution reaction

The previous section gave an account of the principal results of studies on equilibria in interpolyelectrolyte exchange reactions where the transfer of polyions is accompanied by the disruption and formation of interpolyelectrolyte contacts of the same type. This section will deal with the equilibria in interpolyelectrolyte substitution reactions where lyophilising polyelectrolytes of different chemical nature participate as competing polyanions. The effect involving the molecular "recognition" of polyions of a definite kind proves as a rule to be very pronounced in such systems. This effect has a bearing on the selective biological action of polyelectrolytes *in vivo* and can be used for the creation of systems for the specific transport of biologically active substances. Therefore, before

proceeding to the discussion of the experimental results, we shall consider briefly the available literature data on the selectivity of interpolymer substitution reactions.

(a) Molecular selectivity of interpolymer substitution reactions

The principal feature of interpolymer reactions is their cooperative character. The sharp increase in the stability constant of the polymeric complex as a function of the degree of polymerisation of the reacting macromolecules may serve as proof of this. It is described by the equation[29,30]

$$K_\nu = K_1^\nu = \exp(-\nu\Delta G_1^\circ/RT), \quad (10)$$

where K_ν is the equilibrium constant for the binding of the oligomer incorporating ν chains of the long chemically complementary chain-matrix and $K_1 = \exp(-\Delta G_1^\circ/RT)$ is the effective constant for the binding of the oligomer unit to the matrix unit. The term "oligomer" is conventional and indicates merely the fact that its chains are shorter than those of the matrix. Since the binding constant K_ν increases rapidly with increase in the degree of polymerisation of the oligomer, it follows that, in a system containing oligomer chains of identical structure but of different lengths, one should expect the manifestation of selective binding of the longest chains. Such a case has been analysed theoretically.

Experimental confirmation of the model examined by Papisov and Litmanovich[29] has been obtained.[28] It was found that the fraction with the highest molecular weight participates in the reaction between polymethacrylic acid (PMAA) and a mixture of three fractions of poly(ethylene glycol (PEG) having different degrees of polymerisation $\overline{P}$:

$$\text{PEG}(\overline{P}=32\,000)+\text{PEG}(\overline{P}=180)+\text{PEG}(\overline{P}=30)+\text{PMAA} \Leftrightarrow$$
$$\Leftrightarrow \text{IPC[PMAA}-\text{PEG}(\overline{P}=32\,000)]+\text{PEG}(\overline{P}=30\,180). \quad (11)$$

The "selective complex formation" reaction (11) can be regarded in essence as an interpolymer substitution reaction. Indeed, at the instant of the mixing of the reactants, interpolymer complexes incorporating different oligomers are apparently formed and, as a result of the substitution of the relatively short oligomer chains by long ones, are converted into stable interpolymer complexes containing oligomer molecules. The selectivity of the binding of oligomers of the same chemical nature but with different degrees of polymerisation examined above, manifested strikingly in interpolymer reactions, is one of the fundamental features of polymer chemistry and has no analogue in the chemistry of low-molecular-weight compounds.

Apart from chain lengths, factors such as the chemical nature of the reactants, the structural complementarity of the interacting chains, the pH of the medium, etc. exert a significant influence on the occurrence and nature of the interpolymer reactions. We shall consider in what way each of these factors influences the equilibrium in reactions with participation of polymeric complexes.

The polymeric complex formation reactions in a system containing simultaneously high-molecular-weight chains and two kinds of complementary oligomers of different chemical structure were first investigated by Papisov et al.[26] and Bednar et al.[32] The objects of study were a high-molecular-weight polymethacrylic acid and the relatively short chains of poly(ethylene glycol), poly-*N*-vinylpyrrolidinone (PVPD), and poly(vinyl alcohol) (PVA). The interpolymer complexes formed in aqueous media in such systems are stabilised by the hydrogen bonds between the protonated carboxy-groups of the polymeric acid and the hydroxy-groups of poly(vinyl alcohol) or the corresponding nucleophilic groups of poly(ethylene glycol) and poly-*N*-vinylpyrrolidinone.[86] Hydrophobic interactions also play a significant role in the stabilisation of such interpolymer complexes.[18] In systems of this kind, the equilibria in the interpolymer substitution reactions (12) and (13) are displaced almost wholly to the right:

$$\text{PC(PMAA}-\text{PEG})+\text{PVPD} \rightleftarrows \text{PC(PMAA}-\text{PVPD})+\text{PEG}, \quad (12)$$

$$\text{PC(PMAA}-\text{PVA})+\text{PVPD} \rightleftarrows \text{PC(PMAA}-\text{PVPD})+\text{PVA}. \quad (13)$$

The highly selective binding of poly-*N*-vinylpyrrolidinone to polymethylacrylic acid in the multicomponent systems indicated is strikingly manifested in the processes involving the matrix polymerisation of methacrylic acid in a mixture of poly(vinyl alcohol) and poly-*N*-vinylpyrrolidinone [or a mixture of poly-(ethylene glycol) and poly-*N*-vinylpyrrolidinone]. In each of these cases, the rate of polymerisation of methacrylic acid is equal to its rate of polymerisation in the presence of poly-*N*-vinylpyrrolidinone alone and is independent of the presence of either poly(ethylene glycol) or poly(vinyl alcohol) in the polymerising system.[26] Under these conditions, the selectivity of the binding of polymethacrylic acid decreases in the sequence PVPD > PEG > PVA.

The substitution reactions can also be observed in systems containing two types of macromolecular matrices of different chemical nature and an oligomer capable of being bound to either of them. An example of such interpolymer reactions is provided by the substitution reactions in solutions of polymethacrylic acid of the interpolymer complex formed by polyacrylic acid (PAA) and poly(ethylene glycol):[27]

$$\text{IPC(PAA}-\text{PEG})+\text{PMA} \rightleftarrows \text{IPC(PMAA}-\text{PEG})+\text{PAA}. \quad (14)$$

The formation of a new interpolymer complex (PMAA–PEG) and the quantitative displacement into the solution of the polyacrylic acid previously incorporated in the initial interpolymer complex were observed in such a system by IR and NMR spectroscopic methods and also by the polarised luminescence method. Reaction (14) is endothermic and is accompanied by a gain in the entropy of the solvent (water). This can be explained by the fact that hydrophobic interactions play a decisive role in the stabilisation of the interpolymer complex (PMAA–PEG).[18] The important conclusion has also been reached that the matrix polymerisation of methacrylic acid in the presence of the interpolymer complex (PAA–PEG) is accompanied by a substitution reaction of type (14), whose rate is comparable to the rate of the polymethacrylic chain propagation in radical polymerisation, i.e. the substitution reaction takes place over a period of the order of 1 s.[27]

The influence of the chemical structure of the macromolecules on the selectivity of the interpolymer interaction in multicomponent systems has been examined.[28] Macromolecules capable of reacting with polymethacrylic acid with formation of the corresponding interpolymer complexes can be arranged in the following sequence in conformity with their ability to compete in substitution reactions:

$$\text{PEG}(\overline{P}=32\,000) > \text{polyacrylamide}\ (\overline{P}=80) > \text{PVPD}(\overline{P}=100) > \text{PEG}(\overline{P}=70) > \text{PVA}(\overline{P}=1000). \quad (15)$$

As can be seen, the influence of the molecular weight and of the chemical nature of the chain are manifested simultaneously in the intermacromolecular reactions. Thus, depending on the molecular weight, poly(ethylene glycol) can exhibit different reactivities in substitution reactions.

Systems in which the influences of both factors — the chemical nature and length of the chain — are manifested simultaneously lead to the possibility of the fine regulation of the matrix polymerisation processes. Cases of matrix polymerisation in the presence of two types of matrices differing in their chemical nature, namely "short" but "strong" and "long" but "weak", have been examined theoretically.[87] Model calculation showed that an interpolymer complex of the daughter chain with the shorter but "strong" matrix should be formed initially. Subsequently the daughter chain attains a length comparable to that of the matrix and an interpolymer reaction accompanied by the formation of a more stable interpolymer complex of the daughter chain with the long but "weak" matrix should take place.

The pH of the medium can play an important role in the selective interpolymer interaction. The influence of the pH on reactions of this type has been investigated[28] in relation to a three-component system containing a weak polymeric acid (polymethacrylic acid), a weak polymer base [poly-2-vinylpyridine (P2VP) or oligoethyleneimine (OEI)], and a non-ionogenic polymer [poly(ethylene glycol) or poly-*N*-vinylpyrrolidinone]. In an acid medium, the weak polymeric acid (polymethacrylic acid) exists predominantly in the unionised form, as a result of which an interpolymer complex between polymethacrylic acid and poly-*N*-vinylpyrrolidinone or poly(ethylene glycol), stabilised by a hydrogen bond, is mainly formed. In a neutral medium, both the polymeric acid and the polymeric bases are partly charged, so that a polyelectrolyte complex stabilised by salt bonds is produced. In an alkaline medium, where polymethacrylic acid is fully dissociated while the weak base is uncharged, the formation of both a polyelectrolyte complex and an interpolymer complex stabilised by hydrogen bonds is impossible, i.e. the interpolymer reaction does not occur at all. Thus the pH of the medium influences significantly both the ability of polymer chains to react with one another and the nature of the interactions stabilising the interpolymer complex.

Yet another important factor influencing the nature of the selective interpolymer interaction is the structural complementarity of the reacting chains. It has been shown[28] that the steric disposition of the functional groups is a decisive factor in the selective interaction in the following systems:

$$\text{P4VP} + \text{P2VP} + \text{PMAA} \rightleftarrows \text{IPC(PMAA} - \text{P4VP}) + \text{P2VP}, \quad (16)$$

$$\text{PGA} + \text{PEG} + \text{PMAA} \rightleftarrows \text{IPC(PMAA} - \text{PEG}) + \text{PGA}, \quad (17)$$

where P4VP is poly-4-vinylpyridine and PGA is polyglutamic acid. A characteristic feature of system (16) is the possibility of the formation of an interpolymer complex both as a result of electrostatic interpolymer interactions and as a consequence of the formation of interpolymer hydrogen bonds. Bearing this factor in mind, the formation of the interpolymer complex (PMAA–P4VP) in the presence of P2VP was explained precisely by the impossibility of the formation of strong hydrogen bonds between the polymethacrylic acid and poly-2-vinylpyridine units owing to steric hindrance. For the same reason the electrostatic interactions between the oppositely charged groups in the interpolymer complex PMAA–P2VP are much weaker than in the interpolymer complex PMAA–P4VP. The conformation of the polymeric reactants plays a decisive role in the reaction. In acid media, where reaction (17) was carried out, polyglutamic acid exists in the α-helical conformation, where the distance between the carboxy-groups of the acid does not correspond to the distance between the oxygen atoms in the neighbouring poly(ethylene glycol) units. The steric correspondence between the polymethacrylic acid and poly(ethylene glycol) chains is much better, as a result of which the insoluble interpolymer complex PMAA–PEG is formed predominantly in the PMAA–PEG–PGA ternary system. This is indicated by the results of the analysis of the supernatant, which contained almost the entire polyglutamic acid in the α-helical conformation introduced into the reaction.

(b) The influence of the degree of polymerisation of the polyions and of the chemical nature of the small ions on the equilibria in interpolyelectrolyte substitution reactions

We shall now proceed to the consideration of the equilibria in interpolyelectrolyte substitution reactions. An example may be provided by the reaction occurring in mixtures of solutions of the NPEC* formed by the high-molecular-weight labelled NaPMA* (P_W = 4100) and poly-*N*-ethyl-4-vinylpyridinium bromide (P_W = 170), and sodium polyphosphate (NaPP):[88–90]

$$\text{NPEC*(NaPMA*} - \text{PEVP}) + \text{NaPP} \rightleftarrows$$

$$\rightleftarrows \text{NPEC(NaPP} - \text{PEVP}) + \text{NaPMA*}. \quad (18)$$

The position of the chemical equilibrium in reactions of type (18) varies markedly, changing the direction of the process as a consequence of the change in the free energy of contact between a pair of units of the chemically complementary macromolecules. As already stated above, this is due to the cooperative nature of the interpolymer reaction.

Fig. 3 illustrates the dependence of the degree of conversion q on the NaCl concentration in reaction (18), which was carried out by mixing solutions of the NPEC* with sodium polyphosphate fractions with different $\overline{P}_n$. On addition of a salt-free solution of sodium polyphosphate to a salt-free solution of the NPEC*, the luminescence intensity does not change, i.e. in the absence of a low-molecular-weight electrolyte reaction (18) hardly occurs. The introduction of even insignificant amounts of NaCl into a system containing sodium polyphosphate with $\overline{P}_n$ = 230 leads to an appreciable increase in I (curve *1*). Hence it follows that the high-molecular-weight sodium polyphosphate substitutes NaPMA* in the initial NPEC*. However, with decrease in the length of the sodium polyphosphate chains, the rate of increase in I diminishes (curves *2*

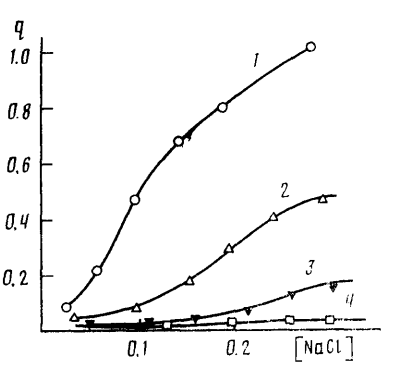


Figure 3. Dependence of the extent of reaction q in reaction (18) on the salt concentration in mixtures of solutions of the labelled non-stoichiometric polyelectrolyte complexes (NPEC*) NaPMA*–PEVP and sodium polyphosphate having different degrees of polymerisation: *1*, 230; *2*, 70; *3*, 50; *4*, 20; pH 10; [NaPMA*] = [NaPP]; φ = [PEVP]/[NaPMA*] = 0.33.[88]

and *3*) and finally does not change at all in solutions containing sodium polyphosphate with $\overline{P}_n$ = 20 (curve *4*). This means that in the last case reaction (18) hardly proceeds from left to right.

In order to elucidate the question whether kinetic or thermodynamic factors limit the occurrence of reaction (18), a study was made of the reverse reaction. It was found that, when [NaCl] > 0.05 M, the values of *I* for mixtures of the non-stoichiometric polyelectrolyte complex NaPP–PEVP and NaPMA* are identical with the values of *I* for mixtures having the same composition but obtained by adding sodium polyphosphate to NPEC*. This means that, when the ionic strength exceeds 0.05 M, reaction (18) is kinetically unhindered and equilibrium is established during the experiment. Consequently the observed dependence of *q* on the degree of polymerisation of sodium polyphosphate is determined by thermodynamic factors.

Fig. 4 shows that, by replacing one alkali metal cation, playing the role of the counterion in relation to PMA* and polyphosphate anions, by another alkali metal cation, it is possible to alter the direction of reaction (18) for fixed degrees of polymerisation of the polyelectrolytes. The addition of sodium polyphosphate ($\overline{P}_n$ = 70) to a solution of NPEC* in the presence of KCl does not alter *I* (curve *3*), i.e. the equilibrium in reaction (18) is fully displaced to the left. On the other hand, in LiCl solutions for [LiCl] > 0.05 M, equilibrium (18) is fully displaced to the right (curve *1*). An intermediate solution occurs in NaCl solutions (curve *2*).

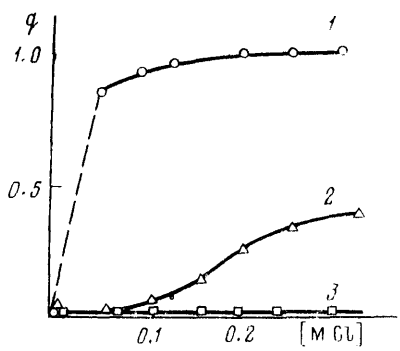


Figure 4. Dependence of the extent of reaction *q* in reaction (18) on the salt concentration [MCl] in mixtures of solutions of labelled non-stoichiometric polyelectrolyte complexes (NPEC*) NaPMA*–PEVP and sodium polyphosphate (P = 70) in the presence of various salts MCl: *1*, M = Li; *2*, M = Na; *3*, M = K; the conditions are the same as in Fig. 3.[88]

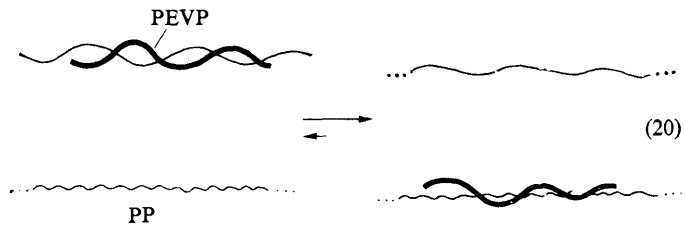
It must be emphasised that, over the entire range of variation of the concentrations of the salts and for any equilibrium position in reaction (18), almost all the units of the polycation are linked to the units of NaPMA* and sodium polyphosphate.

In order to account for the observed effects, we shall represent the free energy change in reaction (18) as the sum of two components:

$$\Delta G = \Delta G_r + \Delta G_s, \qquad (19)$$

where ΔG_r is the free energy change on replacement of the NaPMA*–PEVP contacts by the NaPP–PEVP contacts, while ΔG_s is the difference between the free energies of the reaction of the counterion with sections of the chains of the PMA* and polyphosphate polyanions.

If the degree of polymerisation of both polyanions is greater than that of the polycation, then the number of species in the system remains constant;



(20)

It follows from Fig. 3 that in NaCl solutions (curve 2) the equilibrium in such a reaction is displaced to the right, i.e. $\Delta G' = \Delta G'_r + \Delta G'_s < 0$. However, the decrease in the sodium polyphosphate chain length displaces the reaction equilibrium in the opposite direction, i.e. the overall free energy change in reaction (21) becomes positive: $\Delta G'' = \Delta G''_r + \Delta G''_s > 0$.



(21)

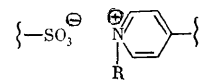
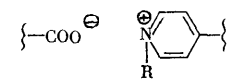
Since ΔG_s is independent of the chain length, i.e. $\Delta G'_s = \Delta G''_s$, the observed effect should be explained by the increase in $\Delta G''_r$, i.e. $\Delta G''_r > \Delta G'_r$. When the total number of salt bonds between the polyions is retained, the occurrence of reaction (21) is less favourable from the standpoint of entropy than that of reaction (20) owing to the decrease in the number of polymeric species in solution. This is correlated with data concerning the influence of the degree of polymerisation of sodium polyphosphate on the stability of the stoichiometric polyelectrolyte complexes NaPP–PEVP in salt media.[89]

For a fixed degree of polymerisation of the polyelectrolytes, ΔG_r remains unchanged on replacement of the alkali metal cation introduced into the system by another and it follows from the comparison of curves *1*, *2*, and *3* in Fig. 4 that the change of sign of ΔG is caused by the change in ΔG_s. The observed effect should be attributed to the difference between the free energies of the reaction of the PMA* and polyphosphate anions with different alkali metal cations. It follows from the turbidimetric titration curve[89] that the critical salt concentration at which the polyelectrolyte complex NaPMA*–PEVP dissociates decreases in the sequence KCl > NaCl > LiCl. In the case of the polyelectrolyte complex NaPP–PEVP, the series is reversed.

By replacing the counterion, it is possible to increase the reactivity of the short chains of the polyphosphate anion. In solution in LiCl, the polyphosphate anions with $\overline{P}_n$ = 20 are already capable of competing with the polymethacrylate anions in reaction (21). On the other hand, in KCl solution even long chains of polyphosphate anions with $\overline{P}_n$ = 230 are almost totally lacking in the ability to replace the polymethacrylate anions.

Thus the equilibrium in the interpolyelectrolyte reaction can be effectively regulated by the simple dissociation or growing of

polyion chains, i.e. by altering the degree of polymerisation. The replacement of one alkali metal cation by another can also induce a qualitative change in the state of multicomponent polyelectrolyte systems. The observed phenomena have no analogues in polymer systems. Presumably such cooperative effects constitute the basis of the regulatory processes in natural biopolymer systems.

The differences between the free energies of the reaction of polyanions of different chemical nature with the polycation as well as the differences mentioned above, observed in the interaction of the polyanions with different alkali metal cations, are evidently caused by the contribution of specific interactions together with the usual Coulombic forces. When such differences become considerable, they actually determine the direction of the inter-polyelectrolyte reaction. Thus polyanions containing sulpho-groups, including heparin, sodium polystyrenesulphonate, sodium polyanetholesulphonate, potassium polyvinylsulphate, etc., almost wholly substitute polymeric carboxylate anions in their polyelectrolyte complexes with different polycations.[58,61,91] This is a consequence of the greater stability of the cooperative system of contacts of the type  compared with the contacts  in aqueous salt media (NaCl solutions) in which substitution reactions were investigated. Indeed, the dissociation of polyelectrolyte complexes formed by polyanions with sulpho-groups and by poly-*N*-ethyl-4-vinylpyridinium bromide requires a NaCl concentration higher by a factor of 4 than for the dissociation of the polyelectrolyte complex NaPMA–PEVP.[58]

(d) The influence of the length of the *N*-alkyl substituent in the poly-4-vinylpyridinium cation on the equilibrium in the substitution reaction

It has been observed[92] that the direction of the substitution reaction

$$\text{NPEC*(NaPMA*}-\text{PVPAlk)}+\text{NaPP} \rightleftarrows \text{NPEC(NaPP}-\text{PVPAlk)}+\text{NaPMA*} \qquad (22)$$

is determined, other conditions being equal, by the number of carbon atoms in the *N*-alkyl substituents of quaternised poly-4-vinylpyridines (PVPAlk). Virtually completely quaternised ($\beta > 90\%$) PVPAlk with $\overline{P}_W = 130$ as well as NaPMA* containing 11 pyrene labels and having $\overline{P}_W = 4100$ and sodium polyphosphate with $\overline{P}_W = 250$ were used in the experiments. Fig. 5 presents the dependence of the degree of conversion q in reaction (22) on the concentration of the added salt NaCl for PVPAlk with *N*-alkyl substituents for Alk = Me, Et, or Pr. The points on the curves correspond to equilibrium values. It follows from Fig. 5 that the number of carbon atoms in the *N*-alkyl substituent in PVPAlk determines the direction of reaction (22) at a fixed ionic strength of the solution. Thus the introduction of sodium polyphosphate into a solution of NPEC* incorporating PVPPr leads to a very slight alteration of q (curve *3*), i.e. equilibrium (22) is displaced to the left. On the other hand, in NPEC* solutions containing PVPMe the equilibrium is significantly displaced to the right (curve *1*), while an intermediate situation arises in solutions of a non-stoichiometric polyelectrolyte complex with PVPEt (curve *2*).

Such alteration of the direction of the interpolyelectrolyte substitution reaction (22) agrees with the difference between the stabilities of the corresponding initial polyelectrolyte complexes and the reaction products in aqueous salt solutions. In sodium chloride solutions, the stabilities of both the complexes NaPP–PVPAlk and the complexes NaPMA–PVPAlk diminish consistently in the sequence PVPMe > PVPEt > PVPPr.[93] Such decrease in the ability of the complexes to resist the disruptive effect of the salts in the homologous series of PVPAlk can apparently be accounted for by the steric shielding of the oppositely charged groups of polyions. However, it is significant that this effect is more marked in the case of the complexes NaPP–PVPAlk, where the replacement of one *N*-alkyl substituent in poly-4-vinylpyridine by another leads to more significant changes in stability. For the same reason, with increase in the length of the *N*-alkyl substituent in PVPAlk, the difference between the stabilities of the corresponding complexes decreases, which agrees with the decrease in the degree of conversion q in the substitution reaction (22) in the sequence PVPMe > PVPEt > PVPPr (Fig. 5).

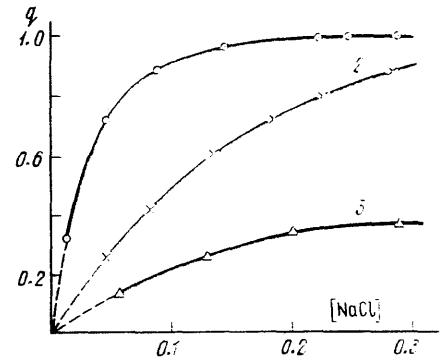


Figure 5. Dependence of the extent of reaction q in reaction (22) on the salt concentration in solutions containing different alkylated poly-4-vinylpyridines: *1*, PVPMe; *2*, PVPEt; *3*, PVPPr; φ = [PVPAlk]/[NaPMA*] = 0.2; [NaPP] = [NaPMA*]; pH 10.[92]

Thus, by virtue of the cooperative nature of the inter-polyelectrolyte reactions, even very slight differences between the free energies of the interaction between pairs of units of chemically complementary chains is entirely sufficient to alter completely the direction of such processes. In many instances, a strikingly high selectivity of the interaction of the oppositely charged chains is manifested in systems of this kind. In a solution containing relatively long and relatively short polyanions with the same chemical structure, the polycation prefers to combine with long chains. By the method of trial and error, the cation recognises and selects that of the two cations which forms with it a more stable polyelectrolyte complex even if the difference between the energies of reaction per pair of oppositely charged units is very small. By adding different alkali metal salts to the reaction mixture (i.e. by varying the nature of the low-molecular-weight counterions), it is possible to alter the affinity of the competing polyanions for the polycation and to regulate thereby the direction and equilibrium position of the interpolyelectrolyte substitution reaction. The presence in the polyanion of a small number of groups (1 per hundreds of chain units), capable of interacting specifically with the units of the complementary chain in the non-stoichiometric polyelectrolyte

complex formed, can ensure the preferential binding, i.e. "recognition", by the polycation of a modified polyanion of this kind among the unmodified macromolecules.

This is responsible for the exceptionally high selectivity of the interpolypolymer interactions and the striking tendency of such systems to undergo self-organisation and also ensures the "self-assembly" of the non-stoichiometric polyelectrolyte complex species in aqueous salt solutions. The factors influencing the direction of the reactions investigated can be an effective means for regulating the interpolyelectrolyte exchange and substitution.

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Translated from *Uspekhi Khimii* **60** 1596–1612 (1991) U.D.C. 541.64;546.28;542.953

Three-dimensionally growing polyorganosiloxanes. Possibilities of molecular construction in highly functional systems.

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ABSTRACT. An analysis is carried out of general aspects of the construction of three-dimensionally growing structures with an organic or an inorganic skeleton. Problems in the synthesis of novel polymeric forms based on organosilicon monomers are examined. Ways are discussed for overcoming steric effects in the surface layer, caused by the characteristics of the formation of three-dimensionally growing structure.

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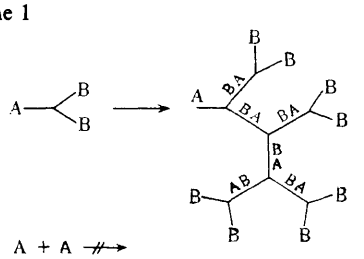
I. Introduction

The present review is based primarily on the material of a report which was presented at the first international school-seminar on non-traditional methods of polymer synthesis.[1] However, a considerable amount of work in this area has appeared recently, as a result of which it can be said that polymer chemistry has developed in a new direction which may be described as the "synthesis of dendrimers" or, more poetically, of polymers of the "starbust" type. The principal achievements and problems and also the characteristics of formation of these structures, including theoretical prerequisites for the emergence of the new polymeric forms, have been reviewed by Tomalia et al.[2] Publication of this detailed review simplified our task to a considerable extent. Here we shall consider only the results and problems arising in the course of the synthesis of three-dimensionally growing organosiloxanes or organosilicon dendrimers. Data for the organic analogues will be used only to the extent that is necessary for an understanding of the similarities in the problems investigated and of the differences in the synthetic approach to their solution.

II. Basic prerequisites, concepts, and general schemes

The basic prerequisites for the creation of macromolecular dendritic systems can be traced back to the work of Flory,[3] who suggested that highly functional systems could lead to the formation of highly branched polymers rather than cross-linked or polycyclic types. To achieve such a result, one main condition, specified by Flory, must be satisfied. Thus, if a monomer contains two or more functional groups, one of which is A, and the others are of type B, and if A does not react with A, or B with B, but the interaction of A with B results in the formation of a chemical bond A–B, then it is possible that a non-crosslinked and non-polycyclic polymer will be formed, as shown in Scheme 1.

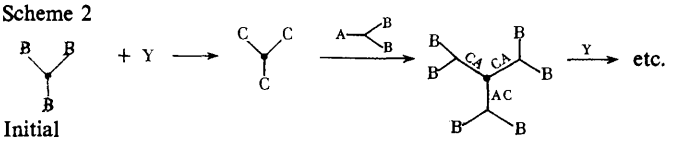
Scheme 1



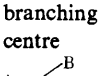
A + A ⇸
B + B ⇸
A + B ⟶ AB

If, however, in the initially formed oligomer itself, not only does A not interact with A, or B with B, but A also does not interact with B; and if it is possible at a certain stage to convert B into C, a group which can form a chemical bond by interaction with A, then such a scheme can be used to obtain completely controlled growth of the molecule (Scheme 2):

Scheme 2



Initial branching centre



main reagent

A + B ⇸
A + A ⇸
B + B ⇸
B + Y ⟶ C
C + A ⟶ AC

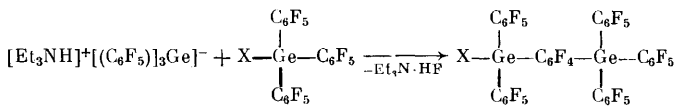
Practically all systems synthesised at the present time can be described in general form by means of Schemes 1 and 2 and we shall therefore make use of these frequently for appraisal of the characteristics of one or another real system.

III. Examples of real structures, and corresponding general schemes

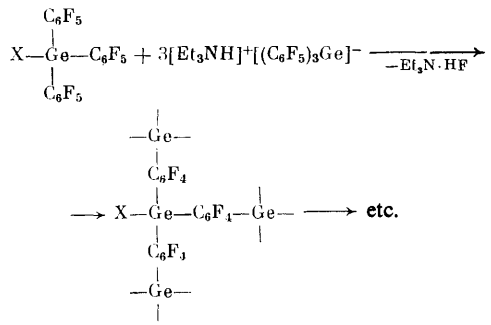
Scheme 1 is well illustrated by work[4,5] using organoelement compounds. During a study of the chemical characteristics of the hydrides of germanium and silicon, with perfluorophenyl substituents at the heteroatom, an interesting fact was discovered. The presence of three perfluorophenyl substituents at the atom of the element leads to such a significant redistribution of the electron density in the molecule, such that on the addition of a base, triethylamine, charge separation occurs with the separation of hydrogen as a proton rather than hydride.

$$(C_6F_5)_3GeH+Et_3N\rightarrow[Et_3NH]^+[(C_6F_5)_3Ge]^-.$$

This fact, in combination with the reactivity of the *p*−F atoms of the perfluorophenyl substituents at the atom of the element, in particular germanium, leads under these conditions to a process at every reaction centre, which can be depicted by the following general scheme:



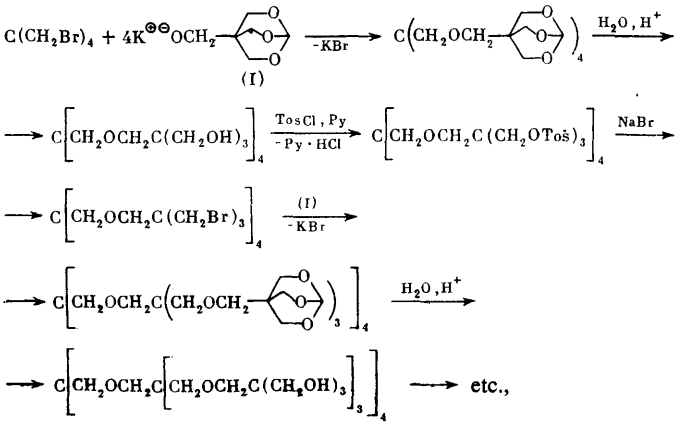
or, bearing in mind the molecule as a whole:



In this system the germanyl hydride grouping (in accordance with the condition of Flory) is the functional group A, and the atom of fluorine in the *para* position of all three perfluorophenyl groupings is the functional group B (Scheme 1).

Let us consider briefly the remarkable properties of this system. First of all, the ease with which reaction occurs at room temperature should be noted: from the moment of introduction of triethylamine to the completion of the reaction and the formation of a polymer, less than a minute elapses. As a result a "live" polymer is formed. The reaction may be resumed again after separation of the precipitate of triethylamine hydrofluoride and the introduction of new portions of reagents. Such an operation can be repeated more than once. In addition, it is possible to obtain a polymer with a molecular mass of several millions, as determined by light scattering. From electron microscope data, the polymeric molecules obtained are seen to be spherical.

The most complete illustration of the general Scheme 2 is possible by a consideration of the following system:[6]



in which the basic reagent is the potassium salt of the tricyclo-orthoester, 4-(hydroxymethyl)-2,6,7-trioxabicyclo[2.2.2]octane (I). Conversion of the functional group B:

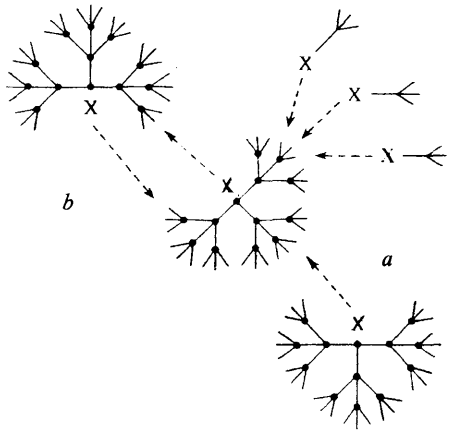


into the form C[−C(−CH_2Br)$_3$] occurs in three stages—hydrolysis, tosylation, and bromination, after which the process is repeated again. As a result, branched dendrimers are obtained (Fig. 1).[6]

Comparing the two basic schemes for the construction of three-dimensionally growing systems, or dendrimers, several principal points should be noted. Scheme 1 occurs in a single step and does not involve regulation of the structure at the molecular level. On the other hand, in accordance with Scheme 2 (and this is confirmed both theoretically and in practice) it is possible to form the structure of the molecule layer by layer with the possibility of termination at any stage. However, such a delicate control of the structure and dimensions of the molecule at the molecular level demands certain sacrifices, both in terms of the purely synthetic target (since a complex and multistage synthesis is involved), and also in general scientific terms (since the molecule grows in an orderly fashion to a definite size, after which there is a rapid reduction in rate on account of steric hindrance). The fact is, that the surface of the molecule grows more slowly than the number of functional groups, leading at a certain stage to steric difficulties.[6] At the same time, the unregulated system (Scheme 1) controls its own growth and therefore in every layer as many functional groups as possible are used without steric complications. In accordance with Scheme 1, polymers can be obtained with a molecular weight of > 1,000,000 a.m.u. The authors[4,5] did not analyse certain additional, purely structural processes, which can take place during the unregulated formation of three-dimensional structures. The basic difference between systems 1 and 2, as schemes for the formation for these structures, is that in the regulated version, if the interaction of the growing molecules between themselves is excluded then growth of the macromolecule is accomplished only by the addition of monomeric units at the growing centre, whereas in the non-regulated variant, the growing molecules are fully able to interact between themselves, especially in the early stages. On the one hand, therefore, it is possible that entire regions of the surface of the growing molecule may become

shielded (Scheme 3, process *a*), but on the other, cyclisation may occur (Scheme 3, process *b*):

Scheme 3



The principles and basic schemes for obtaining macromolecular dendrimeric systems have thus been considered and attention will now be turned to the main subject of this brief review: three-dimensionally growing polyorganosiloxanes.

IV. Three-dimensionally growing polyorganosiloxanes

With the whole expansion of possibilities for controlling the structures of organosilicon polymers, and so also to a certain extent the properties of materials based on them, a search was carried out for new, convenient methods for the synthesis of organosilicon polyfunctional oligomers with reactive functional groups.

From the point of view of choice of reagents, suitable for the construction of three-dimensionally growing systems, organosilicon monomers are not themselves convenient, because of the limited choice of functional groups in comparison with normal organic monomers. This applies especially to the construction of polymers with a purely siloxane skeleton. Analysis of data in the literature showed, in particular, that amongst the organosilicon monomers reported, there were none which could have met the necessary requirements sufficiently (i.e. would have allowed the aim of conversion by general Scheme 2 to be achieved). The majority of traditional monomers employed for obtaining siloxane polymers by polycondensation methods contain functional groups that are the same, undergo exchange with each other, are insufficiently stable, or enter into reaction with one and the same reagent.

The basic reaction, therefore, is not sufficiently selective for the preparation of simple branched oligomers by the use of such organosilicon monomers, or for the subsequent development of the functional system.[7–15] All of these facts stimulated work on the creation of monomers containing two or more differing functional groups. In this connection, our attention was attracted to the alkoxysilane-alkali metal hydroxide system, which, in spite of conflicting reports in the literature,[16–19] allowed one to hope that monomers with independent functional groups could be obtained, containing simultaneously sodiumoxy- and alkoxy-groupings attached to atoms of silicon. The synthesis of such compounds proved to be very simple and the yield of the main substance in the majority of cases reached 95%.[20]

$$\mathrm{RO{-}Si{-}OR} + \mathrm{NaOH} \longrightarrow \mathrm{RO{-}Si{-}ONa} + \mathrm{ROH},$$

R=Et; R′=R″=Me; R′=R″=OEt; R′=Me, R″=OEt.

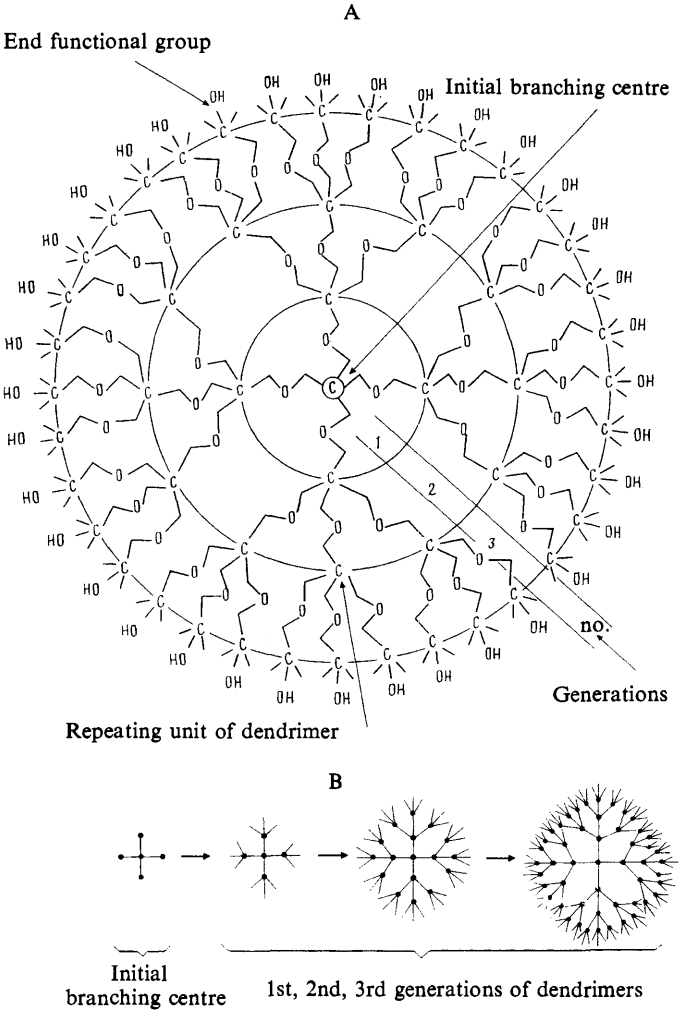
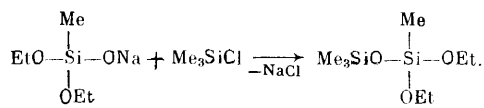


Figure 1. Planar projection of "starbust dendrimer" (A) and scheme for its formation (B).

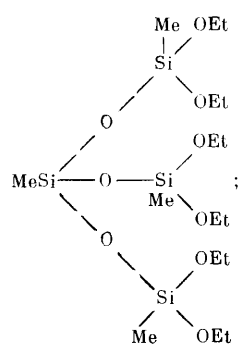
Although it was initially apparent that the presence of two or more identical functional groups in a molecule of alkoxysilane does not permit high selectivity to be achieved in this reaction, a more detailed study of the NaOH–$(RO)_2SiR'R''$ system showed subsequently, that selectivity is an entirely natural result of the marked redistribution of electron density in the molecule of

alkoxysilane that follows the introduction of sodiumoxy-groupings into its structure.[21] A study of the properties of the sodiumoxy-organoalkoxysilanes that were obtained led us to the conclusion that under certain conditions, alkoxy groupings can be considered as latent functional groups or as protected groups that may be activated to become reaction centres ($\geq$Si—Cl). These assumptions were most simply confirmed and utilised by a one-step transformation of the alkoxysilyl grouping into chlorosilyl (Scheme 4). The transformation of $\geq$Si—OR into $\geq$Si—Cl allowed the primary cycle of conversion to be completed and the molecular construction of siloxane systems to commence immediately.

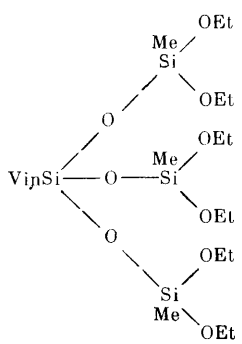
In contrast to the majority of sodiumoxy-derivatives or organosilicon monomers, sodiumoxyorganoalkoxysilanes dissolve readily in practically all organic solvents including those such as hexane, toluene, diethyl ether, etc. The first reactions carried out with the use of the novel reagents have already demonstrated the "independence" of their functional groups; in particular, we have shown that it is possible to carry out the reaction between organochlorosilanes and sodiumoxy groupings with formation of a siloxane bond, whilst preserving the inviolability of the alkoxy groupings. Thus, during treatment of the monomers with trimethylsilyl chloride (a process used by us for the identification of synthesised compounds and estimation of their yield) the formation of by-products was not observed.



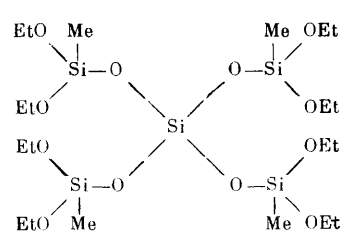
The use of tri- or tetra-functional silanes such as $RSiCl_3$ (R = Me, vinyl) and $SiCl_4$ in these reactions, instead of trimethylchlorosilane, allows the first generation of oligomers to be obtained.



62%



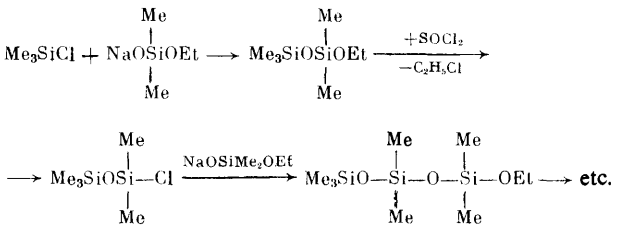
65%



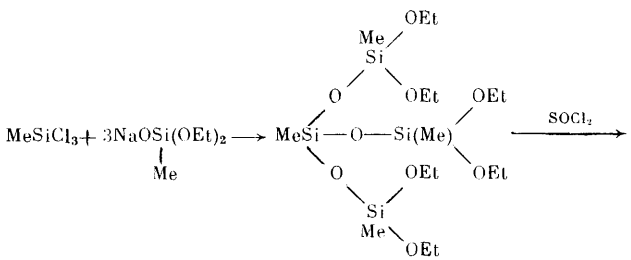
30%

Differences in the yields are explained by the different stabilities of the central, branching centres towards nucleophilic reagents. Further development of the process—conversion of the functional groups from the form B into C (in accordance with the general Scheme 2)—was carried out through replacement of the alkoxy groupings by chlorosilyl as in the scheme:

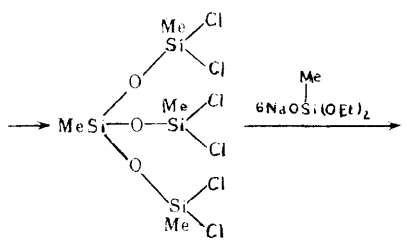
Scheme 4



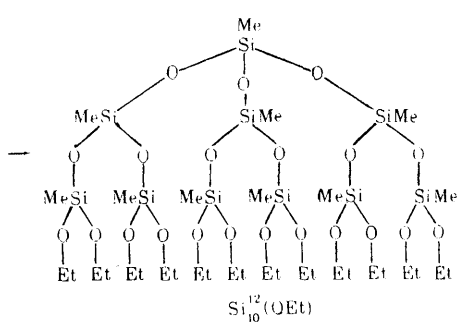
or by use of a trifunctional branching centre.



$Si_4^6(OEt)$



$Si_4^6(Cl)$



$Si_{10}^{12}(OEt)$

In the accepted designation of three-dimensionally growing oligomers the upper index shows the functionality of the oligomer, the lower index shows the number of silicon atoms in the structure of the oligomer, and the type of functional group is shown in brackets.

The high yields of first and second generation oligomers and the absence in the reaction mixture of products resulting from fission of the siloxane bond, show that the reaction conditions chosen were suitable. Since compounds with chlorosilyl groupings were already used in the first stage of reaction (by interaction with sodium-oxyorganoalkoxysilanes), then the process for obtaining second generation oligomers did not give rise to special difficulties. It was also found that the yield of the oligomer $Si_{10}^{12}(OEt)$, was significantly higher than the yield of $Si_4^6(OEt)$ and that this tendency was repeated for the conversion of $Si_{10}^{12}(OEt)$ to $Si_{22}^{24}(OEt)$, facts that may be

accounted for, apparently, by the characteristics of the structure of the synthesised oligomers and, in particular, the extensive screening of the siloxane skeleton by the surface functional groups. Thus, if the primary branching centre and the surface reaction centres are chemically identical, there is less possibility of fission of the siloxane bonds under the action of sodiumoxy-derivatives. Four generations of oligomer, $Si_4^6(OEt)$, $Si_{10}^{12}(OEt)$, $Si_{22}^{24}(OEt)$ and $Si_{46}^{48}(OEt)$ are reported,[22] providing indisputable evidence of correspondence with the cited Scheme 4 and the conditions for formation of three-dimensionally growing systems mentioned above. From Scheme 4 it is possible to see all stages of formation of the molecular structure by the use of methyltrichloro-silane as the branching centre and sodiumoxymethyldiethoxysilane as the basic reagent. The reaction of chain growth (accumulation of layers) proceeds by the interaction of sodiumoxy groupings with chlorosilane groupings at the branching centre, whilst the ethoxy groups act as protecting groups for the future reaction centres at which, after their conversion into the active form, a new "layer" in the structure of the growing molecule will be formed.

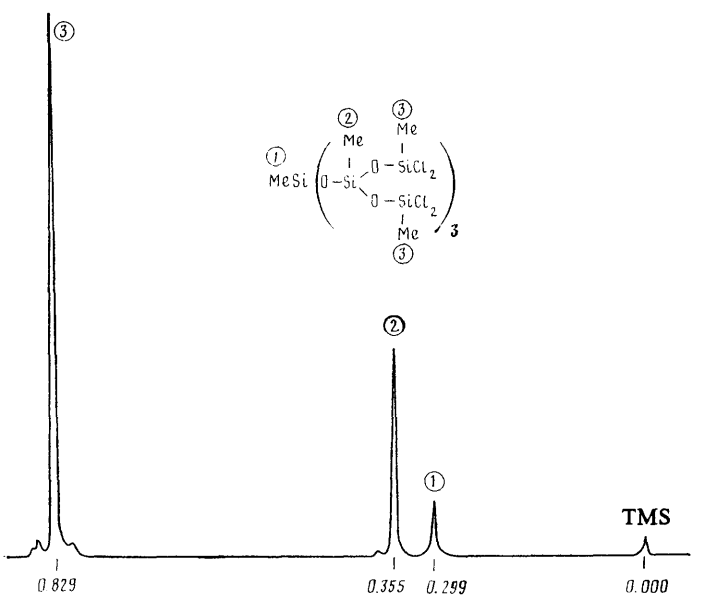
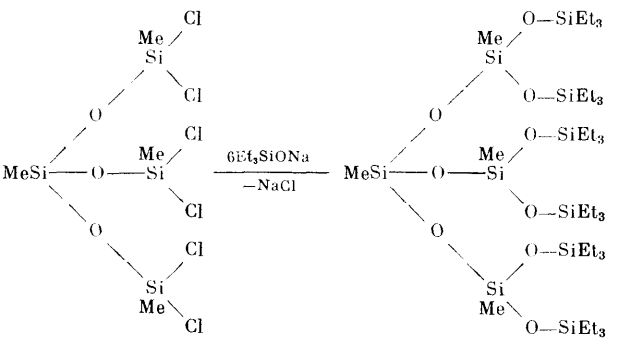


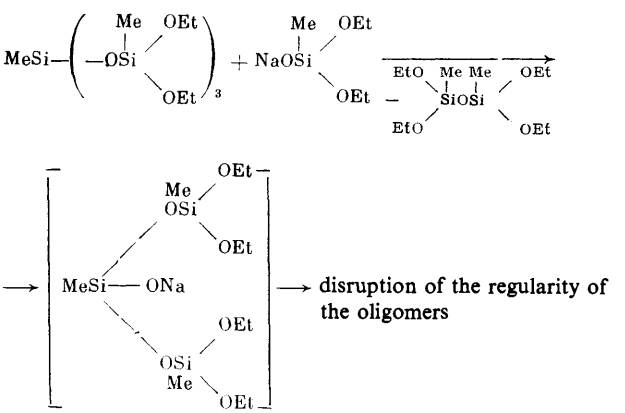
Figure 2. ^1H nmr spectrum of the oligomer $Si_{10}^{12}(Cl)$ in CCl_4 (spectrum recorded on Bruker WP-200 instrument).

The three-dimensionally growing oligomers are obtained as transparent mobile liquids. For identification of the synthesised oligomers a number of methods were used, including functional and elemental analysis, ^1H and ^{29}Si nmr spectroscopy, and high performance liquid chromatography (HPLC). In Fig. 2, the ^1H nmr spectrum of the oligomer $Si_{10}^{12}(Cl)$ is given as an example, showing well resolved signals for three species of methyl group attached to silicon in the central, first and second (external) layers. The integration ratio for the intensities of these signals (1 : 3 : 6) is in complete accordance with calculation. Still more informative is the ^{29}Si nmr spectrum. In particular, for the oligomer $Si_{10}^{12}(OEt)$, three signals are observed in the regions $\delta_1 = -67.91$, $\delta_2 = 67.44$, and $\delta_2 = 51.47$ ppm, corresponding to the central silicon atom and the atoms of silicon of the first and second layers.

At the same time, in the analysis of the oligomers that were obtained, account was taken of the specific character of the highly-functional and very reactive systems under investigation. Because of the high reactivity of chlorosilyl derivatives, the use of HPLC for confirmation of purity was preceded by an additional step involving blocking of the functional groups by triethylsilyl groups to give non-functional derivatives:

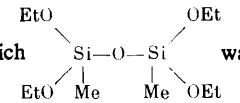


These non-functional derivatives of the three-dimensionally growing oligomers were studied by the method of HPLC and it was shown that the resolving ability of the apparatus, with a column efficiency of 24 000 theoretical plates, was sufficient for the separation of oligomers of the 1st, 2nd, 3rd and 4th generations. HPLC was used to confirm the purity of the standard obtained by Scheme 4 and also proved to be helpful in the selection of optimum reaction conditions for the basic synthetic scheme. The latter circumstance is especially important, as it is known that the siloxane bonds which form the skeleton are sensitive to both the nucleophilic reagent (sodiumoxy-organoalkoxysilane) and the electrophilic reagent (thionyl chloride) which are used at different stages of the synthesis. It was shown that to carry out the synthesis under non-optimum conditions can lead to disruption of the ordered structure of the oligomers as in the following scheme:



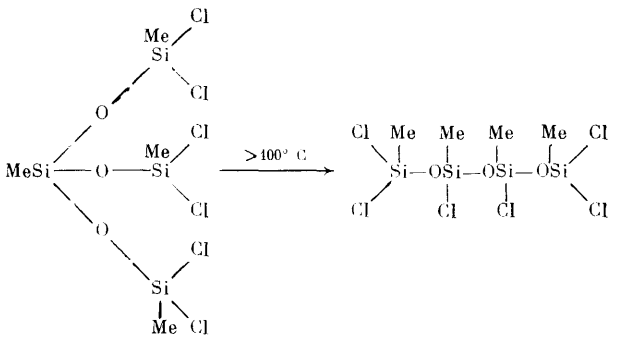
i.e. the fear that the siloxane skeleton of the oligomers may not be stable is not without foundation. Indeed, under certain conditions the fission of the grouping $\diagdown Si-OC \diagup$ by sodiumoxyorgano-alkoxysilanes can proceed quantitatively. Concerning fission of the

$\diagdown$Si—O—Si$\diagup$, grouping, interaction of the sodiumoxy-derivative $NaOSiMe(OEt)_2$ with the oligomer $PhSi[OSiMe(OEt)_2]_3$, gave

products among which  was identified, showing

clearly that this type of interaction should also be borne in mind in the systems under investigation.

There are further experimental factors confirming the instability of the siloxane skeleton. Thus, for example, we have shown[24] that to heat oligomers which contain chlorosilyl functional groups above 100 °C is extremely undesirable, as it can lead to rearrangement.



However, in the presence of chlorosilyl groupings, the oligomer shows desirable stability both of the siloxane skeleton and of the molecule as a whole. It is sufficient to say that the oligomer $Si^{24}_{22}(OEt)$, which has a molecular mass of 2356, was distilled under vacuum without showing any tendency to rearrangement. A knowledge of these processes, of the temperature ranges at which they occur, and of their characteristics, ensures the possibility of accurate control of the formation of products. As a result, the majority of oligomers were made and characterised as individual chemical compounds. It can therefore be affirmed, that by carrying out the reactions under optimum conditions, the synthetic schemes shown can be realised without any perceptible side reactions.

V. Separate problems of synthesis of three-dimensionally growing siloxanes

In spite of considerable differences in methods of synthesis for three-dimensionally growing polyorganosiloxanes and their organic analogues, systems of the type under examination develop according to general and objective rules. It was therefore natural to consider the question of saturation of the surface layer by functional groups and the negative consequence of this phenomenon for regular growth of the molecule. We first encountered this in the course of the synthesis of three-dimensionally growing siloxanes, having found that at a definite stage in the progress of the synthesis, the characteristics of the products obtained began to change in a way that was not in accordance with previously observed tendencies. Thus, in Fig. 3, the relationship is given of refractive index, specific viscosity and density for three-dimensionally growing oligomers with ethoxy functional groups, to the ordinal number of the oligomer. It is easy to see that in all cases of change from oligomers of the 6th generation to those of the 7th, these curves show a break, which we believe to be associated with a loss of regularity in the oligomer, on account of arising steric difficulties. The same phenomenon was encountered but at an earlier stage in the blocking of functional oligomers. Thus in the case of the 4th generation oligomer, Si^{48}_{46}, we found that the number of blocked end groups which could be introduced did not correspond to that calculated theoretically. For this reason we do not have available the corresponding chromatograms, confirming the individuality of synthesised oligomers that contain more than 46 atoms of silicon. This earlier breach of the regularity of the system is explained, first of all, by the use of monomeric reagents, and it is not therefore surprising that the increase in the functionality of the oligomer quite quickly outstrips the increase of the surface at which they may be able to attach themselves.

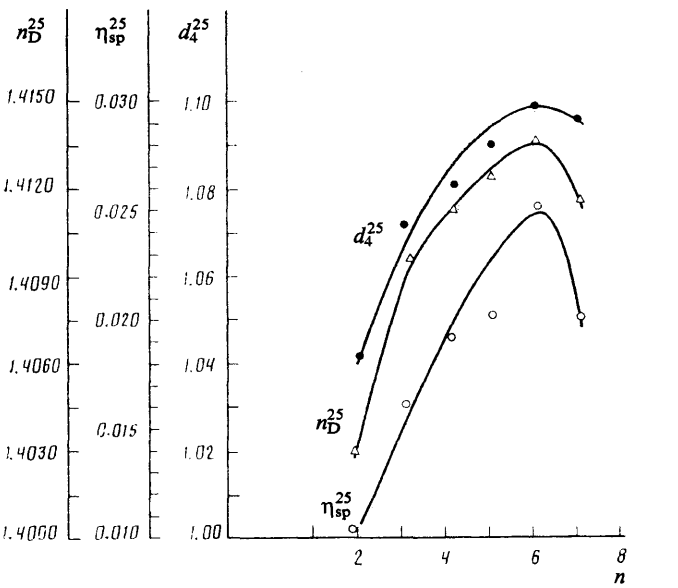


Figure 3. Relationship of density, (d_4^{25}), specific viscosity (η_{sp}^{25} for a 1% solution in toluene) and refractive index (n_D^{25}) for three-dimensionally growing polyethoxymethylsilsesquioxanes to the ordinal number of the oligomer in the homologous series.

The limit to the regular growth of dendrimers should not, however, be considered as an insurmountable problem but should rather stimulate efforts to overcome these difficulties in the field of molecular construction of such polymers. In principle this is possible. A mathematical correlation can be made between the length of the linear section of an oligomer and its functionality, for which steric difficulties on the synthetic pathway for oligomers of a definite size will not arise. There is also another way for solving this problem. In particular, we have shown that during accumulation of

a further layer of monomer, it is possible to use a structure which is different from that of the basic structure.[22]

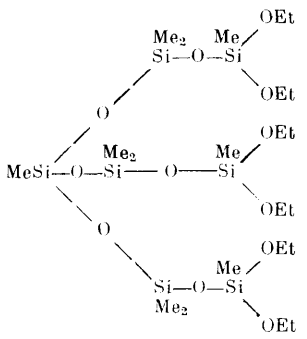
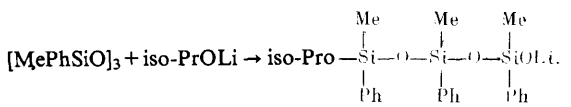


Table 1. Properties of blocked oligomers.

Unit blocked	Blocking group	t_{vit}, °C	η Pa s
$MeSiCl_3$	Et_3SiO-	−138.4	$2.5\cdot10^{-3}$
$Si_4^6(Cl)$	Et_3SiO-	−133.0	$2.5\cdot10^{-2}$
$Si_{10}^{12}(Cl)$	Et_3SiO-	−120.0	0.1
$Si_{10}^{12}(Cl)$	$Me_3SiOSiO-$ (Me, Me)	−110	–
$Si_{22}^{24}(Cl)$	Et_3SiO-	−101.0	6.5
$Si_{46}^{48}(Cl)$	$C_{10}H_{11}-$	−48.0	$2\cdot10^{-2}$
$Si_{46}^{48}(Cl)$	$(CF_3CH_2CH_2)_3SiO-$	−63.8	0.28
$Si_{46}^{48}(Cl)$	Me_3CO-	−85.0	–
$Si_{46}^{48}(Cl)$	$CH_2=CH-SiO-$ (Me, Me)	–	–

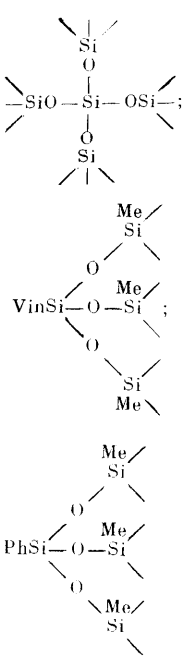
From the chemical formula given, it is seen that the use of a difunctional monomer leads to an increase in the size of the oligomer and consequently also, in the size of its surface, with preservation of the number of functional groups. Such an operation can be described as a distinct "thinning out" of the reaction centres, averting the onset of steric difficulties. Undoubtedly, the effectiveness of such a thinning out is proportional to the length of the linear section between the last branch in the structure and the functional groups. In such a scheme for the siloxane systems considered, there is the prospect of using individual oligomers, synthesised as follows.[25]



It is necessary at once to make the reservation, that the operation of "thinning out" of the functional groups is closely connected with a change in the intramolecular packing of the three-dimensionally growing molecules, and at present it is not clear whether such thinning out has any effect on the properties of the oligomer as a whole. The influence of the surface layer on the properties of the oligomer, especially in blocked oligomers, is considerable, since the blocking groups constitute 50% of the structure of three-dimensionally growing oligomers (out of the total number of monomeric units) and being concentrated in the surface have an independent significance.

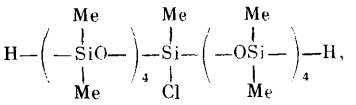
It appeared to be possible within fairly wide limits to change the intermolecular interaction of the oligomers by the use of different organic substituents at the atoms of silicon in the surface layer. For this purpose it was shown to be possible to use blocking compounds such as Me_3CONa, $Me_3SiOSiMe_2OH$, $(CF_3CH_2CH_2)_3SiONa$, and $C_{10}H_{11}MgBr$.[23] For illustration we can use the data in the Table 1, which shows oligomers having identical molecular skeletons but differing in the features of the surface layer as a direct consequence of the use of different blocking agents. From the data that are presented it is seen that both the viscosity of the oligomers and also their temperatures of vitrification vary widely.

The problem of molecular construction in such systems are not exhausted by a guarantee of the possibility of layered growth but require maximum flexibility of approach in order to control the form and density of intramolecular packing and also the quantitative and qualitative composition of the functional groups in the surface layer of the oligomer. Comparing the schemes for dendrimers with organic and inorganic skeletons, it can be noted that in both cases it is possible to use different initial branching centres. Thus Newkome[26] demonstrates tri- tetra- and hexa-functional branching centres for organic systems. For organosiloxane systems in the same way it is possible to use various compounds, for example;[22]

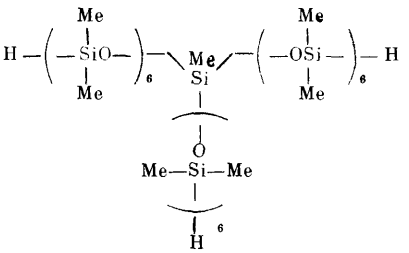


As regards the choice of reagents that meet the requirements for the use of general Scheme 2 for the construction of regular dendritic structures, it can be noted that the number of organosilicon monomers exceeds that of the organic analogues, although at the

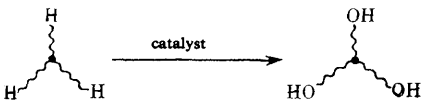
present time they are almost all of the same type. Organic reagents are notable for their diversity, making it possible to obtain amidoamino and polyoxyalkylenic oligomers, in addition to those based purely on carbon. Furthermore, it is clear, that in the use of siloxane systems both the process of building up of the layers, and the conversion of functional groups into the active form involve two reactions, whereas in the majority of organic systems that have been investigated, the conversion of functional groups into the active form requires four different chemical reactions.[6,26] More recently a short communication[27] has appeared on the synthesis of polyorganosiloxanes of the starburst type using a different functional basis and reagents of a larger size than were considered by us above. In this case, the following was taken as a particular reagent:



and as a branching centre:



Conversion of form B into form C was carried out according to the following scheme:



This example also shows that in the field of organosilicon polymers, three-dimensionally growing systems are not excluded and that the reagents which are used can themselves be diverse.

In conclusion let us refer to possible trends in the uses of three-dimensionally growing polyorganosiloxanes. Firstly they find application, as do the organic analogues,[2] as standards for HPLC, electron microscopy, and the calibration of membranes. There are prospective uses in biology and medicine for three-dimensionally growing polyorganosiloxanes as soluble polyfunctional matrices, with variable characteristics in the surface layer at which different biomolecular assemblages can be attached. There are also good prospects for the use of new polymers in the fields of microelectronics, conducting materials, and membrane separation technology, etc. However, in the course of making these new materials, still wider investigations will be necessary into the development of the necessary basic reagents, the properties of three-dimensionally growing polymers of different structure and composition, and new synthetic approaches to the control of structure and properties.

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Translated from *Uspekhi Khimii* **60** 1617–1644 (1991) U.D.C. 541.636:541.127:547.26'118

Steric effects: the problem of their quantitative assessment and manifestation in the reactivity of hetero-organic compounds

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ABSTRACT. Literature data on the methods of quantitatively assessing steric effects and their manifestation in the reactivity of various hetero-organic compounds is systematised. The authors' own results are considered in the light of a model of frontal steric effects and of a calculated scale of steric constants R_s, the high effectiveness of which has been demonstrated in more than 100 reaction series involving organic and hetero-organic compounds.

The bibliography contains 202 references.

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I. Introduction

Current ideas on the effects of the spatial structure of molecules on their reactivity embrace many diverse phenomena. The overall interaction of substituents with a reaction centre is assumed to be subdivided into inductive, resonance and steric components.

When attempting a quantitative assessment of the steric component investigators have frequently encountered a problem when choosing parameters reflecting the steric effect of substituents. The presence of many steric scales complicates such a choice. The assessment of spatial effects in the chemistry of hetero-organic compounds (HOC) was problematical until recently owing to the uncertainty of its overall theoretical character. Whether steric effects actually influence the reactivity of HOC was still in question.

The present review is devoted to a discussion of studies affecting both aspects of the problem. In addition to an analysis and comparison of the existing methods of calculating steric effects attempts will be made to use these methods for the analysis of the reactivity of HOC. In those cases when the material of the present review partially overlaps reviews published already the appropriate references are given.

II. Quantitative methods of assessing steric effects

1. General concepts of steric effects

a) History of their development

It is considered (see Ref. 1 and literature therein) that the idea of a steric effect was introduced for the first time by Khermann in the mid-nineteenth century to explain the chemical inertness of substituted quinones by the steric effect of *ortho* substituents. Up to the thirties of the present century the concept of a steric effect was widely drawn upon by Hofman, Menshutkin, Holleman, Conant and other authors to explain chemical phenomena. However the development of steric effect theory later went into a decline caused by the predominant attention paid by investigators to the inductive effect of substituents.

Subsequently the reactivation and blossoming of steric effect theory was linked mainly with the precise quantitative investigations carried out by Ingold, Brown and Taft (see Ref. 2 and literature therein).

At present the steric effect shown by a substituent is recognised as steric hindrance or cooperation in the course of a reaction as a result of which there is a change in valence angles and coordination number of the reaction centre during the reaction or on activation.[3] The concept of a substituent shielding a reaction centre is widely used.[4] The drawing together of molecules in space is considered to be the most important factor determining the energy of activation.[5,6] According to contemporary ideas[7–9] steric effects for processes occurring in solution reduce in many cases to the hindrance which a substituent creates for solvation of the reaction centre. Finally, steric effects of substituents may be manifested by the inhibition of resonance structure formation.[4]

These factors of structure and reactivity have been considered in adequate detail for organic compounds in the review literature.[3,10–13] For hetero-organic compounds these aspects have not as yet been generalised in any appreciable manner although there are individual reviews concerning compounds of phosphorus, silicon and nitrogen[9,14–18] and a whole series of individual papers and series of papers on the chemistry of other elements in which some aspects of the spatial effect of substituents are considered. It must be noted that the possibility of the actual manifestation of steric effects in HOC chemistry was discussed comparatively recently,[19] although there are numerous investigations, including some carried out at the quantitative level,[20,21] pointing in favour of the existence of such an effect.

An extremely important factor moderating the study of steric effects until now has been the absence, in spite of many experimental data, of a satisfactory physical model of steric interactions, although the latter are linked in a sense with the spatial structure of

molecules.[3] Taft, for example, considers that the more bulky (or more branched) the interacting group is and the closer it is located to the reaction centre then the stronger these interactions will be. It is assumed that these correspond to repulsive forces.[13,22]

At the present time quantitative methods of calculating the steric effect comprise quantochemical, topological, structural and experimental approaches.

2. Methods of molecular mechanics and quantum chemistry

In the theoretical approach to the study of steric effects it is most important[3] to consider the combination of phenomena united by the term 'spatial effects of substituents' as a part of the more general problem of conformational analysis. Consequently a quantitative calculated–theoretical approach to the study of spatial effects must be based on the achievements of theories of conformational analysis,[4] i.e. on quantochemical calculations of the total energy of a molecule as a function of the angles of rotation, which enable the most stable conformation to be established.

It is accepted (see Ref. 2 and literature therein) that the general theory of spatial effects was first formulated in 1946 by Hill who showed that the energy of any molecule (or activated complex) may be described as the sum of the van der Waals potential energy (for the interaction of non-valently linked atoms) and the energy required for the deformation of bond lengths and valency angles of the molecule.

$$SE=E_r(r)+E_\theta(\theta)+E_\varphi(\varphi)+E_{nb}(d), \quad (1)$$

where SE is the system energy, E_r is the energy for deformation of bond length, E_θ is the energy for deformation of valency angles, E_φ is the torsional energy and E_{nb} the energy of non-bonding interactions.

The energy minimum corresponds to the optimum conformation of the molecule. The mathematical problem therefore reduces to varying the structural parameters in the search for the energy minimum.

The approaches of various authors have differed, as a rule, by ignoring some or other of the components of Eqn. (1) or by including additional terms and by the form of the potential function, the force field and by the mathematics and programs provided.

The method,[23] which has received the name atom–atom potential functions, was first applied to the calculation of the spatial influence of substituents in substitution reactions at a saturated carbon atom.[24] The agreement of calculated and experimental data was fairly satisfactory considering that the calculations were carried out manually. After a twenty-year break the studies were continued using computers (see Ref. 2 and literature therein). Initially the calculation plans were most simple, being stepwise, and were then improved by considering an analysis of the energy differences linked with a change in each coordinate of a mobile atom. The Engler 73 and Allinger 71 force field programs were developed.

The approach modified in this way, called the force-field or molecular-mechanics method, is better than previous methods since the set of structural parameters and deformation values used is appreciably improved, the choice of potential function is easier and the calculation procedure for the user is simplified.

The method of molecular mechanics has been used in various branches of organic chemistry. The results of the previous studies of Ingold on the S_N2 process have been re-examined (see Ref. 2 and literature therein) using more precise models. The method proved to be applicable to explain the processes of solvolysis of carbocations and their rearrangements and for conformational calculations of molecules and certain reactions.

DeTar[25] has proposed assessing steric effects using hydrocarbon models. The method considered afforded an explanation of the results of certain reactions[26] and proof of the steric sense of the experimental Taft constants, E_S.[27]

In a series of studies Kalamov and Kuzmin[28–32] developed and verified an approach to the assessment of the steric factors of reactivity based on calculation of the energy of the various conformations of a substrate and an intermediate within the framework of a force field model. By varying the torsion angle and the distance to a reactant a picture was constructed of the potential surfaces which enabled the reactivity of the compounds investigated to be analysed qualitatively and the stereochemical result of a reaction to be explained.

The steric index of reactivity (SIR) was introduced by these authors[28–32] for the quantitative description of the steric effects. This correlates satisfactorily with the E_S constants of alkyl groups and also with the rate constants for the hydrolysis of various esters. Such an approach also enables the stereochemical result of the reduction of α-substituted β- and γ-ketoesters to be explained.

Another approach[33] to the quantitative assessment of steric effects is based on the analysis of the overlap volumes of van der Waals shells of pairs of reactants. A good agreement of calculated and experimental data was achieved. This and methods similar to it are applied mainly to the correlation of biochemical data and biological activity (see Ref. 2 and literature therein).

Recently *ab initio* quantum methods have been developed for the calculation of potential barriers to internal rotation and of the total energy of a molecule as a function of the angles of internal rotation.

The approach proposed by Becker[34–36] is considered to be the most fundamental among this group of methods. Steric effects of substituents are proposed as the manifestation of particular conformational relationships.[34–36] However at the basis of Becker's method there are complex mathematical calculations and parameters which are difficult to determine and which hamper its practical use. It is necessary to mention the work of Bohle[37] on the development of optimisation programs based on Becker's approach in which a satisfactory description of the steric effect of alkyl substituents was achieved with specific assumptions. However it is also unlikely that this modification will be successful in the short term.

Periodically studies have appeared using various methods of disregarding differential overlap in calculations, such as CNDO, CNDO/2, MNDO, CS-INDO.[38–42] However the results of calculations did not always agree with the experimental data.

Various MO methods have been applied with varying success to the calculation of rotational barriers[43,44] and the investigation of various reactions.[45,46]

3. Topological methods

Topological indices have been applied in chemistry comparatively recently and have already acquired a wide reputation (see Refs. 2 and 47 and literature therein).

The development of topological approaches is linked with the application of graph theory. Usually an abstract mathematical structure, the so-called 'molecular graph', is characterised by two matrices, a proximity matrix A and a distance matrix D. The topological indices are quantitative characteristics of such graphs and represent various combinations of the elements of both matrices and reflect some aspect of the structure of the molecule.

The topological index was first introduced by Weiner (see Ref. 2 and literature therein). He introduced the W index denoting the number of edges connecting all pairs of apices to one another and showing the extent of branching of the molecule. Like W the I indices, the Platt index f, and the index N_2 derived from it, depend on the number of linking edges but in a different manner. The Hosoi index Z reflects the distance between all the unconnected apices. The indices of Gutman (M_I), Randic (χ) and Kier–Hall (h_x) are indicators of the extent of substitution at each apex.

A new group of informational indices I_{PC} and $\bar{I}_{PC}$ was introduced by Bonchev. These indices are combinations of indices W, Z and χ.

The group of centric indices of Balaban reflect the structure of a tree-like graph and is also linked with the geometric structure of the molecule.

The topological indices represented above and certain others are considered in a more detailed manner in the review[2] and in the literature cited in it.

Topological indices are intuitively linked with the structural parameters of molecules[2] but there are very few quantitative investigations of them. Recently Balaban[48] has correlated 14 known topological indices with molecular refraction and van der Waals volume. The best correlations were obtained for the indices W, I, χ and the informational indices I_D^W and I_D^E. This enabled a conclusion to be drawn on the similarity of these indices with the experimental constants E_S and v_X. In addition it turned out that all 14 of the indices investigated were linked linearly to one another which prevented the creation of a new superindex of the linear combination of several of the known indices. However in several cases the correlation of experimental data with the indices of Randic[49] and Kier–Hall[50] proved to be successful. A linear connection between the Randic indices and steric constants has also been recorded.[49]

The lack of consideration of the conformation of a molecule is a considerable drawback to the use of the indices mentioned. This drawback is removed when using the DARC system of Dubois (see Ref. 2 and literature therein). However this system is an order of magnitude more complicated than the 'disordered' topological indices.

The topological indices may be and already are being used for the calculation of steric effects, for example in computer synthesis programs. However the absence of a clear physical and geometric meaning and also the lack of consideration of the conformation of molecules restrains their application.

4. Structural and geometric scales

The approaches to the modelling of steric effects using various structural, geometric and physical parameters differ from the previous two by the considerable simplification of the mathematics used, by its more graphic nature and by a clear geometric meaning. As a rule available structural parameters, such as valence angles, atomic, covalent, van der Waals radii of atoms and bond lengths, are used as the initial data.

Attempts to create similar accessible methods for the calculation of steric effects were undertaken long ago and were unsuccessful initially. For example some authors compared distances between chemically unbonded atoms with the sum of their van der Waals radii.[51] Such a comparison was usually uninformative but sometimes this method gave acceptable results.

Intramolecular covalent radii, proposed by Bartell[52] as a measure of steric effects, have also not been widely applied.

Tolman's method of cone angles has proved to be more popular. The plane angle subtended at the apex of a cone tangential to the whole ligand was proposed as a measure of the steric effect of the ligand in transition metal complexes.[14,53] However the precision of the measurements conducted at the scale of the model was not high and the method has not enabled linear relationships to be obtained between the stability of complexes and the steric effect of ligands. It succeeded only in explaining qualitatively the effect of some ligands and in placing them in a series according to the order of increasing steric effect.

$$(CH_3)P < (C_2H_5)_3P < (C_3H_7)_3P < (C_6H_5)_3P < (\text{iso-}C_3H_7)_3P < < (\text{sec-}C_4H_9)_3P < (\text{t-}C_4H_9)_3P < [2,4,6\text{-}(CH_3)_3C_6H_2]_3P.$$

Tolman's cone angle model has been further developed in a series of studies[54–59] which has appeared recently. It is proposed to use the idea of 'coordination space' for the quantitative description of steric effects in the coordination sphere of a metal atom in complexes. This space is set by the Tolman cone angles of the ligand at a fixed (ionic) radius of the metal and the van der Waals radii of the atoms in the ligand. The concept of a packing function characterising the density of packing of ligands was also introduced.

This approach has enabled the molecular structure of several complexes to be explained. Rules have emerged for packing saturation, the geometrical parameters of complexes have been calculated and agree with data of X-ray structural analysis. Based on an analysis of the packing function the course of certain reactions has been successfully explained, such as the disproportionation and ligand insertion reactions.

The Tolman cone angle concept has also been extended to cluster systems.[60]

Tolman cone angles have been recalculated by Imyanutov[61,62] using a simple mathematical device and new values have been obtained. The more recent individual values for the extent of screening Λ_c of a central atom, characterising the part of the sphere occupied by the cone angle, proved to be applicable in coordination and organic chemistry and served (for a while) as a basis for a new scale of Λ_c constants.[63] However this scale does not always correlate well with the experimental E_S scale; the authors confined themselves only to a graphical correlation.

Tolman's approach served as a basis for the creation of the solid angle method. Initially[64,65] the steric hindrance generated by a substituent at a carbon atom was assessed on a semiquantitative basis. The solid angles cast by the atoms of a substituent on the sphere of the central atom was used as a measure of the hindrance. The method was used at the quantitative level more recently[66–69] by applying a computer for the calculations. A good correlation was obtained between the stability of a complex and the total solid angles of the ligand. The method also proved to be suitable for the assessment of the screening of individual atomic fragments (such as an individual chemical bond or individual atoms) of the remaining portion of the molecule.[66–69]

The concept of screening a reaction centre by a substituent has been used in many studies. It is thus considered obvious that any substituent screens a reaction centre but the extent of screening is determined by the area cast by the substituent. Approaches to the actual assessment of this area vary.

It was proposed[51,70] to assess the area of screening by the solid angle describing the substituent. The measure of the steric effect is the sum of the ratios $S_L/4\pi R^2$ where S_L is the area screened and R is the distance from each atom to the reaction centre. The equality

of this sum to unity indicates coordination saturation has been reached.

This approach is close in essence to the frontal steric effect model proposed by us two years previously[71] which is based on kinetic collision theory. In it the procedure for calculating the screened area is simpler. A scale of steric constants R_S is proposed which are linked linearly with the available experimental scales. More detail on this method and the different aspects of its application will be considered below.

An ideology almost identical to the ideology of the frontal steric effect served as a basis for the generation in 1989 of a scale of Ω_S constants.[72] This scale differs from the R_S scale only in the use of more complicated methods of calculation. It also correlates well with the E_S constants, but in contrast to the R_S scale gives distinct relationships for primary, secondary and tertiary alkyls. The Ω_S constants also correlate with certain experimental data.

Another direction for assessing steric effects is in essence close to the use of topological indices. Here the number of α-, β-, γ-, etc. carbon atoms is used to characterise the shape of the molecule.[73,74] This is less convenient since it requires several numbers for the description of a substituent[73] and it does not have such a clear geometric and physical sense as is possessed by scales based on the screening of a reaction centre by a substituent. For the same reason it is inconvenient to use parameters characterising the geometric shape of the molecule, such as the length and width in various directions proposed independently by Balaban[75] and by Verloop (see Ref. 2 and literature therein).

The number of carbon atoms in the sixth position in relation to the reaction centre in reactions of addition to an unsaturated system known as the 'six-number' of Newman[76] is used fairly widely (see Ref. 2 and literature therein) and is linked with the E'_S constants of Dubois.[77]

Steric effects are also characterised by parameters reflecting the size and shape of a molecule such as molecular weight or van der Waals volume. However these methods have not had particular success.

Structural methods, as a rule, describe fairly precisely the steric effect of a substituent. Their drawbacks are considered to be that they calculate for only one conformation, they have a static character and they ignore the second reactant. For the usual investigational purposes this is frequently not necessary. Special problems linked with a dynamic change in conformation may occasionally be resolved within the framework of these methods but requires other approaches. The solution of some of these problems will be considered below using the frontal steric effect model.

5. Experimental methods

Experimental methods of determining the steric effect developed completely by another independent route have been applied widely. These methods, proposed by Ingold and Taft,[3,13,78] are based on the principle of the linearity of free energies (LFE). This has been carried out for an enormous number of chemical processes and among them it is possible to pick out those in which the influence of one of the effects predominates. Taft[13,22] proposed that in aliphatic compounds there are powerful steric effects of substituents which must be separated from the electronic. He proposed assessing steric effects using the hydrolysis of carboxylic acid esters.[79] The inductive constants of aliphatic substituents were assessed at the same time.

$$\sigma^* = \frac{1}{2.48}[\lg (k/k_0)_B - \lg (k/k_0)_A],$$

$$E_S = \lg (k/k_0)_A,$$

where σ^* is the constant for a substituent depending exclusively on the overall polar effect of the substituent (corresponding rate constant k), k_0 is the rate constant for a standard compound with substituent CH_3, E_S is the constant of the substituent reflecting its steric effect, the indices A and B refer to the reaction of alkaline and acidic hydrolysis of carboxylic acid esters identical in all other respects. The factor 2.48 is a constant introduced with the aim of making the polar scale of σ^* within the limits of the same scale as applied by Hammett.

The E_S constants have been and still are widely applied in contemporary chemistry in reactions of nucleophilic substitution and fission at a saturated carbon atom (their use is possible both in reaction series analogues to the standard and in very different series) and in unsaturated systems, in catalysis and polymerisation processes, in the chemistry of free radicals, in processes of association in solution and in the gas phase and in spectroscopy. Periodically refined values of constants appear for certain substituents.[80] Correlations of E_S have been obtained with steric energy (ΔSE) calculated by the method of molecular mechanics[27] which, in the authors' opinion,[27] neatly proves the steric nature of the E_S constants.

The Taft E_S scale has been modified by Hancock[81] using a value of $h = 0.306$, calculated by MO methods, for the reaction series of ester hydrolysis, with the aim of calculating the contribution of the hyperconjugation of C–H bonds. The corrected values of the steric constants E_S^c, obtained in this way are linked with the Taft E_S values by the following expression:

$$E_S^c = E_S + 0.306(n-3),$$

where n is the number of hydrogen atoms on the first carbon atom of the substituent being considered and 3 is the same figure for the standard substituent CH_3.

The values of E_S^c lead in several cases to a marked improvement in correlations[82–84] compared with results obtained using E_S constants.

Pal'm has proposed taking into consideration the hyperconjugation of C–C bonds as well.[85]

$$E_S^0 = E_S - 0.33(3-n_H) + 0.13n_C.$$

Several scales similar to E_S have also been introduced. One of them (E_N) is based on the principle of isostericity for substituents at a nitrogen atom,[86] a second on the approach of DeTar[87] and a third on the E_S(Si) constants of Cartiedge.[88] Particular mention must be made of the E'_S scale (MacPhee, Panaye and Dubois[89–91]) determined from the acid esterification of carboxylic acids.

$$RCOOH + CH_3OH \xrightarrow{H^+,\ 40^\circ C} RCOOCH_3.$$

The E'_S scale is similar to the E_S scale for all substituents, except for the very bulky.

An E_S^* scale of constants, similar to the E'_S scale, has been introduced for reactions the transition state of which is analogous to that in hydroboration reactions.[92]

The scale of v_X constants, proposed by Charton,[93] is based on several other principles. The Charton scale may be described as semiempirical since v_X constants may be calculated fairly simply from

the following equation for monoatomic and for highly symmetrical substituents of the A_3B type.

$$v_X = r_{v_X} - r_{v_H} = r_{v_X} - 1.20,$$

where r_{v_X} and r_{v_H} are the van der Waals radii of the groups X and atom H. In addition an equation has been obtained within the framework of the standard reaction series of hydrolysis of carboxylic acid esters

$$\lg k_X = \varphi v_X + h,$$

permitting an empirical route for determining v_X constants for complex unsymmetrical substituents. Charton gave values for 61 v_X constants and also carried out an analysis of the correlation ratios between the experimental data and v_X, E_S, E_S^c and E_S^0 constants for data on 22 reactions of esterification and acidic hydrolysis. It turned out that v_X constants gave the best correlation.

The insignificance of electronic effects of substituents was shown[94] in a continuation of the study of alkaline hydrolysis of esters. Correlation with v_X constants again gave excellent results.

In reactions occurring by an S_N2 mechanism,[95] the use of v_X constants did not lead to a very good result since in this case the type of reaction centre, and consequently the structure of the activated complex, is changed. Introduction of a v' scale of constants for substituents at a sp^2-hybridised reaction centre enabled successful application of correlation analysis to these systems. It transpired that the sizes of the steric effects in S_N2 reactions are greater than in esterification reactions.

Finally v_X constants have been used in the study of the kinetics of $E1$ and $E2$ processes, of internal rotational barriers, the hydrolysis of amides and the racemisation of chiral biphenyls (see Ref. 73 and literature therein).

The v_X constants have been shown to be additive.[96] In addition they proved to be applicable to the study of reactions with substituents present on atoms of oxygen, nitrogen, sulphur and phosphorus (see Ref. 97 and literature therein).

The investigation of the effect of branching in a substituent on the value of v_X constants is a logical completion of the studies on v_X constants.[73] The steric v_X parameters of alkyl, alkoxyl, thioalkyl and dialkylamino groups and also values of v' for alkyl groups have been described using Eqn. (2) with a good correlation.

$$v_X(v') = an_\alpha + bn_\beta + cn_\gamma + dn_\delta + i. \qquad (2)$$

Here the parameters n_α, n_β, n_γ and n_δ reflect the number of α-, β-, γ- and δ-carbon atoms. The correlation Eqn. (2) enables assessment of values of the v_X constants of a very large number of groups. In this scheme the E_S^c constants of Hancock and the E_S^0 constants of Pal'm are simpler steric parameters correlating only with the value of n_α, the coefficients a in which are different from those for v_X.

In spite of the wide and fairly successful application of the empirical scales they are constantly subjected to critical analysis and are occasionally disputed. The main attention of critics is paid to the E_S scale of Taft and the scales derived from it.

In particular it has been shown[98] that the observed rate constant for the standard ester hydrolysis reaction is an effective (but not a simple) constant. The dissecting out of the rate constant for the primary bimolecular stage enabled E_S^b constants to be determined based on it, the values of which are different from the values of the Taft E_S constants. A dependence was also detected for the E_S constants on σ* constants having the form of several straight lines with the same slope for each individual number of α-hydrogen atoms.[99] This led investigators to the concept of the non-electronic nature of σ* constants, although σ* constants work successfully in many cases.[100] On analysis of the experimental data on the hydrolysis of carboxylic acid amides it was proposed[101] that the Taft σ* constants for alkyl groups do not reflect the electronic effect of alkyl groups. More recently Charton[102] discovered that the Taft constants correlate well with the degree of branching of the alkyl group at the α and β positions. From this it was concluded that the σ* constants reflect principally the steric effect of substituents.

Other authors have arrived at the same conclusion. When investigating σ*, σ_I and E_S constants DeTar[103] drew the following notable conclusions. The σ* constants of alkyl groups are inaccurate values which comprise a residual steric effect and experimental error. The use of any other nonsteric values for alkyl groups is also erroneous. References to the nonsteric effects of alkyl groups are based on incorrect data. The alternative scales, such as E_S^c and v_X have no special merit and should be rejected.

One of the main errors of Taft when determining the E_S scale has been considered[90] to be the *a priori* assumption that the various reaction series (acidic and alkaline hydrolysis) used for calculations have identical sensitivities to steric effects.

The lack of consideration of the conformational state of a substituent is described[2] as an appreciable drawback of the E_S scale although the importance of the influence of conformation on the steric effect of a substituent has been recognised by many authors.[73,104–106]

Much attention has been paid to the problem of the additivity of E_S constants. Taft himself recorded[13] that E_S constants were nonadditive but show a telescoping effect (the change of a constant in relation to the position of the substituent at the reaction centre). However certain authors[107,108] use ΣE_S in correlation analysis.

There is another possible approach to the consideration of the additivity of the constants. The following equation has been proposed.[107]

$$E_S(C_{XYZ}) = aE_S(X) + bE_S(Y) + cE_S(Z),$$

which enables various conformations of substituents to be taken into account and the E_S constants of any complex group to be calculated.

Much work has been devoted to a study of the physical significance of the E_S scale. Numerous attempts have been made to find the interconnection between the E_S constants and the various geometric and structural parameters of a molecule. For example, a linear relationship was discovered between E_S constants and the φ_{R_1} scale,[109] reflecting the contribution of the spatial stress built up by α, β and γ C–H bonds. Attempts to link the E_S values directly with the number of α, β and γ carbon atoms were not particularly successful[73] since a correlation was detected only with the number of α carbon atoms. Inherent geometric parameters of a substituent such as its length or width in two orthogonal directions proved to be completely unconnected with the E_S scale.[75]

Taking the results of all these investigations into account and also the recent work of Kramer[110,111] on the nature and additivity of E_S constants, it may be regarded as established that the E_S scale has on the whole a steric nature, its successful use in correlations is well founded in principle but it does not have a clear physical and geometric sense. It is not known which of the aspects or what proportions of steric effects it reflects. Certain actual values of the E_S constants need refinement, such as the E_S constants for the

t-BuMe$_2$C and t-Bu(t-BuCH$_2$)MeC substituents.[90] Recent achievements in solvation theory enable consideration of the appreciable contribution of solvation effects to the size of E_S constants. Thus the conclusion of Motoc and Balaban[75] on the need to create a new scale of spatial constants with a clearer physical, geometric or topological meaning is entirely well founded.

The E_S^c and E_S^0 scales, being derived from the E_S scale, have absorbed all of its drawbacks and virtues. In addition they proved to have their own specific defects. It has been made clear[90] that the size of the hyperconjugation coefficient h on both scales depends appreciably on the choice of reaction series and solvent which significantly reduces their universal nature. Pal'm[3] was guided by these same considerations when justifyng the need for the correction of the E_S^c constants. However it has been considered[90] that the E_S^0 scale is not completely free from the indicated drawbacks.

Even in the early studies of Charton doubt was expressed on the expediency of estimating the hyperconjugation components in the E_S^c and E_S^0 scales.[112,113] More recently these doubts became stronger[93] and then grew in confidence.[114] It was shown that all the results previously explainable by hyperconjugation may be interpreted by drawing on electronic, steric and polarisation effects alone and there is no need to use the E_S^c and E_S^0 scales. Istomin and Baranskii arrived at the same conclusion almost simultaneously.[115]

The ν_X scale being semiempirical has nonetheless acquired the drawbacks of the experimental scales, namely a dependence on the conditions and precision of the experiment. In its calculated portion it is also not completely reliable for large and unsymmetrical substituents.[90] Charton himself acknowledged that the values of ν_X for such groups may have not one but at least two values, a minimum and a maximum.[112] It turned out that neither correlates with the value of log k determined experimentally or with the experimental ν_X constants.

In conclusion it must be noted that in spite of a proposal to give up the use of experimental scales,[116] they still remain a common and useful instrument in correlation analysis and are a good basis for creating, testing and developing a new generation of steric constants.

III. Steric effects in the chemistry of hetero-organic compounds

Historically organic chemistry was the first area where the theory of steric effects was applied. There are examples demonstrating the influence of steric effects on the course of the nucleophilic substitution reaction.[117,118] The majority of the existing methods for the quantitative estimation of steric effects are based on the data of organic chemistry. The literature data on this theme are contained in numerous reviews.[3,10–12] Some of these studies have been referred to by us above so we will not consider them in more detail.

There is also the question of estimating steric effects in hetero-organic chemistry. For a long time it was considered[19,119] that steric effects were insignificant in the chemistry of phosphorus and the majority of other elements in view of the large size of the atoms of these elements. Information on steric effects was vague, sketchy and only at the qualitative level.[120,121]

However the experimental results accumulated up to the present indicate that the role of steric effects in the reactivity of HOC is far more substantial than was supposed previously. It is sufficient to note the opinion which is now established in the literature[17,94] that alkyl substituents in general do not exert any effect other than steric.

Numerous studies have appeared (see for example Refs. 15, 16, 53) in which there is a description of a steric effect at the qualitative level in the chemistry of boron, silicon, phosphorus and other elements.

It is recorded[4] that steric effects play a more varied role in HOC chemistry than in carbon chemistry. Spatial effects have an influence in three areas, viz. reactivity, complex-forming ability and conjugation. The majority of the existing steric scales of substituents are applicable only to the first area. Consequently it is probable that the literature data concerning the chemistry of various elements describe mainly the effect of substituents on the acid–base properties of HOC and on their reactivity in reactions of various types. On varying the nature of the reaction centre the problem inevitably arises of the possibility of applying the carbon scales of steric constants. Opinions are divided concerning this. On the one hand it is considered[3] that the carbon experimental scales of the E_S type are inapplicable for describing steric effects in HOC chemistry and the introduction of special scales is required. On the other hand Charton (see Ref. 97 and literature therein), when obtaining scales of ν_X constants for nitrogen, oxygen, sulphur and phosphorus, discovered their linear interrelation and concluded that special calculations were unnecessary and that the carbon steric ν_X constants for substituents may be used to describe the reactivity of any HOC (see Ref. 73 and literature therein). The E_S constants have proved to be applicable in phosphorus chemistry.[20]

Steric Λ_C constants have been calculated for more than 20 atoms[122] and an empirical link has been discovered between the scales obtained, which is characterised by discrete parameters unconnected with dimensions or with any characteristics of reaction centres.

On the whole the situation remains unclear and the same variety of scales of steric constants are applied for the estimation of steric effects in HOC chemistry. The main bulk of data relates to the description of steric effects in the chemistry of nitrogen, sulphur, phosphorus and arsenic.

1. Steric effects of substituents at a nitrogen atom

When studying steric effects in nitrogen chemistry two predominant directions of investigation stand out, viz. effects on the basicity of amines and effects on the reactivity of amines, amides and related compounds in various reactions.

The study of the basicity of amines was begun in the forties with the work of Brown and co-workers. The results of these studies have been published in a review,[1] consequently we will not analyse these results, we mention only that they led mainly to the determination of basicity constants and the discovery of the anomalous order of the change in basicity of the methylamines.

$$NH_3 < CH_3NH_2 < (CH_3)_2NH > (CH_3)_3N.$$

It has been recorded (see Ref. 9 and literature therein) that the changes in basicity of various classes of amines in all solvents are governed by the same rules and are linked with structural changes and special features of the molecule. This is caused mainly by the electronic effects of substituents and the effects of the medium, actual steric effects only apply to branched residues.

However there are examples of successful correlations of pK_B with σ^* and E_S constants (see Ref. 9 and literature therein). A scale of steric constants for alkyl substituents has even been developed[123] and differs from the Taft scale.

According to a contemporary concept[124] the mechanism of the steric influence on the basicity of amines is included in the steric hindrance of solvation. However for a complete solution of the problem of steric influence (including anomalous changes in basicity) it is necessary to think of the change in the configuration of the atomic orbitals of nitrogen, and in the state of the unshared electron pair responsible for basicity, being connected with the change in nature and number of alkyl groups and the symmetry of the alkylamine.[9]

The influence of the structure of amines on their reactivity was even recorded by Menshutkin[125] but attempts to assess steric effects quantitatively were undertaken relatively recently. Carbon scales were also used and new scales of steric constants have been introduced.

However the latter are, as a rule, only modifications or extensions of scales known already. Examples are the constants of Charton $\nu_X(NR^1R^2)$ which correlate well with various experimental data.[126]

A new standard reaction series has been proposed[127] for determining the steric influence in iodo-lactonisation of (*R*)-*N*-allyl-aminoacetic acids but no new scale was built up based on this series.

The best known is the scale of E_N constants,[86] which were obtained using the isostericity principle and are the constants of the corresponding carbon analogue. The E_N constants are applied widely to describe the various reactions of amines with alkyl halides,[128–132] such as the Menshutkin reaction,[133,134] and also nucleophilic addition reactions[135–140] and in the study of catalytic activity.[141]

At the same time the equation generally used

$$\lg k = \lg k_0 + \rho\Sigma\sigma^* + \delta\Sigma E_N,$$

does not enable the reactivity of all amines to be described. The deviations observed are taken[142] to be explained by two reasons, viz. by the imperfections of the principle of isostericity and by the presence of specific non-steric interactions of certain substituents with the reaction centre (by the formation of an intramolecular hydrogen bond for example).

It has been proposed[142] that a third and most important reason may be an incorrect allowance for electronic effects. In view of the combined opinion[87,103] on equating the inductive effects of all alkyl groups to that of a methyl group it was proposed[142] to take only the steric effect into consideration. In this case

$$\lg k = \lg k_0 + \delta E_S' + \rho_H^* n_H \sigma_H^*,$$

where n_H is the number of hydrogen atoms on the nitrogen, $\sigma_H^* = 0.49$ the inductive constant for the H atom, ρ_H^* is a coefficient showing the sensitivity of the reaction centre to substitution of a hydrogen by an alkyl group, E_S' is the modified MacPhee scale,[90] differing from the E_S scale by the larger range of substituents and better self-consistency.

The classical E_S constants have been used for calculations of steric effects in some correlations[143–146] and the E_S^0 constants in a further study.[147]

2. Steric effects in the chemistry of organosilicon compounds

The influence of steric effects of substituents on the reactivity of the most varied organosilicon compounds at the qualitative level has been discussed very widely in the literature. One of the first investigators who attempted a quantitative description of steric effects was Sommer[148] when recording the combined influence of steric and electronic effects in solvolysis and chlorination reactions in compounds containing the R_3Si fragment. The E_S constants for the alkyl substituents on the silicon atom were calculated on the basis of literature and the authors' own kinetic data. Sizes of the deviation from the dependence of log k on σ^* for various reactions taken from the E_S constants were not mutually consistent and had no particular practical importance.

The conclusion has been drawn (see Ref. 149 and literature therein) on the basis of a comprehensive analysis of literature data that the manifestation of steric effects of substituents was important in many reactions of compounds of the R_3SiX and even R_2SiX_2 types (R is an organic substituent and X a functional group). In all cases steric effects were suitable for describing compounds with three alkyl substituents on silicon. Occasionally such an approach is also applied for substituents having iso-structures. In certain reaction series the reaction kinetics were interpreted successfully only using the steric constants E_S^c and E_S^0, for example in the hydrolysis of R_3SiH, the methanolysis of siloxanes, the ozonolysis of silanes and in the hydrosilylation reactions of 1-hexyne.

It has been emphasised[149] that the absence of a direct correlation of reactivity with steric constants does not imply that the steric effect makes an unimportant contribution since in these cases, as a rule, substituents are used which differ little in their steric characteristics.

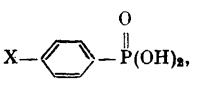
The use of scales based on the degree of branching of substituents[150] and the E_S(Si) steric scale of Cartiedge[88] must also be noted. A series of acid hydrolyses was used as the model.

$$R_3SiOR + H_2O \xrightarrow[-ROH]{EtOH,\ HCl,\ 25^\circ C} R_3SiOH.$$

The E_S(Si) constants obtained correlated best of all with the Charton ν_X constants and possessed the property of additivity. However these scales are not used widely and in several cases (see Ref. 151 for example) correlation with E_S constants was significantly better than with E_S(Si).

3. Steric effects in the chemistry of organophosphorus compounds

Study of the quantitative interrelation between the structure of organophosphorus compounds (OPC) and their reactivity began around 1953. The first studies[152–154] showed that the Hammett equation was applicable to the ionisation of phosphonic acids of the form



where X is the substituent being varied. The Hammett constants and the Taft σ^* constants were used to characterise the influence of the substituent X. With the purpose of building up a scale of similar constants for radicals joined to phosphorus (σ^P), Kabachnik[119] subjected the literature data on the pK_a values of the phosphorus acids $RPO(OH)_2$, $R^1R^2P(S)OH$, $R^1R^2PO_2H$ to quantitative treatment using the Hammett equation in the form

$$pK_a = pK_a' - \rho\Sigma\sigma^P.$$

It must be noted that in all cases only the electronic effects of substituents were taken into account. It was proposed[19,119] that steric effects were insignificant in view of the large size of the phosphorus (or other element) atom.

This opinion has been held for a fairly long time.[120,121] However with the subsequent accumulation of new experimental data the σ^P scale has been subjected to careful analysis and its relation to steric effects has been reconsidered.

It has been shown[115] that the σ^P constants of alkyl groups and electronegative substituents having no α,β multiple bonds or unshared electron pairs on the α atom are combined values and contain inductive and steric components. The inductive and steric components are described adequately by the scales accepted in correlation analysis for the corresponding types of interactions using the σ^* and E_S scales, i.e. the phosphorus atom does not require any special scales.

Consideration of the standard reaction series used as a basis of the σ^P scale also showed[156] that the experimental values are described adequately by a single correlation equation using the σ^* and E_S scales. It was noted that the principal difficulty when considering such broad sets of data obtained by different authors was the lack of self-consistency.[157]

In a review[20] of the results of a correlation analysis of organic derivatives of pentavalent four-coordinate phosphorus it was shown that the σ^P constants widely used in the chemistry of OPC are complex and include contributions from the inductive, steric and resonance interactions of substituents with the reaction centre. The σ^P scale is applicable to those cases when the proportions of the various contributions to the overall effect of a substituent and the structure of the reaction centre in the series of compounds being studied are the same as or close to the values on which these constants are based in the standard reaction series. In other cases a different approach must be sought.

The $\nu_X(P)$ scale of Charton obtained for substituents at a phosphorus atom may serve as one of such approaches to the assessment of spatial effects.[97] The successful use of the carbon ν_X scale in OPC chemistry is also possible. There are also data on the successful application of E_S constants in correlations with pK_b values of alkyldiphenylphosphines.[158]

Relying on data of recent years[101,159] regarding the electrical neutrality of alkyl groups an approach has been suggested[17,21] involving the separation of the σ^P constants into inductive (σ_i^P), resonance (σ_r^Φ) and steric (σ_s^Φ) components. The σ_s^Φ scale was then used successfully to correlate the chemical and biological activity of OPC[160–164] and evidently the approach must be acknowledged to be totally fruitful.

At the same time when separating the σ^P constant into its primary components the authors[17] used certain assumptions which from our point of view were not completely argued through. For example the E_s^0 constants of alkoxyl groups were estimated on the basis of isostericity (from the E_s^0 constants of the isosteric alkyls) and these values were then included in the overall correlation with alkyl substituents virtually giving the isosteric constant the significance of the true constants. In a way this may be one of the reasons for the low quality of the correlation (r = 0.92) in the overall reaction series including alkyl and alkoxyl residues.[17]

Various approaches and combinations of scales are used when describing the influence of steric effects on the reactivity of OPC. The carbon scales are frequently used which is quite understandable because of the discovered similarity of the influence of substituents on the reactivity of compounds of phosphorus and carbon[165] and of phosphorus and silicon.[166]

The stability of complexes of $(RO)_3P$ with R_FI, as has been shown,[167] correlates poorly with the value of σ^P, particularly for branched substituents, the reason for which[167] is the lack of consideration of steric effects. A satisfactory correlation was achieved with the joint use of E_s and $\Sigma(\sigma_i^P + \sigma_r^P)$ constants. At the same time the acid–base properties of R_3PO with alkyl and alkoxyl substituents correlate quite successfully with the σ^P constants.[168] Consequently the σ^P scale works well in some cases[169,170] but must be replaced by different scales in others.[171]

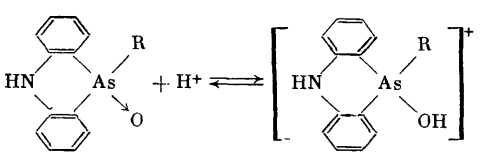
Occasionally it has been proposed in discussion to discard the apparatus of correlation in general and to replace it by methods of linear algebra.[172] However it is doubtful whether this suggestion meets with wide response.

In general the variety of quantitative approaches and the unpredictability of the importance of one or other parameter in the various correlations is extremely inconvenient in practice. A search is needed for a universal scale enabling description as far as possible of all cases of steric interactions in OPC chemistry.

As will be shown below the use of the calculated R_s scale, proposed on the basis of a model of the frontal steric effect,[71] gives good results when describing the very varied reaction series involving OPC.

4. Steric effects in the chemistry of organoarsenic compounds

Steric effects have not been considered in the few quantitative studies of the properties (mainly acid–base) or organoarsenic compounds up to the present time. The available data on the acidity of certain alkyl- and arylphosphonic acids and on arsinic acids in water[173] and in DMF[174] and data on the basicity of tertiary arsine oxides[175] correlated either with the σ^* constants or with σ^P constants. Correlation was better with the Taft inductive constants (σ^*). Analysis of the basicity of 10-alkyl-5,10-dihydrophenarsazines showed a very unusual dependence of pK_b on the σ^* constants.[176]



The values of pK_b for the alkyl-containing compounds in the series R = CH_3, C_2H_5, iso-C_3H_7, t-C_4H_9, $CH_2{=}CH{-}CH_2$, Ph, Ph–C≡C, OH lie on a separate straight line with a positive ρ coefficient although when the inductive influence predominates the value of ρ must be negative. A link was also detected between pK_b and parameters characterising the branching of a substituent. It was concluded[176] that another effect, which requires clarification, exerts an influence.

In our opinion, allowing for all the above-mentioned it may be deduced that the effect in question has a steric nature, although confirmation of this must finally be obtained experimentally. Regrettably there are still very few investigations of that type.

A Japanese study[158] is devoted to the examination of the nucleophilicity of a wide range of alkyldiphenylphosphines and -arsines (reaction with methyl iodide for example). A linear correlation was established between the nucleophility of phosphines and arsines expressed by the equation

$$\lg k_{As} = 0.49 \lg k_P - 3.14.$$

Phosphines are three orders of magnitude more nucleophilic than arsines. The nucleophilicity of both types of compound is described by a two-parameter Taft equation using σ^* and E_S constants.

Similar compounds of arsenic were investigated previously by Soviet authors.[177,178] It was shown that the nucleophilicity of arsines correlates with σ^* constants but does not correlate with σ^P, which the authors link with the possible manifestation of steric effects.

5. Steric effects in the chemistry of organosulphur compounds

The influence of steric effects on the reactivity of sulphur compounds was considered by Charton[97] who showed that the AlkS group possessed a constant electronic effect. The ν_x(SR) parameter for SR substituents was determined using the hydrolysis of alkylthioacetates in 40% aqueous dioxan as the reaction series. The ν_X parameters obtained were used in the analysis of 24 sets of acidic and alkaline hydrolysis. This enabled the conclusion that the effect of alkyl groups joined to sulphur was fairly large and had a predominantly steric nature.

The constants obtained have been used by other authors, for example in the investigation of the catalytic activity of thiols.[179]

The E_S scale is also widely applied in addition to the ν_X parameters. Processes successfully described with it are the oxidation of alkyl aryl sulphides,[180] the electron donating properties of sulphides,[181] the chemoselectivity of alkanesulphonates[182] and the catalytic sulphonylation of phenol with a sterically hindered sulphonyl chloride.[183]

$$RC_6H_4SO_2Cl + HOC_6H_5 \xrightarrow[-HCl]{(C_2H_5)_3N,\ C_6H_6,\ 40^\circ C} RC_6H_4SO_2OC_6H_5,$$

$$R = 2\text{-}CH_3,\ 2\text{-}C_2H_5,\ 4\text{-t-}C_4H_9,\ 2,4,6\text{-}(C_2H_5)_3,\ 2,4,6\text{-(iso-}C_3H_7)_3.$$

In the latter case, in fact, the E_S^0 constants were used.

Regrettably the limited amount of experimental data enabled a conclusion to be drawn only on the appreciable influence of steric effects in the chemistry of organic sulphur compounds but did not enable a comparative analysis to be carried out with compounds of other elements.

6. Steric effects in the chemistry of organometallic compounds

Literally a single study is devoted to steric effects in the chemistry of organometallic compounds (the chemistry of complex compounds is not considered here). Pal'm[3] has drawn attention to the reaction of alkylmagnesium bromide with pinacolin.[184]

$$RMgBr + CH_3\overset{\overset{O}{\|}}{C}C_4H_9\text{-t} \xrightarrow{\text{ether}} \begin{matrix} & CH_3 & & OMgBr \\ & \diagdown & \diagup & \\ & & C & \\ & \diagup & \diagdown & \\ & R & & C_4H_9\text{-t} \end{matrix},$$

which, in his opinion, might be used for obtaining a new scale of 'pure' steric constants. However this was not sustained.[184,185] Of the three parallel processes, viz. reduction, addition and enolisation, taking place in the reaction of pinacolin with RMgBr only the last two are linked with steric effects. The addition reaction is linked predominantly only with the steric effects of alkyl substituents and correlates with the E_S^0 constants. The rate of the uncatalysed reaction of $R_3SnOCOC_2H_5$ with phenyl glycidyl ether[186] and the rate of electroreduction of titanium and zirconium bis-(cyclopentadienyl) chlorides[187] are linked linearly with the same constants.

IV. A model of the frontal steric effect and its application to the analysis of the reactivity of organic and hetero-organic compounds

The numerous approaches to the assessment of the steric effect to describe the reactivity of organic and hetero-organic compounds indicates the need to search for a universal scale of steric constants ready for use in any region of organic and hetero-organic chemistry. Such a scale must probably be based on calculated structural methods such as the experimental scales linked to actual conditions and to the precision of an experiment. It must also consider the conformational state of a substituent. It is necessary, when changing the conformation of a substituent, to obtain refined values of the steric constants fairly simply. Finally, the universal nature of this scale must be subject to broad experimental verification. It is necessary that such a scale should describe, as far as possible, the maximum amount of experimental data correlated by other scales, while retaining a high degree of correlation.

We have attempted to create such a scale and verify it in a large number of different reaction series, including hetero-organic compounds.

1. A model of frontal steric effects and the R_S scale

A model of frontal steric effects and its mathematics have been presented in a fairly detailed manner[71,188] consequently a short description only will be given here. The basis of the model is the concept of the frontal character of the steric effect, i.e. simple mechanical shielding of the reaction centre by a substituent (Fig. 1). This model enables the steric effect of any substituent at any reaction centre to be described, proceeding only from its structure and conformation. Parameters describing the structure of a molecule, i.e. bond lengths and valence angles, are used as the initial data.

It is easy to show, within the framework of kinetic collision theory and a simple mathematical procedure, that the steric effect of a substituent is proportional to the area which it occupies on the sphere separating it from a reaction centre. The final expression for the reaction rate constant of a compound with a particular substituent has the following form:

$$k_R = \left(1 - \sum_{i=1}^{n} r_i^2/4R_i^2\right) Z \exp(-E/RT),$$

where r_i is the radius of each actual atom in a multiatomic substituent, R_i is the distance of this atom from the reaction centre, Z is the frequency of twin collisions and E the activation energy.

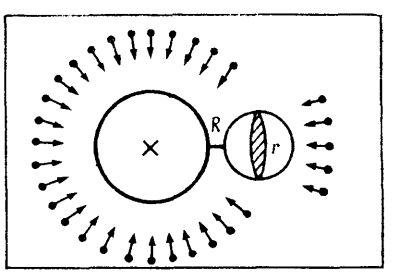


Figure 1. Attack at a substituted reaction centre.

The correctness of the model proposed was verified[71] by comparing values of the steric effect for substituents (first for alkyl and then others), calculated theoretically on its basis, with the existing steric scales E_S, E_S^0 and ν_X, which are based on hundreds of reaction series with steric control. An excellent correlation ($r \approx 0.99$) was obtained in every case covering the whole possible range of variation of steric effects (from +1.24 to −4.0 on the E_S scale), which indicates that proposed model describes steric effects in an adequately correct manner. In order to solve problems insoluble or soluble with difficulty within the framework of the existing experimental scales, a purely calculated steric R_S scale has been proposed which, for the reasons detailed,[71] has been introduced as

$$R_S = 30 \lg \left(1 - \sum_{i=1}^{n} r_i^2/4R_i^2\right).$$

This scale correlates well with the empirical scales and describes adequately the steric effect of the most varied substituents. For example the majority of halogen, hydroxy, alkylthio and alkoxy substituents are described satisfactorily by the relationship of R_S and E_S which applies to alkyl substituents.[71]

$$R_S = (-1.702 \pm 0.032) + (0.730 \pm 0.022) E_S, \quad n=35, \quad r=0.9854, \quad S_0=0.141. \qquad (3)$$

At the same time it must be emphasised that a strict physical interpretation cannot be conferred on such a limitingly simplified steric model.[71,188] In spite of the fact that the better quality of correlation as in (3) would justify assumptions to be made, the steric effects of a substituent undoubtedly cannot lead only to screening of a reaction centre, ignoring completely the energy contributions of other types of steric interactions. The screening effect must be considered as only one component of the steric effect which for some reason (possibly simply formal) is linked linearly with the total effect.

The proposed model is therefore more formal rather than physical. At the same time it represents a fairly successful means for the correct calculation of the steric effects of various substituents and may be extremely useful in solving the most varied problems. This will be illustrated below with some examples.

2. The principle of isostericity

The standard reaction series forming the basis of the empirical scales impose some serious limitations on the possibility of determining the steric constants of substituents. In the E_S scale, and the E_S^c and E_S^0 scales derived from it, the standard reaction series, viz. the hydrolysis of esters, does not permit determination of the steric constants of hetero-atomic substituents such as OR, SR, NR_2, etc.

In practice the isostericity principle is used in these cases, which means that the steric effect of any heteroatomic substituent is equated to the effect of the corresponding (isosteric) alkyl substituent.[3]

Since the model considered above enables direct calculation of the steric effect of any hetero-atomic substituent there is the possibility of verifying to what extent the indicated principle remains within this framework and what are the limits of its applicability. This was carried out[71] using as example a set of alkoxyl and thioalkyl substituents by comparing the R_S constants calculated for them with those for the isosteric hydrocarbon analogues.

It turned out that in each series excellent linear relationships were satisfied.

$$R_S(\mathrm{OR}) = (0.812 \pm 0.115) + (1.256 \pm 0.053) R_S(\mathrm{CH_2R}), \quad n=8, \quad r=0.9954, \quad S_0=0.058;$$

$$R_S(\mathrm{SR}) = (-0.459 \pm 0.039) + (0.976 \pm 0.018) R_S(\mathrm{CH_2R}), \quad n=8, \quad r=0.9991, \quad S_0=0.019.$$

It follows from the correlation equations obtained that the steric constants for OR and SR substituents are linearly related to the constants of the CH_2R group but are not equal to them. Hence it is evident that the isostericity principle must work well in sets of substituents of the same type (for example, only OR or only SR) but will not be effective in mixed sets.

Within the framework of the present model the application of the isostericity principle has a mathematical foundation but at the same time its limitations are clearly evident. However since it is possible to calculate directly the R_S constants for any heteroatomic substituent, the principle of isostericity in general loses its value in this scale.

3. The steric effect of substituents at non-carbon atoms

As was indicated above more data have appeared in the literature recently which indicate the appreciable contribution of steric effects in the reactivity of many hetero-organic compounds. In some studies the presence of a linear relationship between the steric effect of substituents at a heteroatom and at carbon has been suggested.

The R_S constants for 25 substituents at phosphorus, sulphur, arsenic and antimony have been compared with the constants for the same substituents as carbon with the aim of clarifying the sensitivity of various atoms to steric effects and detecting the presence or absence of linear relationships between the steric effects of substituents at these atoms and of the same substituents at a carbon atom.[189] This series has been extended more recently to 43 substituents at 20 elements (from hydrogen to lead).

It has been established[189] that the steric effect of a substituent is reduced uniformly with an increase in the size of the central atom. At the same time there was a strict linear relationship ($r > 0.99$) between the steric effects of substituents at each heteroatom studied and the steric effects of the substituents at a carbon atom.

$$R_S(\mathrm{E}) = A_0 + A_1 R_S(\mathrm{C}),$$

where $R_S(\mathrm{E})$ are the steric constants for substituents at any element and $R_S(\mathrm{C})$ are the steric constants for the same substituents at a carbon atom.

The results obtained are completely in agreement with the literature data mentioned above according to which the steric effects of substituents at various heteroatoms (particularly at atoms of phosphorus, sulphur, oxygen, nitrogen and silicon) are described well by correlation equations using the constants for carbon.

The linear dependence established between the steric effects of substituents at various atoms and at a carbon atom removes the problem of determining the steric constants for substituents for each individual element since it is possible, when analysing the reactivity of hetero-organic compounds, to use the steric constants for substituents at a carbon atom with equal success.

4. Steric effects and the conformation of a substituent

It is evident that the steric effect of any substituent within the framework of the model being considered is linked directly and in an extremely effective manner with its conformation. In particular the parameter R_i in the expression $\sum_{i=1}^{n} r_i^2/4R_i^2$, which corresponds to the distance from each of the atoms contained in the substituent to the reaction centre, is sensitive to conformation. On the one hand this points in favour of the adequacy of the model since the dependence of steric effects on conformation actually occurs.[2,73,104–106] On the other hand such a conformational sensitivity may seem to be an undesirable factor because the conformation may not be known precisely for each substituent. For the majority of substituents the problem of conformational uncertainty is either completely absent or one of several possible conformations is known to be obviously in existence. In such a case it is possible to go over to the reverse procedure, i.e. to determine which conformation exists in those substituents in which the proportion of conformational uncertainty is large. For this it is sufficient to compare the theoretical values of R_S for each of the possible conformations (as a rule there are no more than two) with the experimental parameter log k and to select that which is best described in coordinates of log k and R_S for the general series (a reaction series composed of conformationally unequivocal substituents).

An actual example of such an unusual conformational analysis has been described[71] for the substituents CH_2OCH_3 and CH_2SCH_3. Two of the possible types of orientation of these substituents relative to the reaction centre were examined, viz. the transoid and the conformation with free rotation about the CH_2-E bond. Comparison of the theoretically calculated values of R_S for each orientation with the values calculated according to the correlation Eqn. (3) from the experimental values of E_S showed that the methylthiomethyl substituent has a clearly expressed transoid orientation while it is impossible to exclude free rotation or the existence of a *gauche* form for the methoxymethyl substituent.

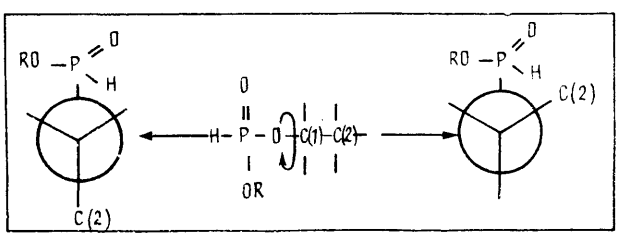


Figure 2. Conformations of alkoxy substituents in the Pudovik and Abramov reactions.

The dynamic stereochemistry of dialkyl phosphorus acids and their anions have been investigated in an analogous manner in the Pudovik and Abramov reactions.[190,191] It was shown that the reactivity and acid properties of the free dialkyl phosphites were well described by a choice of R_S constant corresponding to the least sterically hindered *trans* orientation of the P–O and C(1)–C(2) bonds in both alkoxyl groups on the phosphorus atom. At the same time the best correlation for the dialkyl phosphite anion was observed on proposing a *gauche* orientation for the P–O and C(1)–C(2) bonds in one of the alkoxyl substituents (Fig. 2). It is possible to explain such an orientation for the substituent by the electrostatic interaction of the anion and the alkyl group polarised by it.

Conformational sensitivity is therefore not a drawback of the proposed model but on the contrary makes it more flexible and more useful in a practical sense.

Table 1. Some types of reaction series described using R_S steric constants.

Series number	Type of reaction series	Q	N_{av}	R_{av}	Refs.
1	Existing scales of steric constants E_s, E_s^0, v_x	3	35	>0.98	[71]
2	Reactions of organic compounds of nitrogen	19	6	~0.99	[192]
3	Reactions of organic compounds of oxygen	8	5	~0.96	[192]
4	Reactions of organosilicon compounds	5	7	~0.98	[192]
5	Reactions of organophosphorus compounds	22	5	~0.99	[192]
6	Reactions of organic compounds of sulphur	4	5	~0.98	[192]
7	Reactions of organic compounds of arsenic	4	4	~0.98	[192]
8	Reactions of organomagnesium compounds	1	5	0.958	[192]
9	Dissociation of phosphoric, phosphonic and phosphinic acids in water and in aqueous alcoholic media	9	9	>0.99	[193]
10	Dissociation of dialkyl phosphites in absolute isopropanol	1	5	0.966	[190]
11	Addition of dialkyl phosphites to an unsaturated compound (Pudovik and Abramov reactions)	10	8	>0.98	[190, 191, 194, 195]
12	Complex formation of nickel and cobalt ions with cyclic and acyclic dithio acids of phosphorus	8	7	~0.97	[196]
13	Reactions of cyclic and acyclic isocyanatophosphites with diphenylcarbodiimide	2	4	>0.99	[197, 198]
14	1,3-Dipolar cycloaddition reactions to a phosphorylated allene and an acetylene	2	6	>0.98	[199]
15	Reaction of dithio acids of phosphorus with cumene hydroperoxide	4	66	>0.97	[200]
16	Williamson reaction in the chloromethylphosphine oxide series	2	24	~0.99	[201]
17	Reaction of gelatine with aldehydes	1	6	0.989	[202]
18	*cis-trans*-Isomerism of ethylenes	2	6	>0.97	[188]

Footnote. Symbols used: Q is the number of reaction series, N_{av} the average number of points in the correlation and R_{av} the mean correlation coefficient.

5. Analysis of the reactivity of organic and hetero-organic compounds

Since the proposed model enables steric effects to be calculated fairly simply for any substituent at any reaction centre it is natural that the largest area for its application is the analysis of steric interactions in the reaction series varying most widely and firstly

where the steric effects of substituents are not expressed adequately by the existing scales. This applies primarily to hetero-organic compounds although recently more data have appeared on purely organic reaction series containing complex branched or heteroatomic substituents, the steric effect of which may not be described in the empirical scales. In this case the theoretical calculation of the steric effect remains the only possibility for an effective analysis and prediction of reactivity.

Attempts to apply the proposed approach indicate its high effectiveness in describing the most varied reaction series both under purely steric control and with a mixed influence of electronic and steric factors within the framework of a multiparameter regression analysis.

Certain types of organic and hetero-organic reaction series which are described successfully using R_S constants are shown in Table 1.

The first 8 types of reaction series in Table 1 are literature data which have been processed previously using other steric scales. Comparative analysis of the quality of the correlations shows that the R_S scale describes the given reaction series in every case no worse than the various scales [E_S, E_S^0, ν_X, $\nu_X(NR^1R^2)$, $\nu_X(P)$, $\nu_X(SR)$, $E_S(Si)$, etc.] which were used in the original correlations. Experimental investigation of the remaining reaction series (series 9–18) were carried out by us either independently or in collaboration which is reflected in the corresponding literature references. It follows from Table 1 that the R_S scale gives good results when describing the reactivity of the most varied HOC in different types of reaction, from acid–base properties to processes of complex formation. In this way regularities often became apparent which could not be detected within the framework of the existing experimental scales. For example, on repeating the experimental study of the dissociation of various types of phosphorus acids (phosphoric, phosphonic and phosphinic)[193] not only were the pK_α values of certain acids successfully refined but it was also discovered that there were distinct relationships between pK_a and R_S for these types of acid, i.e. a given reaction series selected as a standard in HOC chemistry was not a single reaction series. This conclusion was also confirmed by studying the Brønsted relationships.

The approach proposed therefore turned out to be extremely effective in the analysis of the most varied chemical processes and also in solving theoretical problems connected with steric effects. Although simple it provides a fairly correct description of the steric interactions developing to a certain extent and of their nature. Using simple and available mathematics it enables calculation of the steric effects of any substituent at any reaction centre, starting from its structure and conformation, and may be useful in understanding and predicting interrelationships between the structure and reactivity of organic and hetero-organic compounds.

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Translated from *Uspekhi Khimii* 60 1645–1679 (1991) U.D.C. 547.425.5

Progress in the chemistry of perhalomethanesulphenyl halides

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ABSTRACT. Results of investigations on perhalomethanesulphenyl halides are systematised and correlated in the review. Methods of obtaining perhalomethanesulphenyl halides are reviewed and their nucleophilic, electrophilic and radical substitution, addition, oxidation and reduction reactions are discussed.

The bibliography contains 232 references.

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I. Introduction

The chemistry of perhalomethanesulphenyl halides began with the synthesis of trichloromethanesulphenyl chloride by Rathke.[1,2] However this region of hetero-organic chemistry had its most rapid development at the beginning of the sixties of the present century after the discovery by Kittleson[3] of the fungicidal properties of *N*-trichloromethanesulphenyl phthalimide and *N*-trichloromethanesulphenyl 1,2,5,6-tetrahydrophthalimide, which have been widely used as standard fungicidal preparations under the commercial names Ftalan and Captan. Trichloromethanesulphenyl chloride is at present the most widely studied perhalomethanesulphenyl halide. Convenient preparative methods (both laboratory and industrial) have been developed for obtaining it, its properties have been studied in detail and areas have been found for its application in practice. The structure of the trichloromethanesulphenyl chloride molecule has been investigated in the gas phase by electron diffraction,[4] from which it was established that the chlorine atom Cl(1) on the sulphur atom and one of the chlorine atoms of the trichloromethanesulphenyl group Cl(4) are in *trans*-disposition. The latter chlorine atom and the sulphur atom are drawn together somewhat because of the deviation of the C–S bond from the three-fold axis of the trichloromethyl residue as a result of which the SCCl(4) bond angle is 102° 5′. Such a peculiarity in the structure of the trichloromethanesulphenyl chloride molecule sets a stamp on its chemical properties. Thus the nonequivalence of one of the chlorine atoms in the trichloromethyl group [as a result of the deviation of the SCCl(4) angle from 109°] is displayed in the increased reactivity of Cl(1) and Cl(4) in free radical processes. The deformation of the SCCl(4) angle also facilitates intramolecular nucleophilic attack of Cl(1) on the carbon atom and makes the generation of dichlorocarbene possible. The other perhalomethanesulphenyl halides known at present have been investigated less and require further study. The interest displayed in the chemistry of perhalomethanesulphenyl halides by many investigators is explained primarily by the synthetic value of these compounds The high lability of the sulphur–halogen bond, its tendency towards heterolytic and homolytic fission, and also two reaction centres (sulphur and carbon) impart the properties of valuable synthons to the perhalomethanesulphenyl halides. On the other hand certain representatives of this class of compound, trichloromethanesulphenyl chloride and dichlorofluoromethanesulphenyl chloride in particular, are widely used in the manufacture of biologically active preparations which are of interest.

Several reviews[3,5–11] partially cover the chemistry of perhalomethylsulphenyl halides up to 1970, however, regretably there are no exhaustive studies. In our view the proferred review may compensate for this omission to some extent. The literature is covered up to 1990.

II. Methods of synthesis of perhalomethanesulphenyl halides

1. Perchloromethanesulphenyl halides

a) Trichloromethanesulphenyl chloride

Trichloromethanesulphenyl chloride was obtained for the first time in 1870 by the chlorination of carbon disulphide with chlorine in the presence of iodine as catalyst.[1,2] For a long time this reaction was the subject of investigation by many scientists with the aim of optimising the process of obtaining trichloromethanesulphenyl chloride both in the laboratory and in industry. This is linked primarily with the fact that in the chlorination of carbon disulphide with chlorine other products are formed in addition to trichloromethanesulphenyl chloride, particularly sulphur mono- and dichlorides and carbon tetrachloride. The probability of forming any particular product is due to a series of factors, mainly by the ratio of reactants, the chlorination conditions and the nature of the solvent. Depending on the ratio of reactants sulphur mono- and dichlorides are formed in addition to trichloromethanesulphenyl chloride in the chlorination of carbon disulphide, as illustrated by the following reactions.

$$2CS_2+5Cl_2\longrightarrow 2CCl_3SCl+S_2Cl_2,$$

$$CS_2+3Cl_2\rightarrow CCl_3SCl+SCl_2.$$

Sulphur mono- and dichloride are formed in the reaction of chlorine with carbon disulphide, the dichloride practically always predominating.[3] The formation of trichloromethanesulphenyl chloride by the reaction of chlorine with carbon disulphide at a ratio

of 2:5 occurs by the following conversions in the opinion of certain authors.[12]

$$2CS_2+2Cl_2\longrightarrow 2ClC(S)SCl,$$
$$2ClC(S)SCl+Cl_2\longrightarrow 2Cl_2C{=}S+S_2Cl_2,$$
$$2Cl_2C{=}S+2Cl_2\longrightarrow 2CCl_3SCl.$$

Although such a mechanism for the chlorination of carbon disulphide is confirmed to a certain extent by the formation of trichloromethanesulphenyl chloride in the reaction of thiophosgene with chlorine,[12,13] it has nevertheless been questioned.[14] These authors[14] considered that the addition of chlorine occurs at the two C=S bonds of carbon disulphide simultaneously with the formation of dichloromethanedisulphenyl chloride, the further chlorination of which leads to the formation of trichloromethanesulphenyl chloride.

$$2CS_2+4Cl_2\longrightarrow 2\left[\begin{array}{c}Cl\\|\\ClS{-}C{-}SCl\\|\\Cl\end{array}\right]\xrightarrow[-S_2Cl_2]{Cl_2}2CCl_3SCl.$$

A change in the ratio of the initial reactants in the direction of increasing the quantity of chlorine leads to a reduction in the yield of trichloromethanesulphenyl chloride and the formation of carbon tetrachloride which arises from the following reaction.[3,15]

$$2CCl_3SCl_2+Cl_2\longrightarrow 2CCl_4+S_2Cl_2.$$

The conversion of trichloromethanesulphenyl chloride into carbon tetrachloride is assisted by sunlight,[3] and also by the presence in the reaction mixture of such metals as iron, tin and copper.[3,5] It is recommended to carry out the chlorination of carbon disulphide with chlorine in the temperature range from 15 to 30 °C.[5] Carrying out this process at higher temperatures assists the formation of carbon tetrachloride, while a reduction in the temperature of the process slows down the rate of chlorination of carbon disulphide. Water,[5] carbon disulphide,[16] organic solvents such as heptane, carbon tetrachloride, etc.[17] are used as reaction medium. In view of the relatively high stability of trichloromethanesulphenyl chloride towards hydrolysis the chlorination of carbon disulphide in an aqueous emulsion is more preferred since the sulphur mono- and disulphides formed in the process are partially decomposed by water to water-soluble products which assists their separation from trichloromethanesulphenyl chloride. Purification of trichloromethanesulphenyl chloride from byproducts is a relatively complex operation. The low-boiling sulphur dichloride and carbon tetrachloride are separated from trichloromethanesulphenyl chloride, which has bp 147 °C, by simple distillation but it is practically impossible to separate sulphur monochloride (bp 136 °C) by simple distillation. Several methods have been developed for purifying trichloromethanesulphenyl chloride from sulphur monochloride. The most widespread are methods comprising steam distillation of trichloromethanesulphenyl chloride[18] and washing trichloromethanesulphenyl chloride with water,[5] or with aqueous solutions of reducing[19] or oxidising[3] agents which convert sulphur monochloride into compounds readily soluble in water. After chlorination the reaction mixture is treated with a fresh portion of carbon disulphide with the aim of converting sulphur mono- and dichlorides to trichloromethanesulphenyl chloride.[3]

$$2S_2Cl_2+CS_2\longrightarrow CCl_3SCl+5S,$$
$$2SCl_2+CS_2\longrightarrow CCl_3SCl+2S.$$

After chlorination, treatment of the reaction mixture with sulphur dioxide has been proposed.[3] This converts sulphur monochloride into thionyl chloride which is readily separable from trichloromethanesulphenyl chloride by simple distillation.

$$S_2Cl_2+SO_2\longrightarrow SOCl_2+S+SO_2.$$

It was reported[3] that the chlorination of carbon disulphide with chlorine in hydrochloric acid leads to the formation of practically pure trichloromethanesulphenyl chloride since sulphur mono- and dichlorides are readily hydrolysed in hydrochloric acid.

$$CS_2+5Cl_2+4H_2O\xrightarrow{HCl}CCl_3SCl+H_2SO_4+6HCl.$$

Other means of obtaining trichloromethanesulphenyl chloride are based on the reaction of chlorine with methane-, chloromethane- or dichloromethanesulphenyl chloride,[3] with dimethyl disulphide,[3] with methyl trichloromethyl sulphide,[3] methyl thiocyanate,[5] dimethyl sulphide,[20] chloromethyltrichloromethyl sulphide,[20] and carbon selenosulphide.[21] However these methods are not widely used due to the low availability of the starting materials, the low yields of trichloromethanesulphenyl chloride and the complexity of isolating it.

b) Trichloromethanesulphenyl bromide

Trichloromethanesulphenyl bromide is formed in quantitative yield by the reaction of trichloromethanesulphenyl chloride with 48% hydrobromic acid at 23–25 °C.[22–24]

$$CCl_3SCl+HBr\longrightarrow CCl_3SBr+HCl.$$

c) Trichloromethanesulphenyl fluoride

The unstable trichloromethanesulphenyl fluoride is formed on heating trichloromethanesulphenyl chloride with activated potassium fluoride and is converted under the reaction conditions into dichlorofluoromethanesulphenyl chloride.[25,26]

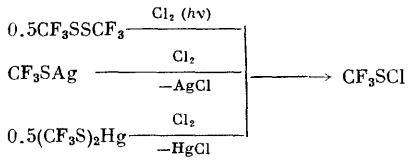
Of the perbromomethanesulphenyl halides only tribromomethanesulphenyl bromide is known and is formed on reaction of dibromochloromethanesulphenyl bromide with 48% hydrobromic acid[22] and by the reaction of bromine with carbon disulphide[8] and carbon selenosulphide.[21]

The formation of the unstable triiodomethanesulphenyl iodide on reaction of carbon disulphide with iodine has been presumed in the literature.[27]

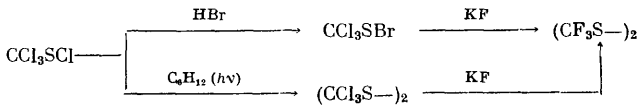
2. Perfluoromethanesulphenyl halides

a) Trifluoromethanesulphenyl chloride

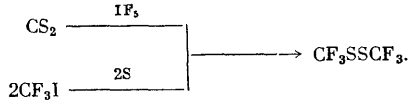
Trifluoromethanesulphenyl chloride is formed in relatively good yield by the reaction of chlorine with hexafluorodimethyldisulphide[8,27] and also with silver[28] and mercury[8,29] trifluoromethylmercaptides.



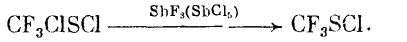
Replacement of the chlorine atoms by fluorine in trichloromethanesulphenyl chloride by the action on it of sodium fluoride,[30] potassium fluoride[31] or hydrogen fluoride[32] also leads to the formation of trifluoromethanesulphenyl chloride, but in low yield, since fission of the C–S bond occurs with the formation of various products in addition to the chlorine–fluorine exchange. Because of this it is more rational to convert trichloromethanesulphenyl chloride into hexafluorodimethyldisulphide as follows.[23]



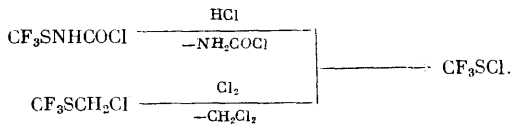
Hexafluorodimethyl disulphide may also be obtained by the fluorination of carbon disulphide or by the reaction of trifluoroiodomethane with sulphur.



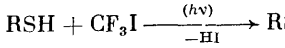
Replacement of chlorine by fluorine in chlorodifluoromethanesulphenyl chloride may be effected with antimony trifluoride.[34]



Fission of the S–N bond of trifluoromethanesulphenamides[35] and also of the S–C bond of trifluoromethyl sulphides[36] by reaction with hydrogen chloride and chlorine also leads to the formation of trifluoromethanesulphenyl chloride.

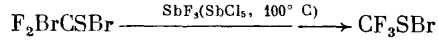


In the latter case the ease of fission of the S–C bond is explained by the structure of the initial sulphide. Consequently there is great interest in the radical perfluorination of thiols[37–39] as a result of which trifluoromethylsulphides themselves of various structure may be obtained.



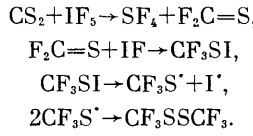
b) Trifluoromethanesulphenyl bromide

Trifluoromethanesulphenyl bromide is obtained in 40% yield by the reaction of bromodifluoromethanesulphenyl bromide with antimony trifluoride in the presence of antimony pentachloride.[34]



c) Trifluoromethanesulphenyl iodide

The unstable trifluoromethanesulphenyl iodide, which readily converts into hexafluorodimethyl disulphide, is formed as an intermediate in the fluorination of carbon disulphide with iodine pentafluoride between 60 and 200 °C.[27]



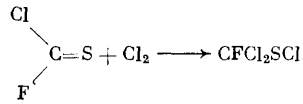
d) Trifluoromethanesulphenyl fluoride

Trifluoromethanesulphenyl fluoride is formed in low yield on exhaustive fluorination of trichloromethanesulphenyl chloride with activated potassium fluoride.[26]

3. Mixed perhalomethanesulphenyl halides

a) Dichlorofluoromethanesulphenyl chloride

Several methods have been developed for obtaining dichlorofluoromethanesulphenyl chloride, however they do not provide a high yield. One of these methods comprises replacement of one of the chlorine atoms in trichloromethanesulphenyl chloride by reaction with potassium fluoride[25,26,31,40] or hydrogen fluoride.[56] Another method is based on the addition of chlorine to the C=S bond of thiocarbonyl chlorofluoride.[24]



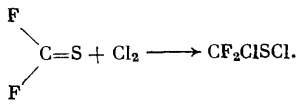
More promising from a preparative standpoint is the replacement of one of the chlorine atoms by fluorine in *N*-(diethyl)-trichloromethanesulphenamide with subsequent fission of the S–N bond in the resulting *N*-(diethyl)dichlorofluoromethanesulphenamide by reaction with hydrogen chloride.[41] A maximum yield (37%) of dichlorofluoromethanesulphenyl chloride was observed at a reactant ratio of 1 : 1, a temperature for fluorination of 55 °C and duration 105 min.



b) Chlorodifluoromethanesulphenyl chloride

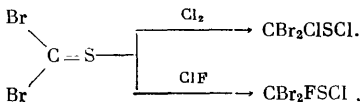
Chlorodifluoromethanesulphenyl chloride is formed in 22% yield on replacing two chlorine atoms by fluorine in *N*-(diethyl)chlorodifluoromethanesulphenamide with subsequent fission of the S–N bond in the resulting *N*-(diethyl)chlorodifluoromethanesulphenamide by reaction with hydrogen chloride.[41] This compound may also be

obtained by the partial fluorination of trichloromethanesulphenyl chloride with potassium fluoride[24] and by the addition of chlorine to the C=S bond of thiocarbonyl difluoride.[8]



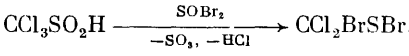
c) Dibromochloromethane- and dibromofluoromethanesulphenyl chlorides

The addition of chlorine or chlorine fluoride to the C=S bond of thiocarbonyl dibromide leads to the formation of dibromochloromethanesulphenyl chloride or dibromofluoromethanesulphenyl chloride in yields of 34 and 18% respectively.[42]



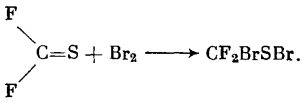
d) Bromodichloromethanesulphenyl bromide

Bromodichloromethanesulphenyl bromide is formed by the reaction of trichloromethanesulphenyl chloride with 48% hydrobromic acid.[3] The formation of this compound has also been mentioned in the reaction of trichloromethanesulphinic acid with thionyl bromide.[43]



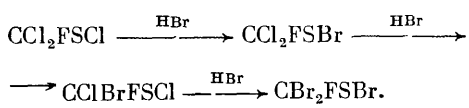
e) Bromodifluoromethanesulphenyl bromide

The addition of bromine to the C=S bond of thiocarbonyl difluoride leads to the formation of bromodifluoromethanesulphenyl bromide in relatively good yield.[44]

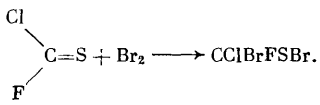


f) Dichlorofluoromethane, dibromofluoromethane- and bromochlorofluoromethanesulphenyl bromides

It has been shown that dichlorofluoromethanesulphenyl chloride is converted by step-wise bromine–chlorine exchange into dichlorofluoromethanesulphenyl bromide, bromochlorofluoromethanesulphenyl bromide and dibromofluoromethanesulphenyl bromide.[24]



Bromochlorofluoromethanesulphenyl bromide is also formed by the addition of bromine to the C=S bond of thiocarbonyl chlorofluoride.[24,44]



III. Reactions of perhalomethanesulphenyl halides

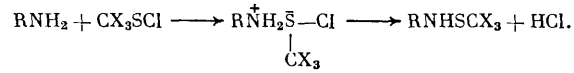
1. Nucleophilic substitution reactions

Perhalomethanesulphenyl halides react vigorously with amines, alcohols, thiols and other nucleophiles with the formation of various perhalomethylthio derivatives. Some of these reactions are fairly unusual compared with the analogous reactions of alkanesulphenyl halides containing no halogen in the alkyl group. In the majority of cases these reactions proceed by an S_N2 mechanism with the formation of a transition state in which the entering and leaving groups are at apices of a trigonal bipyramid.[45]



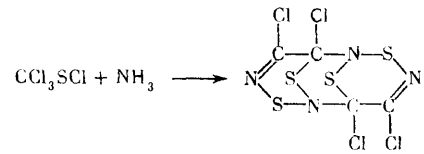
X = Hal.

The possibility of some reactions occurring by an addition–elimination mechanism is not excluded.[45]

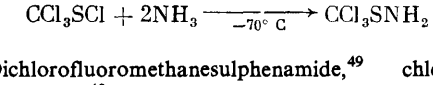


a) Interaction with *N*-nucleophiles

Interaction with ammonia. The vigorous reaction of trichloromethanesulphenyl chloride with ammonia was remarked upon even by Rathke,[1] however the structure of the resulting product was not determined. Significantly more recently the reaction of trichloromethanesulphenyl chloride with ammonia was studied in a heterogeneous medium of benzene and water.[46] The product formed in this reaction was assigned the structure of 3,6-dichloro-1,4-dithia-2,5-diazine, but proved to be more complex.[47] The reaction of trichloromethanesulphenyl chloride with 25% aqueous ammonia solution in a two-phase benzene–water system leads to the formation of 2,3,7,8-tetrachloro-5,10,11,12-tetrathio-1,4,6,9-tetraazatricylo[5,3,11^{2,6}]dodeca-3,8-diene.



Trichloromethanesulphenamide has been proposed[47] as an intermediate in this reaction and was obtained more recently by the reaction of trichloromethanesulphenyl chloride with liquid ammonia in pentane at –70 °C.[48] This unstable compound, which decomposes at room temperature, is preserved at –80 °C without decomposition for 7 days.



Dichlorofluoromethanesulphenamide,[49] chlorodifluoromethanesulphenamide[49] and trifluoromethanesulphenamide,[50] formed by the reaction of the corresponding sulphenyl chlorides with liquid ammonia at –60 °C in trichlorofluoromethane, proved to be more stable. Further reaction of perhalomethanesulphenamides with one

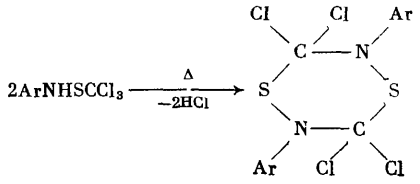
or two moles of perhalomethanesulphenyl chloride leads to the formation of bis-(perhalomethanesulphen)amides and tris-(perhalomethanesulphen)amides.[49,51–53]

$$RSNH_2 + RSCl \xrightarrow[-HCl]{} (RS)_2NH \xrightarrow[-HCl]{RSCl} (RS)_3N,$$
$$R=CCl_2F,\ CClF_2,\ CF_3.$$

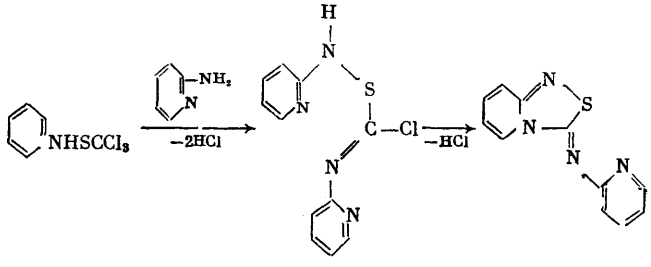
Interaction with amines. The reaction of perhalomethanesulphenyl halides with primary and secondary amines leads to the formation of *N*-substituted amides of perhalomethanesulphenic acids. *N*-Substituted amides have been described for trichloromethanesulphenic,[3,5] trifluoromethanesulphenic,[3,54] dichlorofluoromethanesulphenic,[3,10,55] chlorofluoromethanesulphenic[3,41] and bromochlorofluoromethanesulphenic[3] acids. The formation of *N*-disubstituted trichloromethanesulphenamides has been established in the reaction of trichloromethanesulphenyl chloride with aminals.[56] The instability of *N*-substituted trichloromethanesulphenamides formed by the reaction of trichloromethanesulphenyl chloride with primary amines has been recorded.[10] For example *N*-alkyltrichloromethanesulphenamides are converted into *N*-trialkylguanidines in the presence of alkylamines.

$$AlkNHSCCl_3 + 4AlkNH_2 \xrightarrow[-2AlkNH_2\cdot HCl]{} AlkN{=}C(NHAlk)_2$$

N-Aryltrichloromethanesulphenamides are converted on heating in the presence of alkali into 2,5-diaryl-3,3,6,6-tetrachloro-1,4-dithia-2,5-diazines.[10]



2-(*N*-Trichloromethanesulphenamino)pyridine, formed by the reaction of trichloromethanesulphenyl chloride and 2-aminopyridine, is converted by an excess of the latter into (2-pyridylamino)-3H-1,2,4-thiadiazolo[4,3-α]pyridine.[10,57]



The reaction of perhalomethanesulphenyl halides with tertiary amines proceeds in a more complex manner. For example, the reaction of trichloromethanesulphenyl chloride with triethylamine in benzene at 20 °C leads to the formation of 1,1-bis(trichloromethanesulphenyl)-2-(*N*,*N*-diethylamino)ethylene.[58]

$$2CCl_3SCl + CH_3CH_2N(CH_2CH_3)_2 \xrightarrow[-HCl]{} (CCl_3S)_2C{=}CHN(CH_2CH_3)_2.$$

Interaction with hydrazine derivatives. The reaction of perhalomethanesulphenyl halides with hydrazine derivatives has been studied mainly for trichloromethanesulphenyl chloride. Reactions have been described for trichloromethanesulphenyl chloride with alkylhydrazines,[59–61] arylhydrazines[61] and alkane(arene)sulphohydrazides.[61] Nucleophilic attack at the sulphur atom is, as a rule, effected by the NH_2 group. However, participation of the NH group in such attack has also been recorded. For example the reaction of trichloromethanesulphenyl chloride with benzenesulphonohydrazide in dimethoxyethane leads to the formation of two products, viz. *N*-benzenesulphono-*N'*-trichloromethanesulphenohydrazide and *N*-benzenesulpho-*N*-trichloromethanesulphenohydrazide.[61]

$$PhSO_2NH{-}NH_2 + CCl_3SCl \rightarrow \begin{cases} PhSO_2NH{-}NHSCCl_3 \\ PhSO_2N(SCCl_3){-}NH_2 \end{cases}$$

The trichloromethanesulphenylation of diacylhydrazines has been carried out in aqueous alkaline medium.[61] Replacement of two hydrogen atoms by trichloromethanesulphenyl groups occurs in this way:

$$RCNH{-}NHCR + 2CCl_3SCl \xrightarrow[-2NaCl]{NaOH} RCON(CCl_3S){-}NCOR(SCCl_3),$$

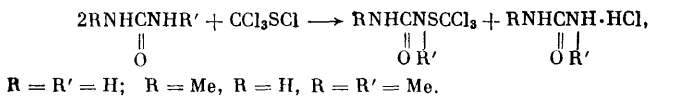
R = H, Me, Et, Ph.

Interaction with amides and amidines of carboxylic acids. Replacement of a hydrogen atom on the nitrogen atom of a carboxylic acid amide takes place with significantly more difficulty than in the case of amines. The structure of the starting material, the nature of the solvent and the sulphenylation conditions play an appreciable role. The presence of strongly electron-accepting groups in the acyl fragment hinder the sulphenylation process, but the presence in the acyl fragment of other reactive functional groups frequently leads to sulphenylation of the acyl fragment and not the amide group, as has been mentioned.[3,62] Strongly basic polar solvents such as dioxan, dimethoxyethane, dimethylformamide, etc. are used as reaction medium. An excess of the amide or an organic base (pyridine, triethylamine, etc.) is used as acceptor of hydrogen halide. The trichloromethanesulphenylation of certain carboxylic acid *N*-monosubstituted amides is effected via the sodium salt.[3] It was shown[63] that the reaction of trichloromethanesulphenyl chloride with amides of aliphatic carboxylic acids in dimethoxyethane or dioxan at room temperature leads to the formation of *N*-alkanoyltrichloromethanesulphenamides in 5–22% yield.

$$2RCON(R')H + CCl_3SCl \rightarrow RCON(R')SCCl_3 + RCON(R')H\cdot HCl.$$

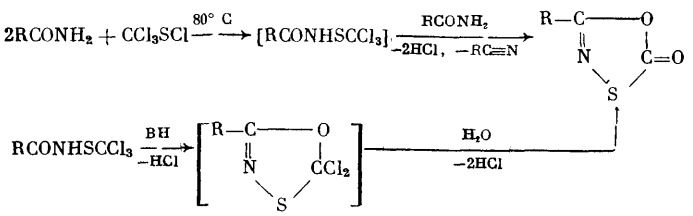
R = R' = H; R = Me, R' = H; R = Et, R' = H; R = n-Pr, R' = H; R = PhCH = CH_2, R' = H; R = H, R' = Et; R = H, R' = n-Pr; R = R' = Me; R = Me, R' = n-Pr; R = Me, R' = n-Bu.

Trichloromethanesulphenyl chloride reacts under analogous conditions with urea and its homologues with the formation of the corresponding *N*-trichloromethanesulphenyl derivatives.[63]



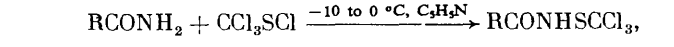
$R = R' = H$; $R = Me$, $R = H$, $R = R' = Me$.

Amides of aromatic carboxylic acids do not react under these conditions but heating the reaction mixture leads to 5-aryl-1,3,4-oxathiazol-2-ones,[64] the formation of which was also observed on reacting *N*-aroyltrichloromethanesulphenamides with bases (NaOH, triethylamine, pyridine, etc.).[65–68]



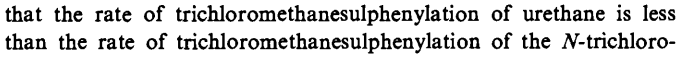
R = Ph; 3-MeC_6H_4; 4-MeC_6H_4; 4-PhC_6H_4; 2-ClC_6H_4; 3-ClC_6H_4; 4-ClC_6H_4; 2,4-$(Cl)_2C_6H_3$; 3,4-$(Cl)_2C_6H_3$; 2-$NO_2C_6H_4$; 3-$NO_2C_6H_4$; 3,4,5-$(MeO)_3C_6H_2$.

It was established[69–71] that the reaction of trichloromethanesulphenyl chloride with amides of aliphatic and aromatic carboxylic acids in dimethylformamide in the presence of pyridine at –10 °C to 0 °C leads to the formation of *N*-acyltrichloromethanesulphenamides in 39–86% yield.

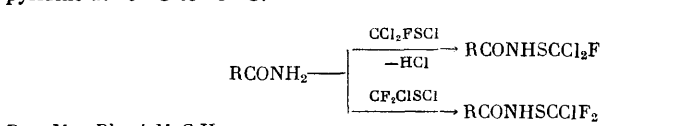


R = Me; n-Pr; n-Bu; iso-Bu; Ph; 3-MeC_6H_4; 4-MeC_6H_4; 3.5$(Me)_2C_6H_3$; 3-$MeOC_6H_4$; 4-$MeOC_6H_4$.

Trichoromethanesulphenyl chloride reacts under analogous conditions with urethane with the formation of *N,N*-bis-(trichloromethanesulphenyl)urethane[72] which is evidently explained by the fact that the rate of trichloromethanesulphenylation of urethane is less than the rate of trichloromethanesulphenylation of the *N*-trichloromethanesulphenylurethane formed as an intermediate.

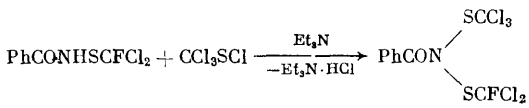


Dichlorofluoromethanesulphenyl chloride is more reactive than trichloromethanesulphenyl chloride in relation to carboxylic acid amides.[3] For example according to the patent literature[73] the reaction of dichlorofluoromethanesulphenyl chloride with carboxylic acids on heating in dioxan leads to the smooth formation of the corresponding *N*-acyldichlorofluoromethanesulphenamides in relatively good yield. Dichlorofluoromethanesulphenyl and chlorodifluoro-methanesulphenyl chloride also react readily with carboxylic acid amides in dimethylformamide in the presence of pyridine at –5° C to –3 °C.[72,74,75]

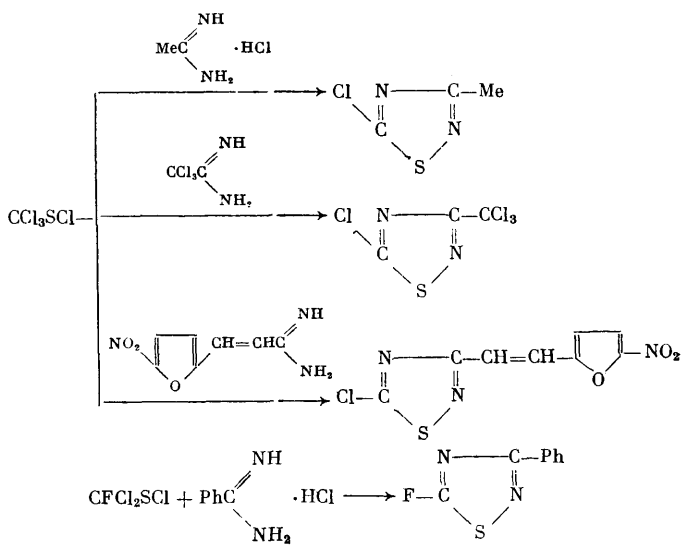


R = Me, Ph, 4-MeC_6H_3.

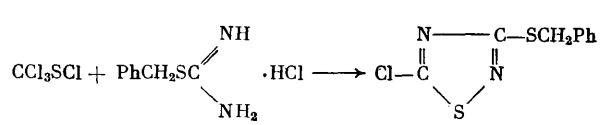
N-Benzoyldichlorofluoromethanesulphenamide reacts with trichloromethanesulphenyl chloride in the presence of triethylamine with the formation of *N*-(dichlorofluoromethylthio)-*N*-(trichloromethylthio)benzamide.[10]



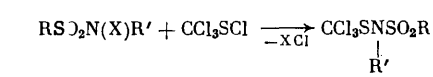
Amidines of carboxylic acids possess a higher reactivity towards perhalomethanesulphenyl halides than do carboxylic acid amides. As a rule both reaction centres (sulphur and carbon) of the perhalomethanesulphenyl halide participate in nucleophilic substitution reactions as a result of which 1,2,4-thiadiazole derivatives are formed.[10,77,78]



S-Alkylisothiouronium salts react like amidines with the formation of 1,2,4-thiadiazole derivatives.

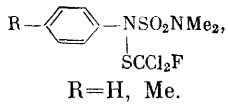


Interaction with sulphonamides. *N*-Substituted amides of alkane- and arenesulphonic acids containing alkyl,[3,80,81] aryl,[3,82] acyl[83] and arenesulphonyl[84,85] groups as substituents react relatively easily with trichloromethanesulphenyl chloride with the formation of *N,N*-disubstituted amides of trichloromethanesulphenic acid. Sulphenylation is carried out in nonaqueous organic solvent (benzene, toluene, chlorobenzene, diethyl ether, etc.) in the presence of organic bases. Occasionally in place of sulphonamides their sodium, lithium or silver salts are used.



R=Alk, Ar; R'=Alk, Ar, RCO, $ArSO_2$, X=H, Na, Li, Ag.

N-Substituted alkane- and arenesulphonamides and also *N,N,N'*-trisubstituted sulphonamides react in a similar manner with dichlorofluoromethanesulphenyl chloride, bromochlorofluoromethanesulphenyl chloride and dibromofluoromethanesulphenyl bromide.[3,86] *N,N*-Dimethyl-*N'*-phenyl-*N'*-dichlorofluoromethylthiosulphonamide and *N,N*-dimethyl-*N'*-*p*-tolyl-*N'*-dichlorofluoromethylthiosulphonamide are the most studied of the *N*-perhalomethylthiosulphonamides formed and are widely used as fungicides under the commercial names "Euparen" and "Euparen-M".[118]



R=H, Me.

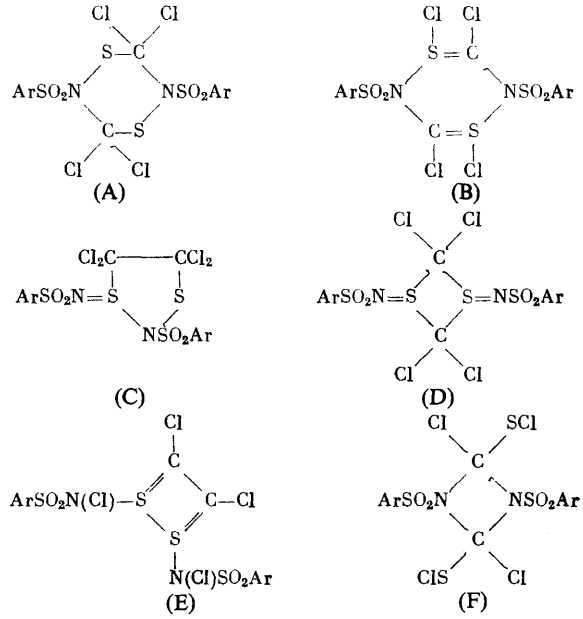
The composition and structure of the products of the reaction of unsubstituted arenesulphonamides with trichloromethanesulphenyl chloride depend on the reaction conditions. It was recorded[87] that the main products of the reaction of arensulphonamides with trichloromethane-sulphenyl chloride in boiling tetrachloroethylene were diaryl disulphides, ammonium chloride and sulphur *N,N*-bis-(arenesulphonyl)diimine. The reaction of arenesulphonamides with trichloromethanesulphenyl chloride in anhydrous benzene in the presence of triethylamine leads to the formation of *N*-arenesulphonyltrichloromethanesulphenamides in 40–60% yield.[88]

$$ArSO_2NH_2 + CCl_3SCl \xrightarrow[-Et_3N\cdot HCl]{20-30^\circ C,\ Et_3N} ArSO_2NHSCCl_3.$$

Arenesulphonamides react similarly with trichloromethanesulphenyl chloride in dimethylformamide in the presence of pyridine at −10 to 0 °C.[67,89] The reaction of arenesulphonamide sodium salts with trichloromethanesulphenyl chloride in carbon tetrachloride at −17 to −10 °C leads to *N,N*-bis(trichloromethanesulphenyl)arenesulphonamides the formation of which was also observed on reaction of *N*-arenesulphonyltrichloromethanesulphenamides with trichloromethanesulphenyl chloride in benzene in the presence of triethylamine.[88]

$$2ArSO_2NHNa + 2CCl_3SCl \xrightarrow[-ArSO_2NH_2,\ -2NaCl]{} ArSO_2N(SCCl_3)_2$$
$$ArSO_2NHSCCl_3 + CCl_3SCl \xrightarrow[-Et_3N\cdot HCl]{Et_3N} \uparrow$$

The reaction of arenesulphonamides with trichloromethanesulphenyl chloride in aqueous alkaline medium leads to the formation of cyclic compounds which were assigned the structure of 2,4-dichloro-2,4-bis(chlorothio)-1,3-bis(arenesulphonyl)-1,3-diazetidines [structure (F)] after analysis of several alternative structures (A–F).[88,90]



These compounds are also formed on reaction of arenesulphonamide sodium salts with trichloromethanesulphenyl chloride in carbon tetrachloride at −1 to +3 °C and also on reaction of *N*-arenesulphonyltrichloromethanesulphenamides with triethylamine.[90]

$$4ArSO_2NH_2 + CCl_3SCl + 4NaOH \xrightarrow[-2ArSO_2NH_2,\ -4NaCl,\ -4H_2O]{-1 \text{ to } 0\ ^\circ C} (E)$$
$$4ArSO_2NHNa + 2CCl_3SCl \xrightarrow[-2ArSO_2NH_2,\ -2NaCl]{-1 \text{ to } 3\ ^\circ C} \uparrow$$
$$2ArSO_2NHSCCl_3 + 2Et_3N \xrightarrow[-2Et_3N\cdot HCl]{} \uparrow$$

Interaction with nitrogen-containing heterocyclic compounds. The reaction of perhalomethanesulphenyl halides with heterocyclic compounds containing an N–H bond leads to the formation of *N*-perhalomethylthio derivatives of the heterocyclic compounds which possess biological activity as a rule. These investigations were particularly widely developed after the discovery in 1951 of the fungicidal properties of *N*-trichloromethylthiophthalimide and *N*-trichloromethylthio-1,2,5,6-tetrahydrophthalimide. As a rule the sulphenylation of heterocyclic compounds is carried out in anhydrous organic solvent in the presence of an organic base (pyridine, triethylamine, etc.). In the case of strongly basic heterocycles an excess of the heterocyclic compound is used as an acceptor of hydrogen halide. Heterocyclic compounds possessing an acidic character are sulphenylated as the sodium salts in aqueous, aqueous-alcoholic or alcoholic solution. *N*-Trichloromethylthio derivatives of the following are known: maleimide,[72] succinimide and its homologues,[91] hexahydrophthalimide and its homologues,[92] pyromellitimide,[93] 2,2-disubstituted malonimide,[94] homologues of

glutarimide,[3] aziridine,[3] caprolactam,[72] pyrrolidine,[95] indole,[3] isatin and its homologues,[96] piperidine,[95] pyrazole and its homologues,[13] imidazole,[3] hydantoin and its homologues,[99,100] uracil,[101] piperazine,[95] benzotriazole and its homologues,[3] benzo-1,2,3-triazin-4-one,[102] oxazolidine-2,4-dione and its homologues,[103] benzoxazolone and its homologues,[3] morpholine,[104] thiazolidine-2,4-dione and its homologues,[103] benzothiazolone,[3] benzoisothiazolone and its homologues,[105] benzoisothiazolone 1,1-dioxide and its homologues,[3] 5-methylthio-1,3,4-thiadiazol-2-one,[3] 5-phenylthio-1,3,4-thiadiazol-2-one,[3] 5-phenyl-1,3,4-thiadiazole-2-thione,[3] phenothiazine[3] and homologues of tetrahydro-1,3-thiazine.[106] The *N*-dichlorofluoromethylthio derivatives of the following have been described:[3,24] phthalimide and 1,2,5,6-tetrahydrophthalimide, hexahydrophthalimide, succinimide, pyrrolidine, homologues of isatin, imidazolin-2-one, benzotriazole, benzoxazolone, 3-methylbenzimidazolone, 1,3,4-oxadiazol-2-one, thiazolidine-2,4-dione, benzothiazolone and benzoisothiazolone 1,1-dioxide and also the *N*-trifluoromethylthio, *N*-dibromofluoromethylthio, *N*-bromodichloromethylthio and *N*-bromochlorofluoromethylthio derivatives of phthalimide and 1,2,5,6-tetrahydrophthalimide. It was shown[107] that the reaction of trichloromethanesulphenyl chloride with hexamethylenetetramine may lead to various products depending on the solvent used. For example 1,3-bis(trichloromethanesulphenyl)hexahydro-1,3,5-triazine is formed in alcohol and 3,7-bistrichloromethanesulphenyl-1,3,5,7-tetraazabicyclo[3,3,1]nonane in dimethoxyethane.

Interaction with other *N*-nucleophiles. The reaction of trichloromethanesulphenyl chloride with an *N*-(trimethylsilyl)-bis(arenesulphonyl)imide[85] or with sulphur *N,N'*-bis(trimethylsilyl)diimine[108] is accompanied by replacement of the trimethylsilyl group on the nitrogen atom by trichloromethanesulphenyl.

$$CCl_3SCl \begin{cases} \xrightarrow[-Me_3SiCl]{Me_3SiN(SO_2Ar)_2} CCl_3SN(SO_2Ar)_2 \\ \xrightarrow[-Me_3SiCl]{(Me_3SiN=)_2S} CCl_3SN{=}S{=}NSiMe_3 \end{cases}$$

b) Reactions with *O*-nucleophiles

Hydrolysis. Trichloromethanesulphenyl chloride is relatively stable towards hydrolysis and may be steam distilled without decomposition. Partial hydrolysis occurs in concentrated sulphuric acid in the presence of a calculated quantity of water with the formation of a chlorocarbonylsulphenyl chloride.[7,8]

$$CCl_3SCl + H_2O \xrightarrow[-2HCl]{(H_2SO_4)} ClC(O)SCl.$$

It was established[109] that the intermediate in this reaction is dichloromethylene sulphoxide, which readily rearranges in concentrated sulphuric acid into chlorocarbonylsulphenyl chloride.

$$Cl_2C{=}S{=}O \xrightarrow{(H_2SO_4)} ClC(O)SCl.$$

Hydrolysis of trichloromethanesulphenyl chloride in the presence of alkali may, depending on the quantity of the latter, lead to the *S*-trichloromethyl ester of dichloromethanethiosulphonic acid[110] or to the sodium salt of dichloromethanethiosulphonic acid.[111] The formation of the *S*-trichloromethyl ester of dichloromethanethiosulphonic acid occurs as follows.

$$2CCl_2SCl + 3NaOH \xrightarrow[-H_2O]{} Cl_2CHSO_2SCCl_3 + 3NaCl.$$

It was proposed[110] that initially hydrolysis of trichloromethanesulphenyl chloride occurs with the participation of the sulphur atom.

$$2CCl_3SCl + 2NaOH \rightarrow 2CCl_3SOH + 2NaCl.$$

Disproportionation of the unstable trichloromethanesulphenic acid then occurs giving trichloromethanesulphinic acid and trichloromethanethiol.

$$2CCl_3CSOH \rightarrow CCl_3SO_2H + CCl_3SH.$$

In its turn the trichloromethanesulphinic acid is converted into dichloromethylene sulphoxide by elimination of hydrogen chloride and subsequent addition of trichloromethanethiol giving the *S*-trichloromethyl ester of dichloromethanethiosulphonic acid.

$$CCl_3SO_2H \xrightarrow[-HCl]{} Cl_2C{=}SO_2 \xrightarrow{CCl_3SH} Cl_2CHSO_2SCCl_3.$$

An excess of alkali obviously leads to saponification of the *S*-trichloromethyl ester of dichloromethanethiosulphonic acid one of the products of which is the sodium salt of dichloromethanesulphonic acid as has been observed.[111] Controlled hydrolysis of trifluoromethanesulphenyl chloride by alkali leads to the formation of the *S*-trifluoromethyl ester of trifluoromethanethiosulphonic acid and hexafluorodimethyl disulphide.[112]

$$4CF_3SCl + 2H_2O \xrightarrow[-4HCl]{} CF_3SO_2SCF_3 + CF_3SSCF_3.$$

Interaction with alcohols and phenols. The reaction of perhalomethanesulphenyl halides with alcohols and phenols leads to the formation of alkyl and aryl esters of perhalomethanesulphenic acids. The esters of trichloromethanesulphenic,[3,112–116] dichlorofluoromethanesulphenic[3] and trifluoromethanesulphenic[3] acids have been described. Sulphenylation of alcohols is carried out in an excess of alcohol or in another organic solvent in the presence of pyridine or triethylamine. Sulphenylation of phenols or naphthols is better carried out as the sodium salts which prevents the competing electrophilic substitution of hydrogen atoms of the benzene ring.[117,118] Reaction of alkoxides instead of alcohols with trichloromethanesulphenyl chloride, especially an excess of the former, leads to the formation of alkyl orthocarbonates.[119] On reaction of trichloromethanesulphenyl chloride with allyl alcohol the resulting allyl ester of trichloromethanesulphenic acid is converted into allyl trichloromethyl sulphoxide as a result of a [2,3] sigmatropic rearrangement.[120–123]

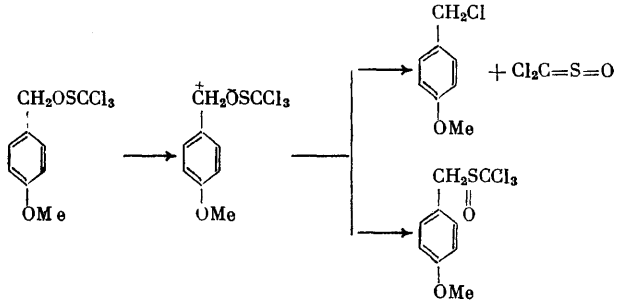
$$CCl_3SCl + HOCH_2CH{=}CH_2 \xrightarrow[-HCl]{C_5H_5N} \left[CCl_3S \begin{matrix} \diagup \\ \diagdown \end{matrix} \begin{matrix} CH \\ O \end{matrix} \begin{matrix} \diagup CH_2 \\ \diagdown \end{matrix} \right] \longrightarrow$$

$$\longrightarrow CCl_3S\underset{\underset{O}{\|}}{CH_2}{-}CH{=}CH_2$$

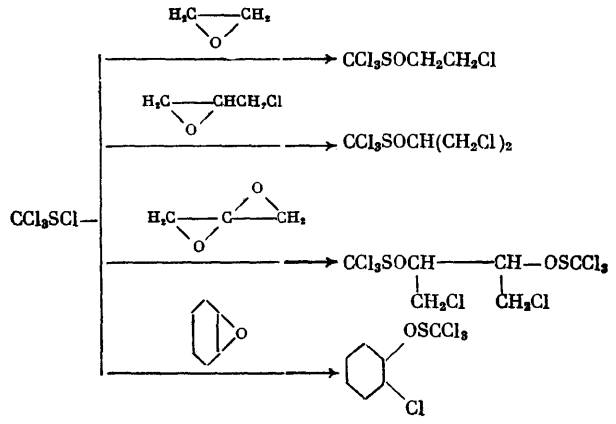
At higher temperatures rearrangement of trichloromethanesulphenic acid allyl ester proceeds without the 1,3-allyl shift with the formation of allyl chloride and dichloromethylene sulphoxide.

$$[CCl_3SOCH_2CH{=}CH_2] \rightarrow CH_2{=}CH{-}CH_2Cl + Cl_2C{=}S{=}O.$$

The propargyl ester of trichloromethanesulphenic acid undergoes an analogous rearrangement.[63] It was noted[123] that trichloromethanesulphenic acid benzyl ester is relatively stable but anisyl esters are rearranged into the sulphoxide and hexane even at 20 °C. Reaction of trichloromethanesulphenyl chloride with anisyl alcohol gives *p*-anisyl chloride and dichloromethylene sulphoxide but trichloromethyl *p*-anisyl sulphoxide is not an intermediate in the process.[123] It was proposed[124] that both rearrangements of anisyl esters proceed according to an ionisation–recombination mechanism by separate schemes.



On reacting trichloromethanesulphenyl chloride with 1,2-epoxides a *trans*-scission of the ring takes place with the formation of β-chloroalkyl sulphenates.[11,125]



Interaction with salts of organic and mineral acids. The reaction of trichloromethanesulphenyl chloride with silver[3,11] and sodium[125,126] salts of carboxylic acids leads to the formation of mixed anhydrides of trichloromethanesulphenic acid and the carboxylic acid.

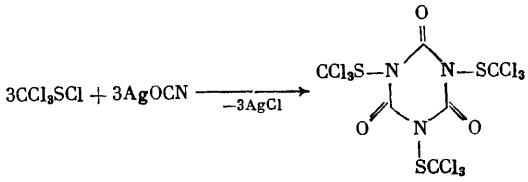
$$RCOOM + CCl_3SCl \rightarrow RCOOSCCl_3,$$

R = Me, Ph, CF_3, *p*-$MeCONHC_6H_4$; M = Ag, Na.

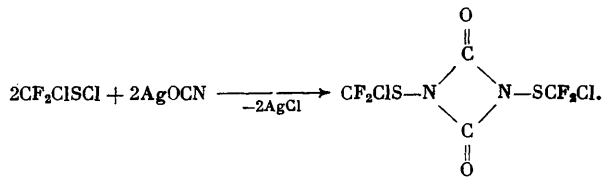
Trifluoromethanesulphenyl chloride reacts ambiguously with silver salts of carboxylic acids. Reaction of it with the silver salt of trifluoroacetic acid leads to the mixed anhydride of trifluoroacetic and trifluoromethanesulphenic acids but a mixture of various products is formed on reaction with the silver salts of chlorodifluoroacetic and pentafluorobenzoic acids.[11,127] Reaction of trichloromethanesulphenyl chloride with silver nitrate leads to the formation of trichloromethanesulphenyl nitrate.[128]

$$CCl_3SCl + AgNO_3 \xrightarrow[-AgCl]{} CCl_3SONO_2.$$

Silver isocyanate reacts with perhalomethanesulphenyl halides with a shift of the reaction centre, i.e. with nitrogen and not oxygen participating in the nucleophilic attack. The character of the reaction products is therefore determined by the form of the perhalomethanesulphenyl halide. For example the product of the reaction of trichloromethanesulphenyl chloride and silver isocyanate is 2,4,6-trioxo-1,3,5-tris(trichloromethanesulphenyl)-1,3,5-triazine which is formed by trimerisation of the unstable trichloromethanesulphenyl isocyanate.[129]



Chlorodifluoromethanesulphenyl chloride reacts with silver isocyanate with the formation of 1,3-bis(chlorodifluoromethanesulphenyl)-2,4-dioxo-1,3-diazetidine.[130,131]



The reaction of trifluoromethanesulphenyl chloride with silver isocyanate leads to the relatively stable trifluoromethanesulphenyl isocyanate.[130,131]

$$CF_3SCl + AgOCN \xrightarrow[-AgCl]{} CF_3SNCO.$$

Interaction with other *O*-nucleophiles. It has been shown[132] that the reaction of trichloromethanesulphenyl chloride with *N*,*N*-diacylhydroxylamines leads to the formation of *N*,*N*-diacyl-*O*-(trichloromethylthio)hydroxylamines.

$$CCl_3SCl + HON(COR)_2 \xrightarrow[-HCl]{} CCl_3SON(COR)_2.$$

c) Reactions with *S*-nucleophiles

Interactions with inorganic sulphur-containing reagents. Perhalomethanesulphenyl halides react with elementary sulphur in the presence of triethyl phosphate with the formation of perhalomethanethiosulphenyl halides.[8]

$$RSCl + S \xrightarrow{140-150\,^\circ C} RSSCl,$$

R = CCl_3, CCl_2Br, CCl_2F.

The interaction of trifluoromethanesulphenyl chloride with hydrogen sulphide leads to the formation of hexafluorodimethyl trisulphide.[133,134]

$$2CF_3SCl + H_2S \xrightarrow[-2HCl]{} CF_3SSSCF_3.$$

In contrast to silver isocyanate silver isothiocyanate reacts with perhalomethanesulphenyl halides with the participation of the sulphur and not the nitrogen atom.[11,135]

$$RSCl + AgSCN \xrightarrow[-AgCl]{} RSSCN,$$
$$R=CCl_3,\ CF_3.$$

Silver isoselenocyanate reacts with perhalomethanesulphenyl halides in a similar manner.[11] The reaction of trichloromethanesulphenyl chloride with sodium trithiocarbonate leads to the formation of bis(trichloromethyl) trithiocarbonate which is converted into thiophosgene on heating.[136,137]

$$Na_2CS_3 + CCl_3SCl \xrightarrow[-2NaCl]{} CCl_3SC(S)SCCl_3 \xrightarrow{130-190^\circ C} 3ClCCl.$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \| \qquad\qquad\qquad\qquad\quad \|$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad S \qquad\qquad\qquad\qquad\quad S$$

Interaction with compounds containing thiol and thione groups. Trichloromethanesulphenyl chloride reacts relatively readily with compounds containing thiol or thione groups with the formation of unsymmetrical disulphides.[119,137–149]

$$XSH(M) + CCl_3SCl \xrightarrow[-H(M)Cl]{} XSSCCl_3,$$
$$X=Alk,\ Ar,\ Het,\ HOCH_2CH_2,\ MeC(O)OCH_2CH_2,$$
$$ROC(S),\ RSC(O),\ NH_2C(O),\ RNHC(O),\ R_2NC(O),$$
$$PhC(S),\ (RO)_2P(O),\ (RO)_2P(S),\ (RS)_2P(S),$$
$$Et_2NC_2H_4;\ M=Na,\ MgBr.$$

In contrast to dithiobenzoic acid which forms an unsymmetrical disulphide with trichloromethanesulphenyl chloride,[137] thiobenzoic acid reacts with trichloromethanesulphenyl chloride with the formation of hexachlorodimethyl disulphide and dibenzoyl disulphide.[150] Esters such as *O*-alkyl thiocarbamates[151] and *O,S*-dialkyl dithiocarbonates[152] react with trichloromethanesulphenyl chloride with the participation of the thione sulphur and elimination of alkyl chloride.

$$XC(S)OAlk + CCl_3SCl \xrightarrow[-AlkCl]{} XC(O)SSCCl_3,$$
$$X=R_2N,\ RS.$$

Thioamides also react with trichloromethanesulphenyl chloride with the participation of the thione sulphur and the formation of unsymmetrical disulphides,[150,153] but the reaction of thiourea and its derivatives with trichloromethanesulphenyl chloride proceeds in a more complex manner.[154,155]

$$RC(S)NH_2 + CCl_3SCl \longrightarrow RC(NH)SSCCl_3 + HCl.$$

In the reaction of trichloromethanesulphenyl chloride with thiiranes a *trans*-fission of the ring occurs and β-chloroalkyl trichloromethyl disulphides are formed.[156,157]

$$RCH(S)CH_2 + CCl_3SCl \longrightarrow R-CH(Cl)-CH_2SSCCl_3.$$

Interactions with sulphinic acids and their derivatives. The reaction of trichloromethanesulphenyl chloride with the sodium salts of sulphinic acids leads to trichloromethyl esters of thiosulphonic acids.[158,159]

$$CCl_3SCl + RSO_2Na \xrightarrow[-NaCl]{} CCl_3SSO_2R,$$
$$R=Alk,\ Ar.$$

Aryl esters of thiosulphinic acids react with trichloromethanesulphenyl chloride with the formation of a mixture of various products.[160]

$$ArS(O)SAr + CCl_3SCl \rightarrow ArSO_2SAr + ArSSCCl_3 + ArSCl.$$

d) Reactions with *P*-nucleophiles

Interaction with inorganic phosphorus-containing reagents. Perhalomethanesulphenyl halides react even at –80 °C with white phosphorus in anhydrous carbon disulphide forming mainly chlorobis(trichloromethylthio)phosphine.[161] The formation of other products has also been recorded, the quantity of which is determined by the perhalomethanesulphenyl halide.

$$CF_nCl_{3-n}SCl + P \rightarrow (CF_3Cl_{3-n}S)_2PCl +$$
$$+ (CF_nCl_{3-n}S)_xPCl_{3-x} + (CF_nCl_{3-n}S)_2 + F_nCl_{2-n}C{=}S.$$

Reaction of trichloromethanesulphenyl chloride with phosphorus trisulphide at 80 °C leads to a mixture of several products including dichloro(trichloromethylthiol)phosphine, *S*-trichloromethyl dithiophosphoric dichloride and bis(S-trichloromethyl) dithiophosphoric chloride.[162]

$$CCl_3SCl + P_2S_3 \longrightarrow CCl_3SPCl_2 + CCl_3SPCl_2 + (CCl_3S)_2PCl.$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \| \qquad\qquad\qquad\quad \|$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad S \qquad\qquad\qquad\quad O$$

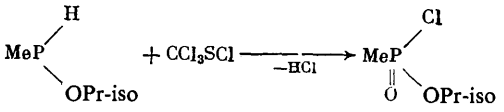
The main product of the reaction of trichloromethanesulphenyl chloride with phosphorus pentasulphide is *S*-trichloromethyl *S*-chloro dithiophosphoric chloride.[8]

$$CCl_3SP(S)(Cl)SCl.$$

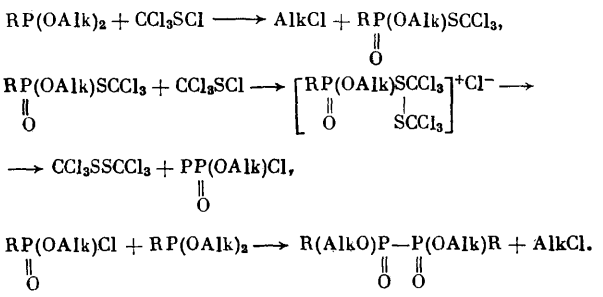
Trifluoromethanesulphenyl chloride reacts readily with phosphine with the formation of bis(trifluoromethylthio)phosphine or tris(trifluoromethylthio)phosphine depending on the ratio of reactants.[50]

$$PH_3 \xrightarrow{2CF_3SCl} (CF_3S)_2PH + 2HCl$$
$$PH_3 \xrightarrow{3CF_3SCl} (CF_3S)_3P + 3HCl$$

The main products of the reaction of isopropyl methylphosphinite with trichloromethanesulphenyl chloride are isopropyl methylphosphonic chloride and thiophosgene.[163]



The reaction of trichloromethanesulphenyl chloride with dialkyl esters of alkylphosphonous acids proceeds in a more complex manner with the formation of a mixture of various products.[164] As was proposed,[164] in the first stage of this reaction the dialkyl esters of alkylphosphonous acids react with trichloromethanesulphenyl chloride by a type of Arbuzov rearrangement with the formation of alkyl halide and an *O*-alkyl *S*-trichloromethyl thiophosphonate which then reacts with the excess of trichloromethanesulphenyl chloride with the formation of the other reaction products.



This process was investigated in a more detailed manner using as example the reaction of trichloromethanesulphenyl chloride with the diethyl and diisopropyl esters of methylphosphonous acid.[163] The authors came to the conclusion that the route of this reaction depends on the reactant ratio, the order of mixing them and the structure of the initial ester. For example, on adding diisopropyl methylphosphonite to trichloromethanesulphenyl chloride at a ratio of 1:1 at −50 °C a mixture of products is formed from which the acid chloride of isopropyl methylphosphonous acid, hexachlorodimethyl disulphide and isopropyl chloride were isolated.

$$CCl_3SCl + MeP(OPr\text{-}iso)_2 \rightarrow MeP(O)(Cl)OPr\text{-}iso +$$

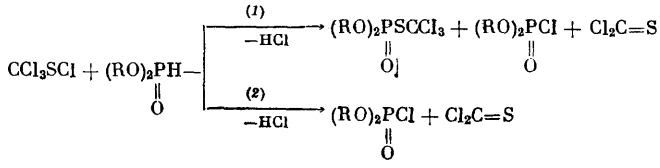
$$+ (CCl_3S-)_2 + iso\text{-}PrCl.$$

On adding one mole trichloromethanesulphenyl chloride to four moles of the diethyl ester of methylphosphonous acid the product formed in 80% yield is that of replacement of all four chlorine atoms.

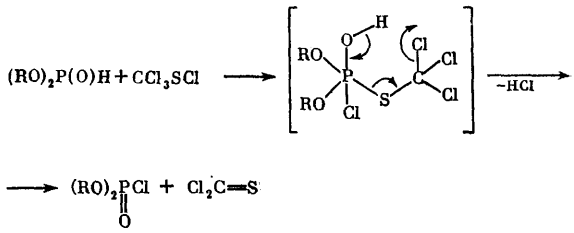
$$4MeP(OEt)_2 + CCl_3SCl \rightarrow$$
$$\rightarrow MeP(O)(OEt)SC[P(O)(Me)OEt]_3 + 4EtCl.$$

In a monograph[165] it was shown that in the case of the diisopropyl ester of methylphosphonous acid no reaction took place due to steric hindrance.

Interaction with dialkyl and trialkyl phosphites. Trichloromethanesulphenyl chloride reacts with dialkyl phosphites according to two alternative routes.[166,167]



The formation of the products of the second route is due to the initially formed phosphorane decomposing according to a six-centre mechanism.[166]



In another study[168] the formation of products by the second route is explained by decomposition of the intermediate salt formed by attack of the dialkyl phosphite at a chlorine atom of trichloromethanesulphenyl chloride.

$$(RO)_2P(O)H + CCl_3SCl \rightarrow [(RO)_2P(OH)Cl]^+(SCCl_3)^- \rightarrow$$

$$\rightarrow (RO)_2P(O)Cl + Cl_2CS + HCl.$$

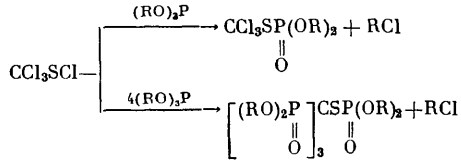
It was shown[169] that reaction of other perhalomethanesulphenyl halides with dialkyl phosphites forms *O,O'*-dialkyl *S*-trihalomethyl thiophosphates mixed with products formed by other routes and with the starting materials which it was impossible to separate by distillation due to the thermal instability of the main products. However reaction of the same sulphenyl chlorides with bis(trimethylsilyl) phosphite or diisopropyl phosphite in anhydrous benzene or toluene at room temperature and a reactant ratio of 2:1 leads to the corresponding *S*-trihalomethyl thiophosphate in quantitative yield.

$$(RO)_2P(O)H + CCl_{3-n}F_nSCl \rightarrow (RO)_2P(O)SCCl_{3-n}F_n,$$

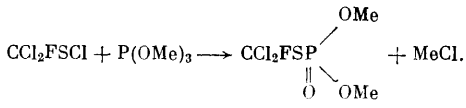
$R = (Me)_3Si$, iso-Pr.

The results of this study formed a basis for the authors[165] to propose that the formation of products of the second reaction route for trichloromethanesulphenyl chloride with dialkyl phosphites may occur during subsequent treatments and not during the reaction. Perhalomethanesulphenyl halides react ambiguously with trialkyl phosphites. For example it was recorded[170–174] that the reaction of trichloromethanesulphenyl chloride with trialkyl phosphites leads to

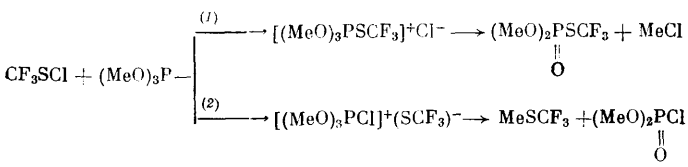
various products, depending on the ratio of reactants, including compounds with three phosphoryl groups.



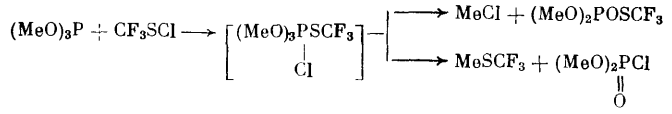
However in more recent work[175] the possibility of forming compounds with three phosphoryl groups on one carbon atom is doubtful based on PMR spectroscopic data. Dichlorofluoromethanesulphenyl chloride reacts with trimethyl phosphite by an Arbuzov rearrangement with the formation of *O,O'*-dimethyl *S*-dichlorofluoromethyl thiophosphate and methyl chloride.[176]



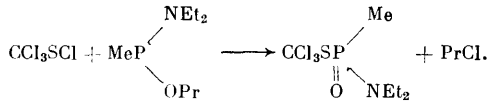
The reaction of trichloromethanesulphenyl chloride with trimethyl phosphite[177] leads to a mixture of four compounds which are formed in pairs as a result of nucleophilic attack of phosphite either at the sulphur atom or at a chlorine atom effecting the two alternative mechanisms (*1*) and (*2*).



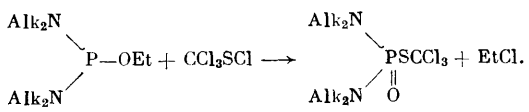
The possibility of forming a compound of five-coordinate phosphorus as an intermediate, which then eliminates methyl chloride or methyl trifluoromethyl sulphide, is not excluded.[177]



Interaction with amidoesters of alkylphosphonous acids, alkoxydiaminophosphines and diamino(hydroxy)phosphines. Trichloromethanesulphenyl chloride reacts with the propyl ester of (diethylamino)methylphosphonous acid according to an Arbuzov rearrangement mechanism.[164]

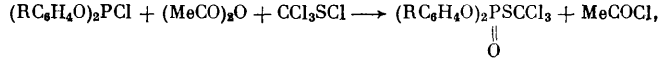


Trichloromethanesulphenyl chloride reacts with alkoxydiaminophosphines in a similar manner.[3]



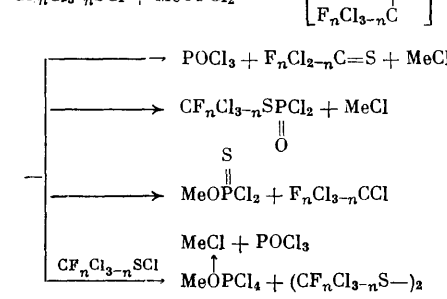
Perhalomethanesulphenyl halides react with tetraalkyldiamino(hydroxy)phosphines with the formation of *S*-trihalomethyl tetraalkyldiaminothiophosphates.[176]

Interaction with chlorodialkoxyphosphines and chlorodi(alkylthio)phosphines. *O,O'*-Diaryl *S*-trichloromethyl thiophosphates, which possess pesticidal properties and are additives for lubricating oils, are formed by the sequential addition of acetic anhydride and trichloromethanesulphenyl chloride to chlorodiaryloxyphosphines.[178]

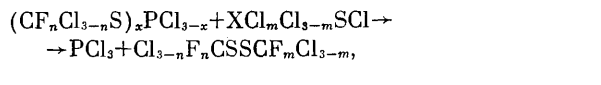


R=H, Me, Cl.

The main products of the reaction of perhalomethanesulphenyl halides $CF_nCl_{3-n}SCl$ (n = 0 to 3) with alkoxydichlorophosphines at −30 to 20 °C are *S*-trihalomethyl thiophosphoryl dichlorides formed in 50% yield.[162] In addition to these compounds *O*-alkyl thiophosphoryl dichlorides, phosphorus oxychloride, alkyl chlorides, bis(trihalomethyl) disulphides, halomethanes (CF_nCl_{4-n}) and thiocarbonyl dihalides ($F_nCl_{2-n}C{=}S$, n = 0 to 2) are formed, the quantity of which varies depending on the ratio of chlorine and fluorine atoms in the sulphenyl chloride molecule. For example it was recorded that on going sequentially from trifluoromethane- to trichloromethanesulphenyl chloride an increase occurred in the yield of *O*-alkylthiophosphoryl dichloride and a decrease in the yield of the corresponding disulphide. It was shown[162] by NMR spectroscopy (^{31}P, ^{19}F) for the reaction of trichloromethanesulphenyl chloride with methoxydichloro-phosphine that an unstable phosphorane was formed as an intermediate, the further conversions of which readily explain the formation of all the reaction products.

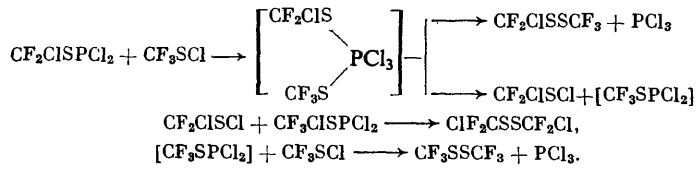


On reacting perhalomethanesulphenyl chlorides with (trihalomethylthio)chlorophosphines at 22−70 °C fission of all the P−S bonds occurs with the formation of unsymmetrical disulphides and phosphorus trichloride.[162]



n, m = 0 to 3; x = 1 to 3.

The formation has also been recorded of a small quantity of symmetrical disulphide and a second sulphenyl chloride which is explained by the formation of a phosphorane intermediate with two perhalomethanethio groups.



$$CF_2ClSPCl_2 + CF_3SCl \longrightarrow \left[\begin{array}{c} CF_2ClS \\ \diagdown \\ PCl_3 \\ \diagup \\ CF_3S \end{array}\right] \begin{array}{l} \longrightarrow CF_2ClSSCF_3 + PCl_3 \\ \longrightarrow CF_2ClSCl + [CF_3SPCl_2] \end{array}$$

$$CF_2ClSCl + CF_3ClSPCl_2 \longrightarrow ClF_2CSSCF_2Cl,$$

$$[CF_3SPCl_2] + CF_3SCl \longrightarrow CF_3SSCF_3 + PCl_3.$$

e) Reactions with *C*-nucleophiles

Interaction with organometallic compounds. Perhalomethanesulphenyl halides react energetically with organomagnesium compounds by a nucleophilic mechanism of substitution of the halogen atom at sulphur by the hydrocarbon radical.

$$CX_3SCl + RMgX \rightarrow CX_3SR + MgXCl,$$

$$X = Hal.$$

As a rule a small quantity (up to 15%) of alkyl halide is formed which hinders isolation of the resulting sulphide. Reactions described include trichloromethanesulphenyl choride with ethylmagnesium bromide[179] and also trichloromethanesulphenyl chloride with alkynylmagnesium halides[180] and arylmagnesium halides.[181] Organomercury compounds react with trifluoromethanesulphenyl chloride in a similar manner to organomagnesium compounds.[182] Simultaneously with substitution of the chlorine atom at sulphur by the hydrocarbon radical, replacement of the mercury halide fragment by chlorine and also demercuration occur.

$$p\text{-}RC_6H_4HgCl + CF_3SCl \rightarrow p\text{-}RC_6H_4SCF_3 + p\text{-}RC_6H_4Cl + PhR,$$

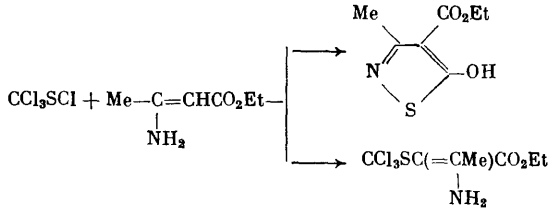
$$R = MeO,\ Me,\ H,\ Cl,\ NO_2.$$

Electron-accepting groups R aid the formation of trifluoromethylthio derivatives and electron-donating groups aid the formation of halogen derivatives.

Interaction with CH-acids and their anions. Perhalomethanesulphenyl halides react relatively easily with compounds containing active methyl, methylene or methine groups with the formation of the corresponding sulphides. For example trichloromethanesulphenyl chloride reacts with nitromethane in an aqueous alkaline medium in the cold with the formation of trichloromethyl nitromethyl sulphide.[182]

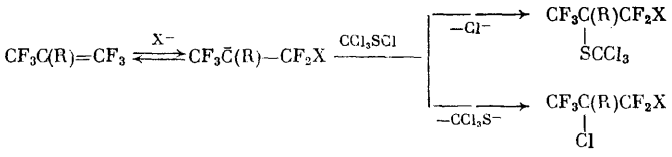
$$CCl_3SCl + CH_3NO_2 \xrightarrow[-NaCl]{0^\circ C,\ NaOH} CCl_3SCH_2NO_2.$$

Depending on the conditions the amino group[183] or the methine group[184] of β-aminocrotonic acid ethyl ester may participate in nucleophilic attack on the sulphur atom of trichloromethanesulphenyl chloride.



$$CCl_3SCl + Me{-}C(NH_2){=}CHCO_2Et \longrightarrow \begin{array}{l} \longrightarrow \text{2-hydroxy-4-ethoxycarbonyl-5-methylthiazole} \\ \longrightarrow CCl_3SC(=CMe)CO_2Et \\ \qquad\qquad | \\ \qquad\qquad NH_2 \end{array}$$

It has been shown[185] that trifluoromethanesulphenylation of CH-acids $RCXCH_2R'$ (X = O, NH; R = Ph, Me; R' = $CONH_2$, CN, $C(S)NHC_6H_4Br$-4) at 0–20 °C in anhydrous chloroform occurs selectively at the α-carbon atom. The reaction of perhalomethanesulphenyl halides with *C*-anions generated by various means occurs by two alternative routes, viz. with the formation of products either of *C*-sulphenylation or of *C*-chlorination. For example the reaction of trichloromethanesulphenyl chloride with carbanions generated by adding fluoride or chloride anions to the multiple bond of fluoroolefins leads to the formation of products of *C*-sulphenylation and *C*-chlorination.



$$CF_3C(R){=}CF_3 \overset{X^-}{\rightleftharpoons} CF_3\bar{C}(R){-}CF_2X \xrightarrow{CCl_3SCl} \begin{array}{l} \xrightarrow[-Cl^-]{} CF_3C(R)CF_2X \\ \qquad\qquad | \\ \qquad\qquad SCCl_3 \\ \xrightarrow[-CCl_3S^-]{} CF_3C(R)CF_2X \\ \qquad\qquad | \\ \qquad\qquad Cl \end{array}$$

The reaction of perhalomethanesulphenyl chlorides with anions of tetraalkyl methylenephosphonates has been investigated.[187] The anions were generated by the action of butyllithium, sodium hydride or metallic sodium on tetraalkyl methylenephosphonates. It was established that products of sulphenylation and of chlorination were formed both in the presence of $AlCl_3$ and in its absence. In the case of dichlorofluoro- and chlorodifluoromethanesulphenyl chloride sulphenylation products were obtained in which the trihalosulphenyl groups were enriched with fluorine compared with the initial sulphenyl chlorides.

$$[(RO_2)P(O)]_2CHM + CCl_{3-n}F_nSCl \xrightarrow{AlCl_3} \longrightarrow [(RO)_2P(O)]_2CHSCCl_{3-n}F_n + [(RO)_2P(O)]_2CHCl +$$

$$+ [(RO)_2P(O)]_2CHSCCl_{2-n}F_{n+1} + [(RO)_2P(O)]_2CHSCF_3,$$

$$R = \text{iso-Pr};\ M = Li,\ Na$$

The formation of products enriched with fluorine in the trihalomethanesulphenyl group occurs, as discussed,[187] by replacement of chlorine atoms by fluorine in the initial sulphenyl chloride and not in the products of sulphenylation. Fluoride anion acts as a fluorinating agent and arises on decomposition of the trihalomethylthio anion which is a byproduct of the chlorination of tetraalkyl methylenephosphonate anion.

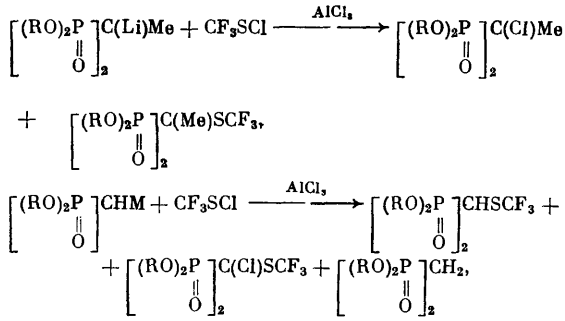
$$[(RO)_2P(O)]_2CHM + CCl_{3-n}F_nSCl \rightarrow$$

$$\rightarrow [(RO)_2P(O)]_2CHCl + CCl_{3-n}F_nS^-,$$

$$CCl_{3-n}F_nS^- \rightarrow Cl_{3-n}F_{n-1}C{=}S + F^-$$

$$CCl_{3-n}F_nSCl + F^- \rightarrow CCl_{2-n}F_{n+1}SCl + Cl^-$$

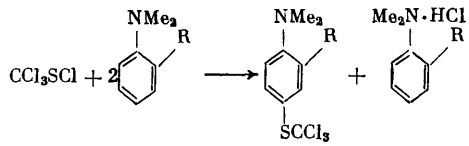
The proportion of chlorination products increases in the sequence $CF_3SCl < CF_2ClSCl \ll CFCl_2SCl$ which is caused[165,187] by the increase in steric hindrance to nucleophilic attack on the sulphur atom by the carbanion. In favour of this explanation is the formation of the product of replacement of a second H atom of the methylene group by chlorine and not by a second trifluoromethylthio group in the reaction with trifluoromethanesulphenyl chloride. In addition, in the reaction of the lithium derivative of tetraisopropyl ethylidenediphosphonate with trifluoromethanesulphenyl chloride in the presence of aluminium chloride products of chlorination and sulphenylation are formed in a 2:1 ratio while in the case of the tetraisopropyl methylenediphosphonate anion under the same conditions the ratio of (trifluoromethylthio)methylene- and (trifluoromethylthio)chloromethylenediphosphonates was 4.6:1.



R = iso-Pr; M = Li, Na.

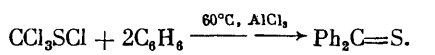
2. Electrophilic substitution reactions

Perhalomethanesulphenyl chlorides react with aromatic compounds by an S_E2 electrophilic substitution mechanism with the formation of trihalomethyl aryl sulphides. The reaction occurs relatively easily with derivatives of benzene and naphthalene containing electron-donating substituents [$N(CH_3)_2$, OH, OCH_3, etc.] but other aromatic compounds react with perhalomethanesulphenyl halides under forcing conditions in the presence of catalysts. For example, trichloromethanesulphenyl chloride reacts relatively easily with dimethylaniline[188] and its derivatives[189] with the formation of the corresponding trichloromethyl aryl sulphides.

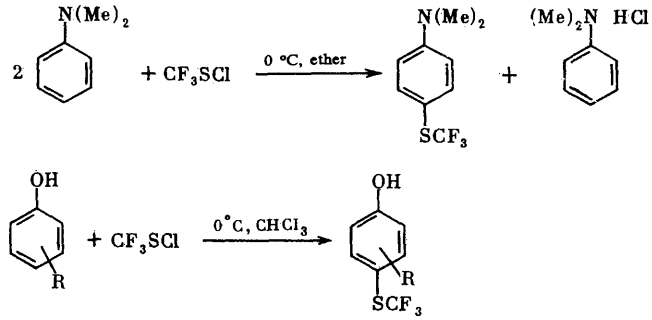


R = H, Me; MeO, MeCOO, $PhCH_2O$.

Trichloromethanesulphenyl chloride reacts anomalously with benzene in the presence of $AlCl_3$ with the formation of diphenyl thioketone.[190]

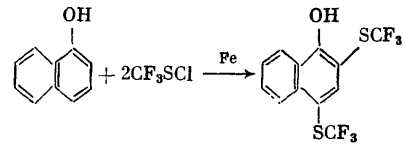


The mechanism of this reaction was not investigated[190] however it is not excluded that thiophosgene is an intermediate in this reaction and as is known,[45] reacts with benzene in the presence of $AlCl_3$ with the formation of diphenyl thioketone. Trifluoromethanesulphenyl chloride reacts with dimethylaniline,[117] and also with phenol and its homologues[118,191] even at 0 °C. The trifluoromethylthio group is directed to the positions *ortho* or *para* to the substituent.

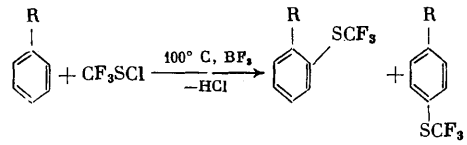


R = H, 2-Me, 3-Me, 2-OH.

Trifluoromethanesulphenyl chloride reacts with α-naphthol in the presence of iron with the formation of 2,4-bis(trifluoromethylthio)-naphthol.[118]



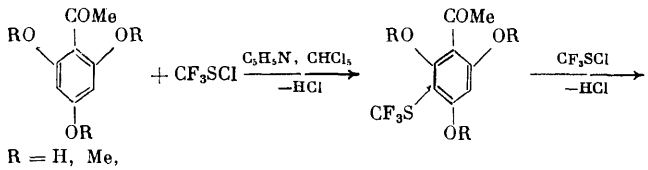
Trifluoromethanesulphenyl chloride reacts with benzene and toluene at 100 °C in an autoclave in the presence of BF_3 with the formation of trifluoromethyl phenyl sulphide and a mixture of 2- and 4-tolyl trifluoromethyl sulphides.



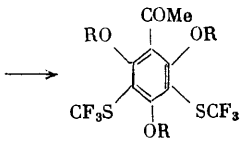
R = H, Me.

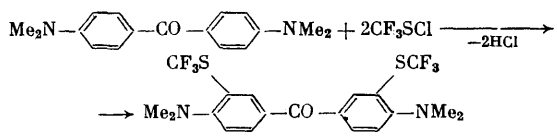
Trifluoromethanesulphonic acid is a more efficient catalyst for the trifluoromethanesulphenylation of benzene, its use enables reduction of the reaction temperature to 20 °C.[192] Introduction of a second trifluoromethylthio group into the benzene nucleus is difficult even in the presence of trifluoromethanesulphonic acid. Trifluoromethanesulphenyl chloride reacts with chlorobenzene under forcing conditions with the formation fo the two isomeric *p*-chloro- and *o*-chlorophenyl trifluoromethyl sulphides.[192] However if there are electron-donating groups (OH, OMe, NMe_2) present in the molecule in addition to electron-accepting groups [MeCO, PhCO, MeOCO, C(O)H], then depending on the conditions one, and in the presence

of iron powder, two or even three trifluoromethylthio groups may be introduced.[191,193]

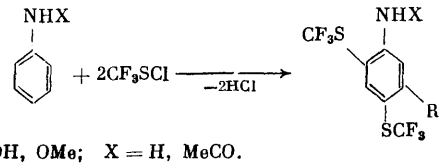


R = H, Me.



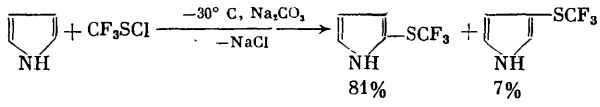


Derivatives of aniline and acetanilide containing the electron-donating groups OH or OMe in the *meta* position also react readily with trifluoromethanesulphenyl chloride with the formation of bis(trifluoromethylthio) derivatives.[194]

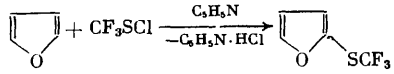


R = OH, OMe; X = H, MeCO.

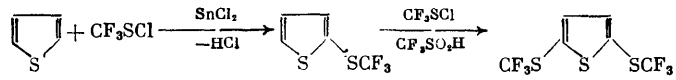
A set of rules has been established[193,195–198] for the electrophilic substitution of hydrogen atoms by the trifluoromethylthio group in heterocycles. For example pyrrole reacts even at –30 °C with trifluoromethanesulphenyl chloride with the formation of 2-trifluoromethylthiopyrrole and a small quantity of 3-trifluoromethylthiopyrrole.[193]



Under the same conditions trifluoromethanesulphenyl chloride reacts with indole with the formation of 3-trifluoromethylthioindole.[193] In the presence of trifluoromethanesulphonic acid two, three or even four hydrogen atoms in the pyrrole ring may be replaced by trifluoromethylthio groups.[195,196] Trifluoromethanesulphenyl chloride reacts with furan in the presence of pyridine with the formation of 2-trifluoromethylthiofuran.[197]



With thiopen, depending on the catalyst used, trifluoromethanesulphenyl chloride forms 2-trifluoromethylthiothiophen or 2,5-bis-(trifluoromethylthio)thiophen.[193,197,198]



3. Radical substitution reactions

Perhalomethanesulphenyl halides react with alkanes and cycloalkanes by a mechanism of radical substitution of hydrogen atom by halogen. For example, trichloromethanesulphenyl chloride reacts in the presence of catalysts of radical processes or under UV irradiation with cyclohexane,[199] n-hexane,[199] n-heptane and other saturated hydrocarbons[200–204] with the formation of the corresponding halogen derivatives and hexachlorodimethyl disulphide.

$$RH + 2CCl_3SCl \xrightarrow{h\nu} RCl + CCl_3SSCCl_3 + HCl.$$

A mechanism has been proposed[199] for the radical chlorination of hydrocarbons with trichloromethanesulphenyl chloride which includes the generation of a trichloromethylthio radical which acts as a chain propagating agent.

$$CCl_3SCl \rightarrow \dot{C}l + \dot{S}CCl_3,$$
$$RH + \dot{C}l \rightarrow R^{\cdot} + HCl,$$
$$R^{\cdot} + CCl_3SCl \rightarrow RCl + \dot{S}CCl_3,$$
$$RH + \dot{S}CCl_3 \rightarrow R^{\cdot} + CCl_3SH,$$
$$CCl_3SH + CCl_3SCl \rightarrow CCl_3SSCCl_3 + HCl.$$

Chain termination may occur by the following processes:

$$R^{\cdot} + R^{\cdot} \rightarrow R{-}R,$$
$$Cl^{\cdot} + Cl^{\cdot} \rightarrow Cl{-}Cl,$$
$$R^{\cdot} + Cl^{\cdot} \rightarrow R{-}Cl,$$
$$R^{\cdot} + \dot{\bar{S}}CCl_3 \rightarrow RSCCl_3,$$
$$CCl_3S^{\cdot} + CCl_3S^{\cdot} \rightarrow CCl_3SSCCl_3.$$

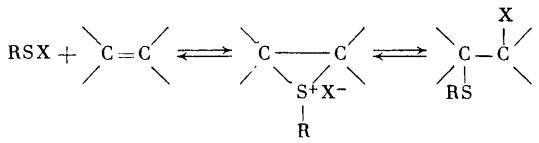
The composition of the mixture of products formed on chlorination of n-heptane with chlorine and trichloromethanesulphenyl chloride has been studied by gas chromatography.[201] It was noted that trichloromethanesulphenyl chloride possesses a higher selectivity than chlorine. Trifluoromethanesulphenyl chloride reacts with saturated hydrocarbons in the same manner as trichloromethanesulphenyl chloride.[199,203,205]

4. Addition reactions

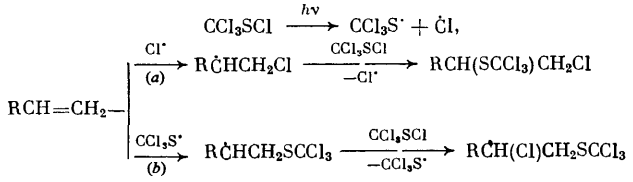
a) Addition to multiple bonds $\diagdown C{=}C \diagup$ and $-C{\equiv}C-$

In contrast to alkanesulphenyl halides the perhalomethanesulphenyl halides react with olefins with difficulty with the formation of β-halogenated sulphides containing a trihalomethyl group. For example, trichloromethanesulphenyl chloride reacts with cyclohexene only on extended heating at 120 °C.[206] Trichloromethanesulphenyl

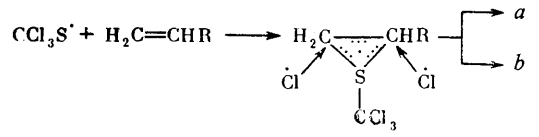
chloride reacts in an even worse manner with allyl chloride and adds to propylene only at 100–110 °C and a pressure of 100 atm. Trichloromethanesulphenyl chloride adds to bicylo[2.2.1]heptene at 100 °C by an ionic mechanism with the formation of *trans*-2-*endo*-chloro-3-*exo*-trichloromethylthiobicyclo[2.2.1]heptane.[207] Addition of trichloromethanesulphenyl chloride to 2,3-dihydrofuran proceeds only in the presence of concentrated hydrochloric acid.[208] Trifluoromethanesulphenyl chloride also adds to vinyl chloride under forcing conditions.[209,210] It was considered[45] that addition of sulphenyl halides to alkenes proceeds by an Ad_E2 mechanism including formation of an episulphonium ion as an intermediate the thermal stability of which, and consequently the thermodynamic advantage, is caused by the character of the R group on the sulphur atom.



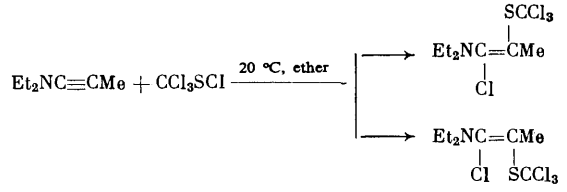
Strongly electron-accepting groups, which trichloro- and trifluoromethyl groups are, reduce the stability and therefore the thermodynamic advantage of the episulphonium ion, which hinders its formation, and consequently the addition reaction. The free radical addition of trichloromethanesulphenyl chloride to cyclohexene, n-hexene, allyl chloride, styrene[211] and aryl vinyl ether[212] proceed readily in the presence of UV light. Depending on the olefin, addition occurs according to two alternative routes with the participation of chlorine radical or of trichloromethylthio radical.



The addition of trichloromethanesulphenyl chloride to styrene, n-hexene and allyl chloride proceeds according to scheme (a)[211] while addition of trichloromethanesulphenyl chloride to aryl vinyl ether, in the opinion of the authors,[212] proceeds by scheme (b). The possibility of forming a non-classical adduct-radical, leading to loss of regioselectivity, is not excluded.[45]

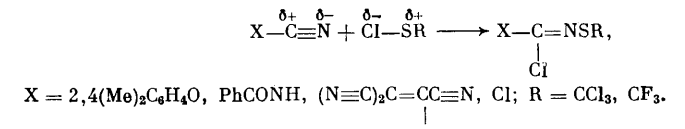


Addition of trichloromethanesulphenyl chloride to the triple bond of ynamines proceeds with the formation of *cis* and *trans* isomers.[213]

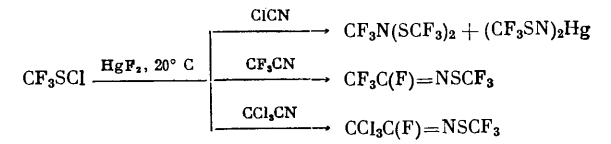


b) Addition to $-C\equiv N$ and $-N\equiv C$ bonds

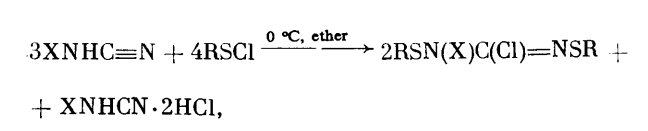
Perhalomethanesulphenyl halides add relatively readily to the polar $-C\equiv N$ bond. As a rule the chlorine atom adds to the electron-deficient carbon atom while the trihalomethylthio group adds to nitrogen with the formation of a S–N sulphenamide bond. Trichloromethanesulphenyl chloride reacts according to this scheme with 2,4-dimethylphenyl cyanate[9] and *N*-benzoylcyanimide,[214] dichlorofluoromethanesulphenyl chloride reacts with cyanogen chloride,[9] trifluoromethanesulphenyl chloride with tetracyanoethylene[215] and cyanogen chloride.[216]



Trichloromethanesulphenyl chloride readily adds to the $C\equiv N$ bond of cyanogen chloride and the nitriles of trichloroacetic and trifluoroacetic acids in the presence of mercury difluoride.[217] Replacement of chlorine by fluorine occurs together with the addition.



Addition of perhalomethanesulphenyl chlorides to the $C\equiv N$ bond of cyanamide and its *N*-alkyl derivatives is accompanied by sulphenylation of the amide group.[218,219]

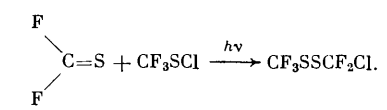


In the case of the reaction of trichloromethanesulphenyl chloride with isonitriles the chlorine atom and the trichloromethylthio group are added to the carbon atom of the isonitrile group.[9]



c) Addition to the C=S bond

Photochemical addition of trifluoromethanesulphenyl chloride to the C=S bond of thiocarbonyl difluoride leads to the formation of trifluoromethyl chlorodifluoromethyl sulphide.[220,221]

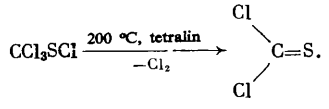


5. Oxidation reactions

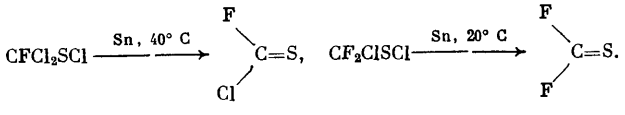
The oxidation of trichloromethanesulphenyl chloride with various oxidising agents is used as a preparative method for obtaining trichloromethanesulphonyl chloride. Oxidising agents include chlorine in aqueous medium,[222,223] chlorine in acetic acid,[224] nitric acid[225] and hydrogen peroxide.[226] These same oxidising agents may be used for converting trifluoromethanesulphenyl chloride into trifluoromethanesulphonyl chloride.[227] *m*-Chloroperbenzoic acid is used for converting trichloromethanesulphenamides into trichloromethanesulphonamides[228] and trichloromethanesulphenates into trichloromethanesulphinates.[229] On heating with nitric acid trifluoro-methyl aryl sulphides are oxidised to trifluoromethyl aryl sulphoxides.[230]

6. Reduction reactions

On reaction with various reducing agents perhalomethanesulphenyl halides are readily reduced to the corresponding thiocarbonyl dihalides. For example heating trichloromethanesulphenyl chloride with tetralin leads to the formation of thiophosgene.[231]



Sulphur dioxide, hydrogen sulphide[232] and tin[44] are also used as reducing agents. In the presence of tin dichlorofluoromethanesulphenyl chloride and chlorodifluoromethanesulphenyl chloride are readily reduced to thiocarbonyl chlorofluoride and thiocarbonyl difluoride respectively.[44]



An attempt has been made in the present review to systematise the available literature data on the methods of synthesis and reactivity of perhalomethanesulphenyl halides in view of the considerable synthetic possibilities which this class of heteroorganic compounds conceals.

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Translated from *Uspekhi Khimii* **60** 1680–1707 (1991) U.D.C. 547.484.2

Aliphatic fluorine-containing amino acids

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ABSTRACT. Data on the methods of synthesising fluorine-substituted analogues of the natural aliphatic amino acids are systematised in the review. The increased interest in these amino acids is explained by the wide spectrum of their biological action and also by the possibility of using them to solve theoretical and practical problems in medicine, biochemistry, enzymology, biotechnology and other related scientific areas. Particular attention is paid in the review to preparative methods of synthesis of the fluorine-containing aliphatic amino acids and to the means of obtaining these compounds in an optically pure state.

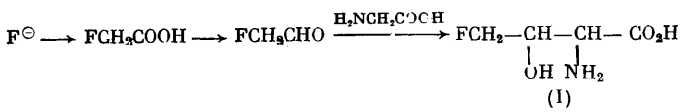
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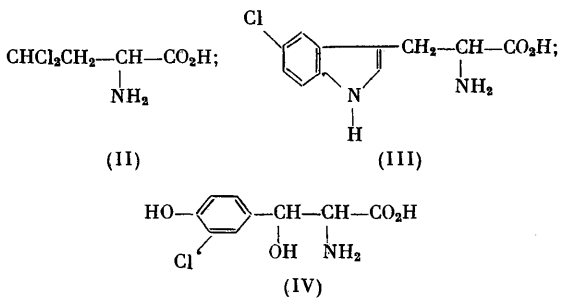
I. Introduction

Until recently fluorine-containing amino acids (FAA) were a unique type of halogen-containing amino acid (AA), having no representatives in nature. Only in 1986 did Japanese investigators[1] describe the first example of FAA biosynthesis, viz. 4-fluorothreonine (I) by the microorganism *Streptomyces cattleya*. It was shown that (I) is a secondary metabolite of monofluoroacetic acid and is formed as follows.



(I)

Chlorine-containing AA, which are the closest analogues of the FAA among halogen-substituted AA, are in contrast fairly widely represented among natural products.[2] The biological activity of chlorine-substituted AA is extremely specific. Many of them are antibiotics or form part of natural peptide or glycopeptide antibiotics. Examples are armentomycin (II), isolated from *Streptomyces armentosus*,[3] 5-chlorotryptophan (III), discovered in the antibiotic longicatenamycin[4] and β-(3-chloro-4-hydroxyphenyl)serine (IV), a structural fragment of the antibiotics actaplanin,[5] vancomycin[6] and aridicin.[7]



(II) (III)

(IV)

All this is a stimulus for broad investigations of other halogen-containing AA.

The most interesting results in the area of halogen-containing AA were obtained when using fluorine atoms for modification, which is explained by the special features of this element compared with the other halogens. Fluorine is the smallest atom after hydrogen and this enables FAA to be incorporated into the metabolism of natural AA (disguise effect).[8,9] On the other hand, the fluorine atom possesses the greatest electronegativity (4.0) of all the elements of the periodic system which is shown in the change of polarisation and an increase in the strength of the C–F bond (451–485 kJ mol^{-1}) compared to the C–H bond (410 kJ mol^{-1}). As a result FAA, incorporated in metabolic processes by organisms by mistake, may in many cases inhibit various metabolic processes partially or completely (blocking effect). The consequences of introducing fluorine atoms into an AA molecule are a change in the acid–base properties of their functional groups and an appreciable increase in the lipophilicity of these compounds, particularly clearly marked when perfluorinated groups are introduced. The manifestation of these factors in the various biochemical processes involving FAA leads to the development of a wide spectrum of biological action. The most important aspects of the biological action of FAA, such as the suicide inhibition of enzymes, the carcinostatic, bactericidal and antiviral activity have been correlated.[10–17]

In addition FAA open the promise of successful application of ^{19}F NMR spectroscopy for the conformational investigation of proteins containing them, of the interaction of AA with receptors, the study of the mechanisms of enzymic reactions,[18,19] and also new routes in biotechnology when selecting microorganisms.[20,21] One rapidly developing use of FAA in medicine is the use of AA labelled with radioactive ^{18}F for the diagnosis of various diseases, the study of pharmacokinetics, the distribution of AA and the products of their metabolism in the tissue and organs of animals and man.[9,22,23]

Intensive study of the biological activity of FAA continually presents synthetic chemists with the problem of developing methods for the synthesis of previously unknown FAA for the testing of biochemical concepts. A second problem is the improvement of methods for obtaining known FAA which may be required in large quantity or in optically pure form.

The methods of synthesis of FAA published up to 1969 have been reviewed.[24,25] The methods of obtaining FAA containing fluorine atoms in the β-position to the amino group have been considered in a recently published review.[26] In addition methods of obtaining FAA have been discussed in studies[10–17] in addition to data on the biological properties of certain FAA. Work discussed in the present review includes the synthesis of fluorine-containing analogues of the natural aliphatic aminocarboxylic acids containing fluorine atoms or fluoroalkyl groups in the carbon skeleton of the AA molecule with the exception of β-fluorine-substituted amino acids.

II. Preparation of fluorine-containing amino acids using classical methods of amino acid synthesis

The possibility of applying classical methods of synthesising AA to obtain aliphatic FAA is determined by the disposition and extent of the effect of the fluorine atoms or fluorine-containing groups on the reaction centres of the molecule and also by the stability of these substituents towards the electrophilic or nucleophilic reagents used. In several cases the influence of fluorine and fluorine-containing groups, which possess a strong electron-accepting effect,[27] proved to be critical for reactions proceeding through the formation of carbocations. However in the majority of cases, when fluorine or the fluorine-containing groups are separated from the reaction centre of the molecule by two or more simple C–C bonds their electronic effects have practically no influence on the course of the reaction. Consequently the classical methods of AA synthesis proved to be suitable for obtaining the majority of fluorine-containing AA.

1. Alkylation of 2-acylaminomalonic acid esters

The classical method of synthesising AA, the alkylation of diethyl 2-acylaminomalonates (AAM) with alkyl halides, has been used for obtaining aliphatic FAA from the first. Alkylation of formamidomalonic ester with 4,4,4-trifluorobutyl iodide or 4,4,4-trifluoro-3-methylbutyl iodide gives the corresponding 6,6,6-trifluoronorleucine (VI) and 6,6,6-trifluoro-5-methylnorleucine (VII).[28]

$$R(CH_2)_2{-}X + R^1{-}CONHCH(COOC_2H_5)_2 \longrightarrow$$
(AAM)

$$\longrightarrow R(CH_2)_2C(COOC_2H_5)_2{-}NH{-}COR^1 \longrightarrow R(CH_2)_2{-}CH(NH_2){-}COOH;$$
(V) (VI)–(XI)

X = Br, I; R^1 = H, CH_3, C_6H_5; R = CF_3CH_2 (VI), $CF_3CH(CH_3)$ (VII), F (VIII), CH_2F (IX), $F(CH_2)_2$ (X), CH_3CHF (XI).

The use of this method for the synthesis of α-amino-ω-fluorocarboxylic acids such as 2-amino-4-fluorobutyric acid (VIII), 5-fluoronorvaline (IX) and 6-fluoronorleucine (X) is complicated. Partial replacement of the fluorine atom by a hydroxyl group occurs with the formation of corresponding α-amino-ω-hydroxycarboxylic acid at the stage of hydrolysing the product of alkylation of the acylmalonic esters (V) with mineral acid.[29,30] Acid hydrolysis of the product (V, R = F) gives a mixture of various quantities of 2-amino-5-fluorobutyric (VIII) and 2-amino-5-hydroxybutyric acids which are separated by crystallisation from aqueous ethanol.[29] It has been shown[30] that on hydrolysis of (V, R = F) a mixture is obtained with a fluorine content from 8 to 39% of the theoretical value for the FAA (VIII).

Replacement of a fluorine atom by an OH group also occurs in the fluoromethylene group and is shown in the preparation of 5-fluoronorleucine (XI).[31,32] 5-Hydroxynorleucine was isolated as well and became the main reaction product on extended heating of compound (V, R = CH_3CHF) with dilute mineral acid.

The synthesis of FAA (IX)–(XI) without contamination by the corresponding hydroxy acids was successfully achieved by hydrolysing the alkylation products (V) with 48% hydrofluoric acid. This approach also enables the preparation of unsaturated aliphatic FAA as was shown in the synthesis of 2-amino-5-fluoro-4,5-dehydroadipic acid (XII).[33]

$$BrCH_2{-}CH{=}CF{-}COOC_2H_5 \xrightarrow[2)\ H_3O]{1)\ AAM} HOOC{-}CF{=}CH{-}CH_2{-}CH(NH_2){-}COOH$$
(XII)

2-Amino-4,4,4-trifluorobutyric acid (XIII), first synthesised[34] in four stages from diazoacetic ester and trifluoroacetic anhydride, may be obtained by the direct alkylation of 2-acetamidomalonic ester with 2,2,2-trifluoroethyl triflate.[35] Attempts to use 2,2,2-trifluoroethyl iodide or 2,2,2-trifluoroethyl tosylate proved to be unsuccessful.

$$CF_3(CH_2)_nOSO_3R \xrightarrow{AAM} CF_3(CH_2)_n{-}C(COOC_2H_5)_2{-}NH{-}COCH_3 \xrightarrow{H_3O^{\oplus}}$$

$$\longrightarrow CF_3(CH_2)_n{-}CH(NH_2){-}COOH$$
(VI), (XIII), (XIV)

n = 1 (XIII), 2 (XIV), 3 (VI); R = CF_3, 4-$CH_3C_6H_4$

5,5,5-Trifluoronorvaline (XIV) is formed similarly from 3,3,3-trifluoropropyl triflate. However, 6,6,6-trifluoronorleucine (VI) is not obtained by the alkylation of 2-acetamidomalonate ester with 4,4,4-trifluorobutyl tosylate. The free (*R*)- and (*S*)-enantiomers of FAA (VI), (XIII), and (XIV) are obtained by enantioselective hydrolysis of their *N*-acetyl derivatives with acylase.

One further method of alkylating acylaminomalonate esters has been used for the synthesis of certain FAA, viz. the Michael addition of activated olefins. 4-Fluoroglutamic acid (XV) is obtained by the condensation of acetamidomalonic ester with the ethyl or methyl esters of 2-fluoroacrylic acid with subsequent acid hydrolysis of the resulting product.[35–38]

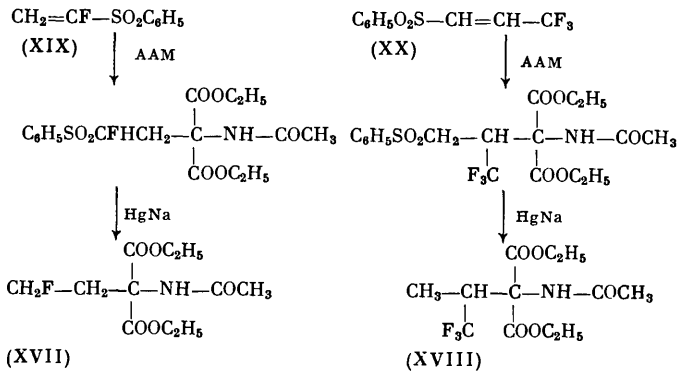
$$CH_2{=}CF{-}COOR \xrightarrow{AAM} C_2H_5OOC{-}CHF{-}CH_2{-}C(COOC_2H_5)_2{-}HN{-}COCH_3 \longrightarrow$$

$$\longrightarrow HOOC{-}CHF{-}CH_2{-}CH(NH_2){-}COOH;\quad HOOC{-}CHF{-}CH_2{-}CH(NH_2){-}CONH_2,$$
(XV) (XVI)

R = CH_3, C_2H_5

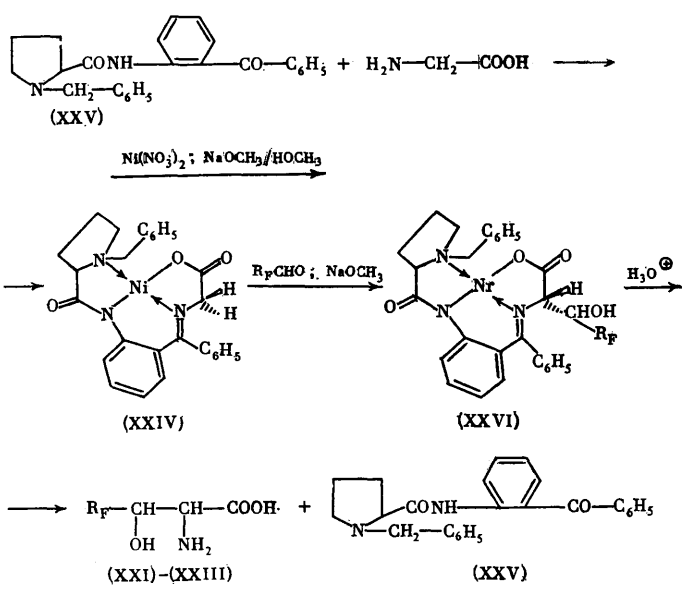
Treatment of the monomethyl ester of 4-fluoroglutamic acid with ammonia gives the corresponding 4-fluoroglutamine (XVI) in low yield.[33]

The ease of removing the benzenesulphonyl group by the action of sodium amalgam on phenyl alkyl sulphones[39] is used in the last stage of synthesising protected 2-amino-4-fluorobutyric acid (XVII)[40] and 4,4,4-trifluorovaline (XVIII).[41] The fluorine-containing vinyl sulphones (XIX) and (XX), readily obtained by the Emmons–Horner reaction from the corresponding benzenesulphonylmethanephosphonates and carbonyl compounds, undergo Michael condensation with 2-acetamidomalonic ester. Subsequent desulphurisation of the resulting products gave FAA derivatives (XVII) and (XVIII) in 40% yield.



2. Alkylation of glycine or its derivatives

A preparative method has been developed recently for the diastereo- and enantioselective synthesis of (*S*)-4,4,4-trifluorothreonine (XXI), (*S*)-*threo*-β-nonafluorobutyl (XXII) and (*S*)-*threo*-β-(ω-hydrododecafluorohexyl)serines (XXIII) using the hydroxyalkylation of the glycine fragment in the chiral Ni(II) complex of its Schiff's base (XXIV) with the appropriate aldehydes.[42]

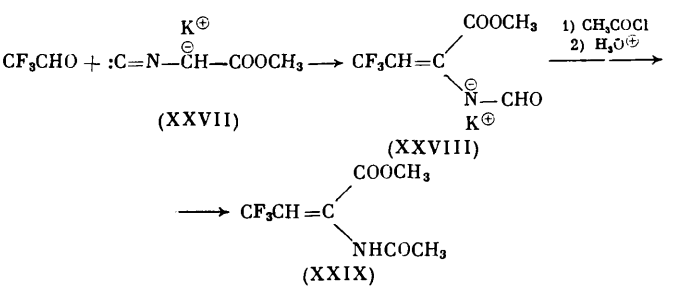


R_F = CF_3(XXI), C_4F_9(XXII), $H(CF_2)_6$(XXIII).

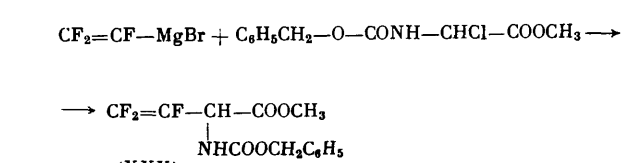
The chiral Ni(II) complex of the glycine Schiff's base is readily assembled from the available (*S*)-2-*N*-(*N*^{1}-benzylprolyl)-*o*-aminobenzophenone (XXV), glycine and nickel nitrate in the presence of sodium methoxide.[43] The hydroxyalkylation of the complex (XXIV) with fluorine-containing aliphatic aldehydes in the presence of sodium methoxide proceeds with high stereoselectivity forming the complex (XXVI) in 70% chemical yield. It was established by X-ray structural analysis that the corresponding FAA (XXI)–(XXIII) with a (2*S*,3*S*)-configuration of the chiral carbon atoms were contained in the complexes (XXVI).

Decomposition of the Ni(II) complexes (XXVI) with 2 N hydrochloric acid gives the free fluorine-containing serines (XXI)–(XXIII) and regenerates the chiral inducing reagent (XXV). It is interesting to record that acetaldehyde gives (*R*)-threonine in the analogous reaction.[44] The total inversion of the stereochemical result of the reaction on using fluorine-containing aldehydes with the complex (XXIV) is apparently linked with the strong influence of the electron-accepting perfluoroalkyl groups on the geminal hydroxyl in the AA fragment formed. In place of the free fluoroaldehydes it is possible to use stable derivatives, such as hydrates or hemiacetals, for the hydroxyalkylation of the glycine-Ni(II) complex. This significantly improves the conduct of the experiment. The diastereoselectivity of the hydroxyalkylation of complex (XXIV) is about 90%. FAA (XXI)–(XXIII) may be obtained with an optical purity of more than 99% after further purification of complexes (XXVI) by chromatography on SiO_2 or by crystallisation.

An interesting example of obtaining fluorine-containing dehydroalanine is shown in the reaction of fluoral with the potassium salt of the isonitrile (XXVII). Acetylation of the intermediate anion (XXVIII) gives a stable imide which is successfully converted regioselectively into the methyl ester of *N*-acetyl-3-trifluoromethyldehydroalanine (XXIX).[45] The electrophilic C=C bond in (XXIX) enables it to be used as a structural unit for obtaining precursors of other FAA.

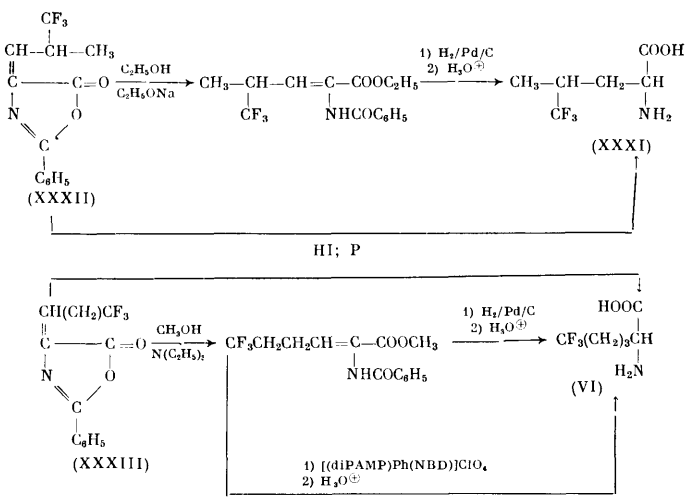


In all the reactions considered above α-anions of glycine or its derivatives and electrophilic fluorine-containing reagents are used. Special mention must also be made of the first example of the use of 'electrophilic glycine' in FAA synthesis. A derivative of α-trifluorovinylglycine (XXX) is obtained in 85% yield by the alkylation of *N*-carbobenzoxy-α-chloroglycine methyl ester with trifluorovinylmagnesium bromide in THF.[46]



3. Azlactone synthesis (the Erlenmeyer reaction)

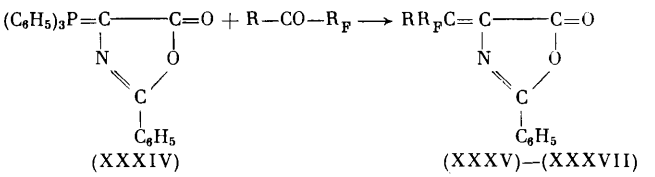
The use of the Erlenmeyer reaction in the synthesis of aliphatic FAA is shown by the preparation of 5,5,5-trifluoroleucine (XXXI) and 6,6,6-trifluoronorleucine (VI).



diPAMP = (1*R*,2*R*)-1,2-bis[(*o*-anisylphenyl)phosphino]ethane, NBD = norborndiene.

A mixture of lead acetate and acetic anhydride in THF is used to form the appropriate azlactones from 2-trifluoromethylpropionic and 4,4,4-trifluorobutyric aldehydes and hippuric acid. This modification enables azlactones (XXXII) and (XXXIII) to be obtained in 100 and 60% yield respectively[47,48] as mixtures of the (*E*)- and (*Z*)-isomers [*E*/*Z* = 13/87 for (XXXII) and *E*/*Z* = 12/88 for (XXXIII)]. The pure (*Z*)-isomers of (XXXII) and (XXXIII) were obtained in 70% yield by crystallisation of the reaction mixture. The pure (*E*)-isomers were isolated by chromatography on SiO_2. The azlactones (XXXII) and (XXXIII) were readily converted by ethanol or methanol in the presence of base into the dehydroaminoacids from which the FAA (XXXI) and (VI) were obtained by reduction with an HI/P mixture. The use of H_2/Pd/C at the reduction stage enabled 5,5,5-trifluoroleucine to be obtained with an 80% excess of the (*S**,*S**)-isomer.[49,50] The optically active methyl ester of *N*-benzoyl-6,6,6-trifluoroleucine was obtained in quantitative yield by the asymmetric hydrogenation of the methyl ester of (*Z*)-*N*-benzoyl-6,6,6-trifluorodehydronorleucine in the presence of a chiral rhodium complex.[48,50] The enantiomeric excess of the corresponding (*S*)-isomer was about 90%.

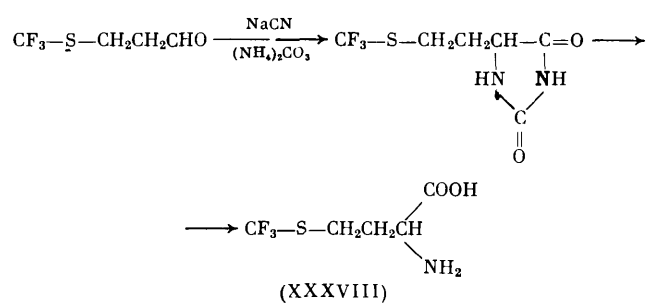
It is possible to use the Wittig reaction between 5-oxo-2-phenyl-4H-oxazolidenetriphenylphosphorane and perfluoroalkyl-containing carbonyl compounds in the synthesis of perfluoroalkyl-containing azlactones.[51] The use of the reagent (XXXIV)[52] enables preparation of the fluorine-containing azlactones (XXXV)–(XXXVII) in far higher yields than using the Erlenmeyer reaction due to the unusual ease of the hydrolytic fission of the azlactone ring in these compounds.[53]



R = R_F = CF_3 (XXXV); R = $COOCH_3$, R_F = CF_3 (XXXVI); R = H, R_F = $CF_2CF_2CF_2CF_2H$ (XXXVII)

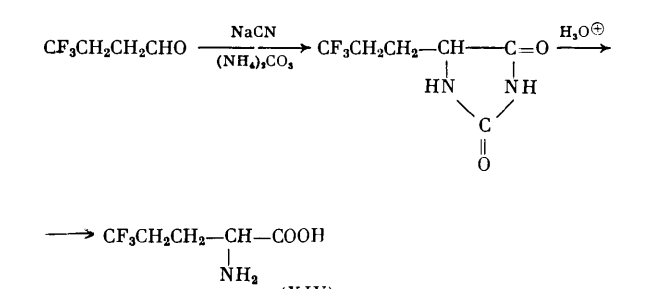
4. Hydantoin synthesis (Bucherer-Bergs reaction)

The synthesis of trifluoromethionine (XXXVIII), a fluorinated analogue of methionine, has been effected with the Bucherer-Bergs reaction.[54] The initial 3-(trifluoromethylthio)propionaldehyde was obtained by addition of trifluoromethyl mercaptan to acrolein.



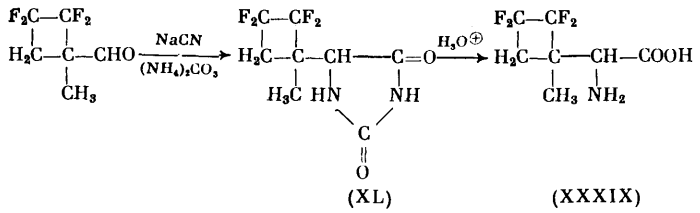
Biological testing showed that trifluoromethionine (XXXVIII) retards the growth of several microorganisms,[55] and is capable of forming *in vivo* the corresponding adenosyl derivative thus inhibiting the demethylation of *S*-adenosylmethionine.[56]

The use of 4,4,4-trifluorobutyraldehyde in the hydantoin synthesis enables preparation of the corresponding 5,5,5-trifluoronorvaline (XIV) in 30% yield.[28]



This approach gives a better result than the Strecker reaction, however in preparative capability it is surpassed by the hydroformylation method, the amidocarbonylation of 3,3,3-trifluoropropene, which is discussed in Section IV.

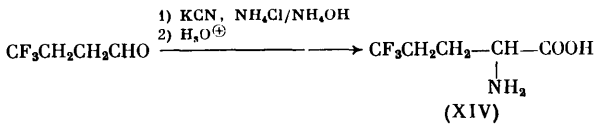
The Bucherer-Bergs reaction has also been used for the synthesis of an unusual AA with a tetrafluorocyclobutyl substituent (XXXIX),[29] in which the hydantoin (XL) is obtained from the corresponding aldehyde in 49% yield. Hydrolysis of hydantoin (XL) with 60% aqueous sulphuric acid gives the FAA (XXXIX).



(XL) (XXXIX)

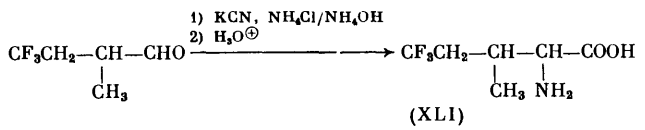
5. Cyanohydrin synthesis (Strecker reaction)

Only β-trifluoromethyl-substituted aldehydes take part in the Strecker reaction. The yield in this case is so low that it does not have the practical value of some of the reactions studied. Thus, 5,5,5-trifluoronorvaline (XIV) is obtained in 4.6% yield by the cyanohydrin method from 4,4,4-trifluorobutyraldehyde.[28]



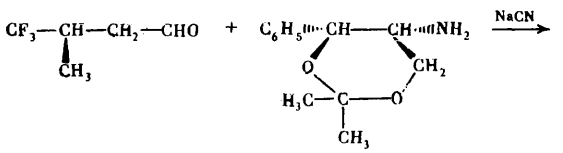
(XIV)

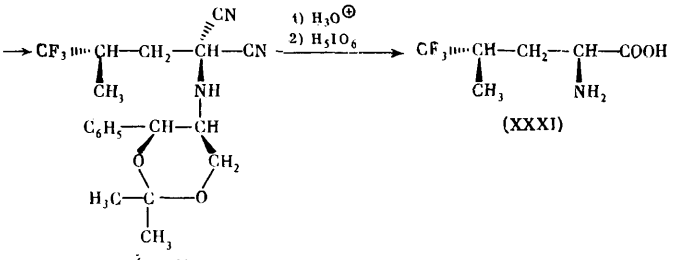
Several methods have been suggested for the preparation of 5,5,5-trifluoroisoleucine (XLI), including the cyanohydrin synthesis based on 2-methyl-4,4,4-trifluorobutyraldehyde.[57] Trifluoroisoleucine (XLI) obtained in this way contains equal quantities of *threo* and *allo* isomers.



(XLI)

The asymmetric synthesis of (2*S*,4*R*)- and (2*S*,4*S*)-5,5,5-trifluoroleucines (XXXI) has been carried out by the Strecker reaction from optically pure 4,4,4-trifluoro-3-methylbutan-1-al and (4*S*,5*S*)-5-amino-2,2-dimethyl-4-phenyl-1,3-dioxan.[58] The ratio of the (2*S*,4*R*)- and (2*R*,4*R*)-diastereomeric aminonitriles (XLII) was 8:2 (60% enantiomeric excess).

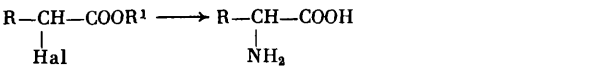




(XLII) (XXXI)

6. Replacement of halogen or hydroxyl group by an amino group.

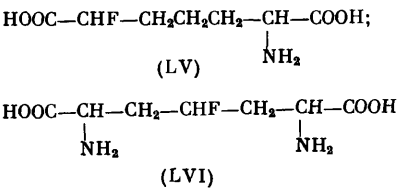
The amination of α-halogen-substituted carboxylic acids is a general method of synthesis for aliphatic FAA. Variants of this approach are manifold. A two stage process is most frequently used. The fluorine-containing α-bromocarboxylic acid or ester is reacted with sodium azide and the azido group is subsequently hydrogenated to an amino group. Another variant is the direct aminolysis of fluorine-substituted α-chloro- or α-iodocarboxylic acids or reaction of them with potassium phthalimide. The choice of experimental conditions is governed by the availability of the fluorine-containing starting material and also by the stability of the functional groups to the action of the reagents used. The following have been obtained by this route: 4-fluoroleucine (XLIII),[59] 4-fluoroisoleucine (XLIV),[60] 5,5,5-trifluoroisoleucine (XLI),[57] β-chlorofluoromethyl- (XLV) and β-chlorodifluoromethylalanine (XLVI),[61] 2-amino-4,4,4-trifluorobutyric acid (XIII),[62] 4,4,4-trifluorovaline (XLVII),[63] 5,5,5,5′,5′,5′-hexafluoroleucine (XLVIII),[64] 2-amino-4-fluorobutyric acid (VIII), 4,4′-difluorovaline (XLIX), 5,5′-difluoroleucine (L), 4-fluorothreonine (I),[65] and several β-perfluoroalkylalanines (LI)–(LIII)[66] and polyfluoronorvalines (LIV) containing in addition bromine or chlorine.[67]



(I), (VIII), (XIII), (XLI), (XLIII)–(LIV

R = $(CH_3)_2CFCH_2$ (XLIII), $CH_3CHFCH(CH_3)$ (XLIV), $CF_3CH_2CH(CH_3)$ (XLI), $CHClFCH_2$ (XLV), $CClF_2CH_2$ (XLVI), CF_3CH_2 (XIII), $CF_3CH(CH_3)$ (XLVII), $(CF_3)_2CHCH_2$ (XLVIII), CH_2FCH_2 (VIII), $(CH_2F)_2CH$ (XLIX), $(CH_2F)_2CHCH_2$ (L), $CH_2FCH(OH)$ (I), $C_2F_5CH_2$ (LI), $C_3F_7CH_2$ (LII), iso-$C_3F_7CH_2$ (LIII), $CF_2XCFXCH_2$, X = Cl, Br, X′ = F, Cl, H (LIV); Hal = Br, Cl, I; R′ = H, C_2H_5.

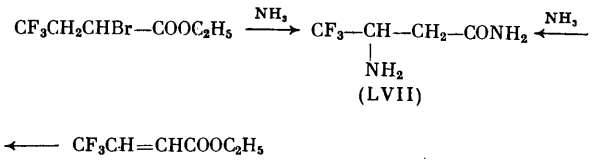
The fluorine-substituted aminodicarboxylic acids 2-amino-6-fluoropimelic (LV) and 2,6-diamino-4-fluoropimelic (LVI) acids may also be obtained by this method.[68]



(LV)

(LVI)

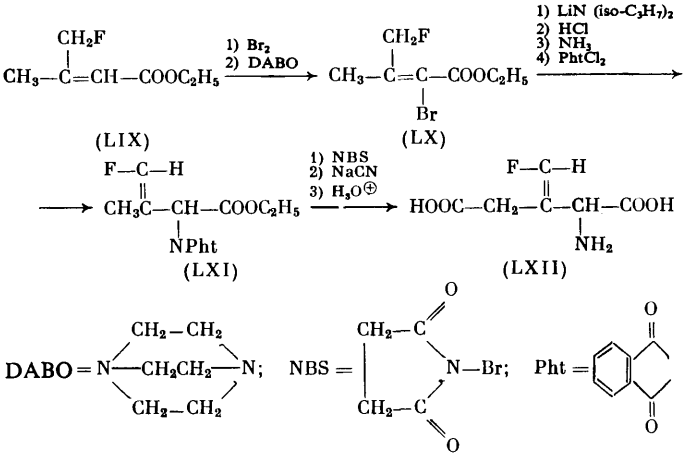
It must be noted that attempts to obtain 2-amino-4,4,4-trifluorobutyric acid (XIII) by the direct aminolysis of ethyl 2-bromo-4,4,4-trifluorobutyrate led to an unexpected product, viz. 3-amino-4,4,4-trifluorobutyramide (LVII),[62] which was obtained by an alternative synthesis from ethyl 4,4,4-trifluorocrotonate (LVIII) and ammonia.[69] The formation of the β-aminoacid (LVII) probably occurs as a result of the dehydrobromination of ethyl 2-bromo-4,4,4-trifluorobutyrate to the ethyl crotonate (LVIII) and subsequent addition of ammonia.[62]



(LVII) (LVIII)

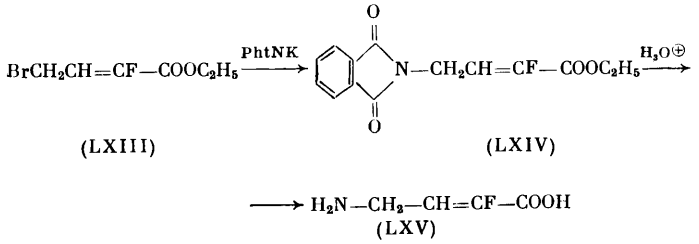
The synthesis of 2-amino-4,4,4-trifluorobutyric acid (XIII) was successfully effected by replacing the bromine atom in ethyl 2-bromo-4,4,4-trifluorobutyrate by an azide group with subsequent reduction over a palladium catalyst.[62]

Replacement of a bromine atom by an amino group has also been used as one of the stages of forming an amino acid molecule in the multistage synthesis of (*E*)-3-fluoromethyleneglutamic acid (LXII).[70]



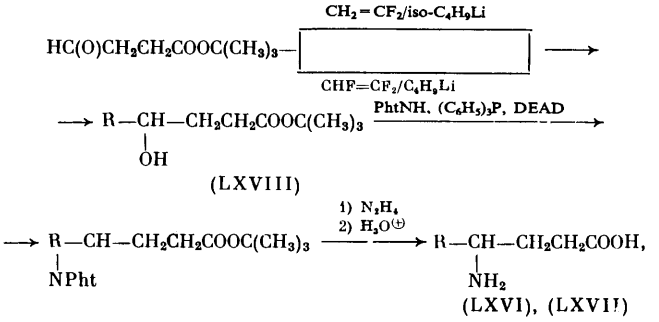
(LIX) (LX) (LXI) (LXII)

Fluorine-containing aliphatic α-amino acids are generally obtained by replacing a halogen atom by an amino group. Obviously this method is also acceptable for the synthesis of other types of FAA as is shown for the example of obtaining 4-amino-2-fluorocrotonic acid (LXIV) from ethyl 4-bromo-2-fluorocrotonate and potassium phthalimide with subsequent acidic hydrolysis of the product (LXIV).[33]



(LXIII) (LXIV) (LXV)

Replacement of an OH group by an amino group by the Mitsunobu reaction was used successfully in the synthesis of the γ-difluorovinyl- and γ-trifluorovinyl-substituted γ-aminobutyric acids (LXVI) and (LXVII).[71] The initial hydroxy derivatives (LXVIII) were obtained by the condensation of t-butyl 4-ketobutyrate with difluoro- and trifluoroethylene by the action of iso-butyl- and butyllithium respectively.

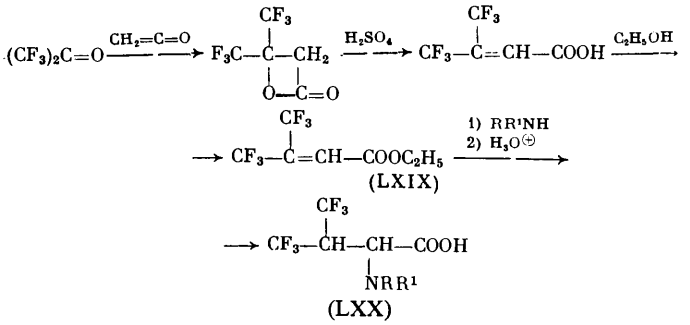


(LXVIII) (LXVI), (LXVII)

DEAD = $H_5C_2OOC-N=N-COOC_2H_5$; R = $CF_2=CF$ (LXVII), $CF_2=CH$ (LXVI)

7. Addition of ammonia or its derivatives to the double bond of acrylate systems

The addition of ammonia or one of its derivatives to a fluorine-containing acrylic acid, as the final stage in the construction of a FAA molecule, is used mainly to obtain derivatives of hexafluorovaline and α-trifluoromethyl-β-alanine due to the fairly high electrophilicity of the C=C bond in the initial unsaturated acid. Hexafluorovaline (LXX) was synthesised for the first time[72] in preparative yield (80–90%) by the addition of ammonia in ether at −80 °C to ethyl β,β-bis(trifluoromethyl)acrylate (LXIX), which was obtained in three steps from hexafluoroacetone and ketene or by the Wittig reaction.[73]



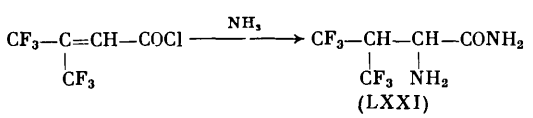
(LXIX) (LXX)

R = R¹ = H (LXX), CH_3, $(CH_2)_4$, $(CH_2)_5$, $CH_2C(CH_3)_2$, $CH_2CHCOOCH_3$; R = H, R¹ = OH; R = H, R¹ = $N(CH_3)_2$; R = H, R¹ = $CH(CH_3)C_6H_5$

Attempts to resolve the hexafluorovaline racemate with enzymes proved unsuccessful.[35,74] This aim was achieved by the crystallisation of the salt of hexafluorovaline (LXX) with *D*-camphor-10-sulphonic acid.[75] Asymmetric synthesis of hexafluorovaline (LXX) in low optical yield may be effected by adding benzylamine to the ester (LXIX) in a solution of methyl *L*-lactate or by the reaction of the optically active *N*-(α-phenylethyl)amide of β,β-bis(trifluoromethyl)-acrylic acid with α-phenylethylamine.[75] It is

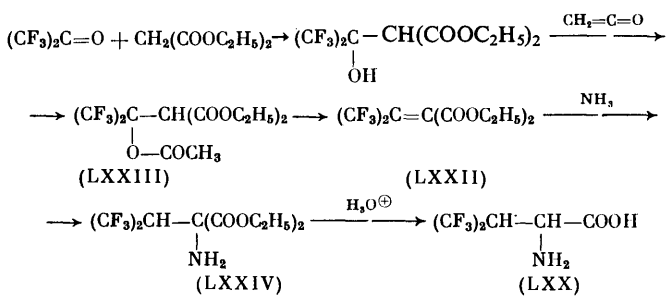
possible to use secondary amines, hydroxylamine and derivatives of hydrazine and aziridine in addition to ammonia in the condensation with the ester (LXIX).[76–79]

Attempts to obtain hexafluorvaline amide (LXXI) by the reaction of ester (LXIX) and ammonia were in vain. Compound (LXXI) was successfully synthesised only by the reaction of ammonia on β,β-bis-(trifluoromethyl)acrylic acid chloride.[72]



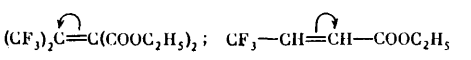
(LXXI)

It is possible to use ethyl α-ethoxycarbonyl-β,β-bis(trifluoromethyl)acrylate (LXXII) instead of ethyl β,β-bis(trifluoromethyl)-acrylate (LXIX) in the synthesis of hexafluorovaline (LXX). The ester (LXXII) is obtained by the low temperature pyrolysis of the *O*-acetyl derivative of the adduct of hexafluoroacetone with ethyl malonate (LXXIII).[80] The addition of ammonia to the diester (LXXII) occurs regioselectively at the α-carbon atom giving the aminodiester (LXXIV), hydrolysis of which gives hexafluorovaline.



(LXXIII) (LXXII) (LXXIV) (LXX)

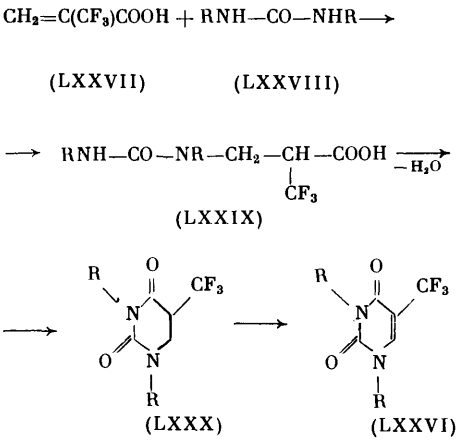
It is interesting to note that in the diester (LXXII) the influence of the two trifluoromethyl groups on the polarisation of the C=C bond proved to be stronger than the action of the two ethoxycarbonyl groups while in ethyl β-trifluoromethylacrylate (LVIII) the reverse polarisation of the C=C bond occurred.[80]



(LXXII) (LVIII)

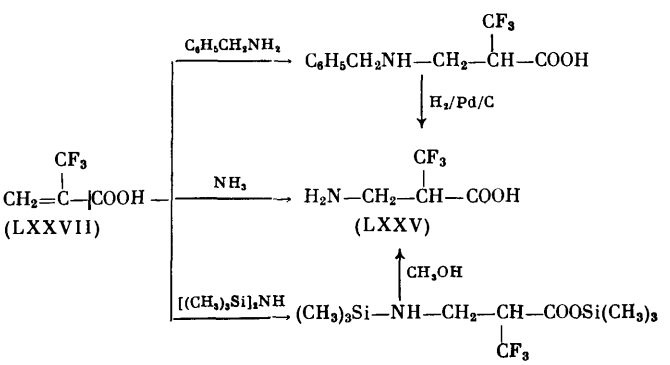
The presence of two trifluoromethyl groups in hexafluorovaline (LXX) is displayed in its physical properties as well as in its biological action. For example hexafluorovaline hydrochloride is insoluble in water.

The development of methods of obtaining α-trifluoromethyl-β-alanine (LXXV) was stimulated by the prospect of synthesising 5-trifluorouracil (LXXVI) from this AA. 5-Trifluorouracil is a fluorinated analogue of thymine and may be used in the synthesis of nucleic acids. The most convenient synthon for obtaining α-trifluoromethyl-β-alanine and its derivatives is seemingly α-trifluoromethylacrylic acid (LXXVII) obtained by the carboxylation of 2-bromo-3,3,3-trifluoropropene. Heating acid (LXXVII) with the ureas (LXXVIII) readily leads to the formation of derivatives of α-trifluoromethyl-β-alanine (LXXIX) which cyclise in the presence of dehydrating agents into the 5-trifluoromethyl-dihydrouracils (LXXX). The conversion of the dihydrouracils (LXXX) into 5-trifluoromethyluracils is effected by bromination and dehydrobromination of the compounds (LXXX).[81,82] Biological testing showed that the derivatives of 5-trifluoromethyluracil possess antiviral activity.



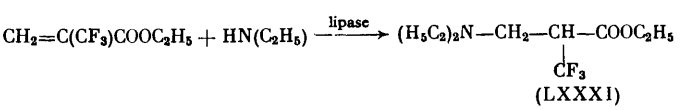
(LXXVII) (LXXVIII) (LXXIX) (LXXX) (LXXVI)

Free α-trifluoromethyl-β-alanine (LXXV) is obtained in high yield by the direct reaction of ammonia with the acid (LXXVII) in methylene chloride at 0–5 °C. Two-stage syntheses through the formation of *N*-benzyl or *N*-trimethylsilyl derivatives have also been studied.[48,50]



(LXXVII) (LXXV)

Asymmetric synthesis of *N,N*-diethyl-α-trifluoromethyl-β-alanine ethyl ester (LXXXI) with a 35% enantiomeric excess has been effected by the condensation of ethyl α-trifluoromethylacrylate with diethylamine in benzene in the presence of lipase modified with lipophilic fluorine-containing compounds.[83]

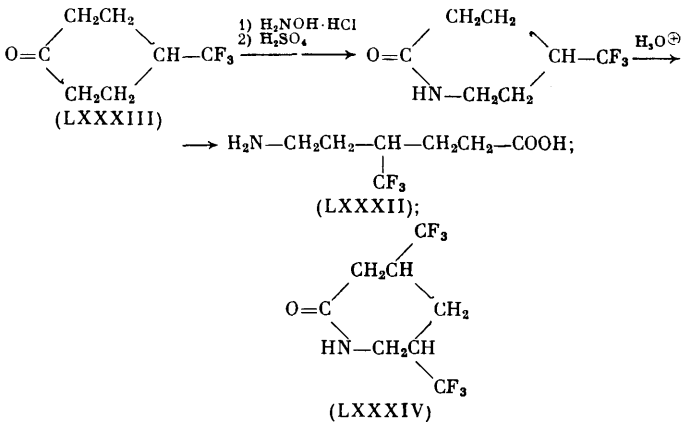


(LXXXI)

8. Beckmann rearrangement

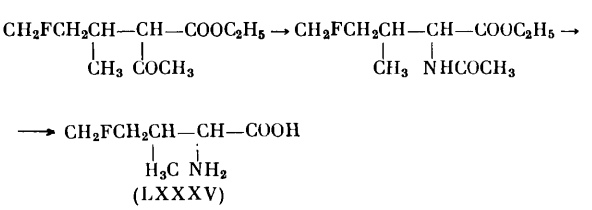
The synthesis of 6-amino-4-trifluoromethylcaproic acid (LXXXII) has been effected from 4-trifluoromethylphenol, which was converted by reduction and oxidation of the resulting alcohol into

4-trifluoromethylcyclohexanone (LXXXIII). The corresponding trifluoromethylcaprolactam was obtained from the ketone (LXXXIII) by the usual scheme of the Beckmann reaction and formed FAA (LXXXII) on acid hydrolysis.[84] The lactam of 6-amino-3,5-bis(trifluoromethyl)caproic acid was obtained from 3,5-bis(trifluoromethyl)phenol in a similar manner.



9. Schmidt rearrangement

The stereoselective synthesis of 5-fluoro-*allo*-isoleucine (LXXXV) has been effected by a Schmidt rearrangement from ethyl 2-acetyl-5-fluoro-3-methylvalerate, which is readily obtained by the alkylation of acetoacetic ester with 3-bromo-1-fluorobutane.[85]

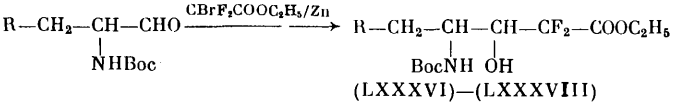


The enantioselective enzymic hydrolysis (using acylase) of the *N*-acetyl derivative of isoleucine (LXXXV) enables the preparation of only the *D*-form of AA (LXXXV) since the *L*-isomer is cyclised under the reaction conditions with replacement of the fluorine atom into *cis*-3-methyl-*L*-proline. It is interesting to note that the preparation of monofluoroisoleucine (LXXXV) by the alkylation of sodium acetamidomalonate with 3-bromo-1-fluorobutane was unsuccessful.[31]

10. Reformatskii reaction

The introduction of ethyl bromodifluoroacetate into the Reformatskii reaction[86] was used in an elegant manner in the synthesis of a 2,2-disubstituted analogue of the unusual AA statin which forms part of the natural pentapeptide pepstatin.[87] Two methods were proposed for the condensation of *N*-t-butyloxycarbonyl-(*S*)-leucinal with bromodifluoroacetic ester in the presence of activated zinc.[88,89] Boiling the reactants in THF gave the *threo*-isomer of (LXXXVI) alone. However partial racemisation (~10%) was observed at the α-carbon atom of the initial leucinal. Conducting the reaction at low temperatures by ultrasound proved to be more preferable and led to the formation of a mixture of the (3*R*,4*S*)- and (3*S*,4*S*)-diastereoisomers of (LXXXVI) (ratio 7 : 3) which was easily separated into the individual isomers. The optically pure diastereoisomers were used in the synthesis of tetrapeptides for study of their ability to inhibit renin, an enzyme playing an important role in the regulation of blood pressure.

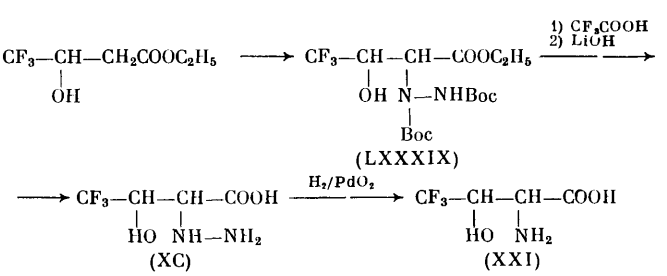
Analogues of difluorostatin containing phenyl (LXXXVII) and cyclohexyl (LXXXVIII) groups in place of the isopropyl group were obtained in a similar manner.[88,89] These compounds were made in order to determine the influence of the lipophilicity of substituents in the *gem* position to the amino group of statin on the biological activity of peptides containing these AA.



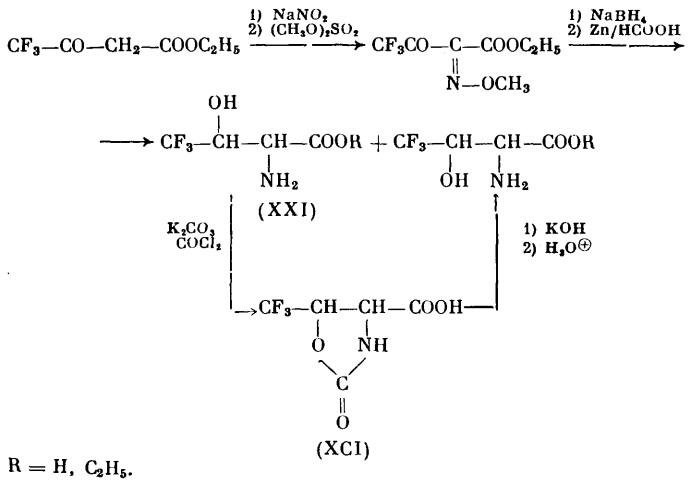
R = iso-C_3H_7 (LXXXVI), C_6H_5 (LXXXVII), cyclo-C_6H_{11} (LXXXVIII); Boc = $COOC(CH_3)_3$

11. Use of other classical methods of AA synthesis to obtain FAA

Several methods have been proposed for the synthesis of trifluorothreonine (XXI) in which 4,4,4-trifluoroacetoacetic ester or products one stage removed from it are used as starting materials. Thus by the sequential action of lithium diisopropylamide and di-t-butyl azodicarboxylate on ethyl 4,4,4-trifluoro-3-hydroxybutyrate a mixture is obtained of diastereoisomers (6 : 1) of protected 4,4,4-trifluoro-2-hydrazino-3-hydroxybutyric acid (LXXXIX), the first representative of the fluorine-containing hydrazinoacids.[90] The free hydrazinoacid (XC), obtained by the hydrolysis of compound (LXXXIX), may be converted readily into trifluorothreonine (XXI) by reduction of the hydrazino group.

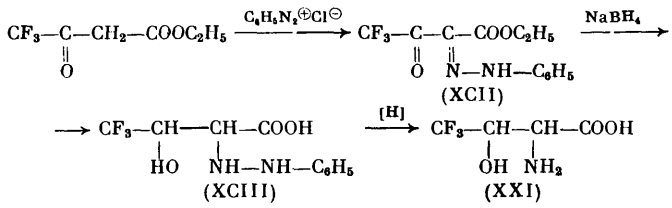


Racemic trifluorothreonine (XXI) has been obtained by the nitrosation of ethyl trifluoroacetoacetate with subsequent methylation of the resulting oxime and reduction of the C=O and C=N bonds.[91] The ratio of *threo* and *allo* isomers in trifluorothreonine (XXI) was 1.5 to 1. Trifluoro-*allo*-threonine may readily be epimerised into the corresponding *threo* isomer through the formation and breakdown of the oxazolidinone (XCI).



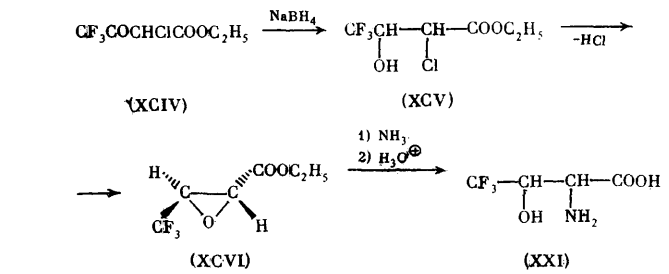
R = H, C_2H_5.

The conversion of the methylene group of 4,4,4-trifluoroacetoacetic ester into an azomethine for subsequent conversion into an amino group may also be carried out by the Japp-Klingeman reaction between 4,4,4-trifluoroacetoacetic ester and phenyldiazonium chloride.

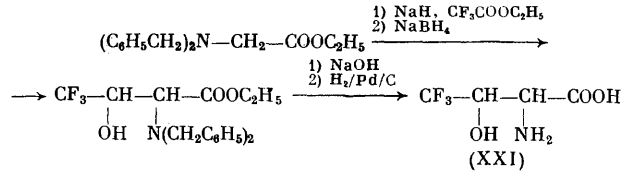


The preparation of 4,4,4-trifluorothreonine (XXI) from phenylhydrazone (XCII) is effected into three stages, viz. reduction of the carbonyl group and azomethine bond, saponification of the ester group and catalytic hydrogenation of the phenylhydrazine (XCIII).[91]

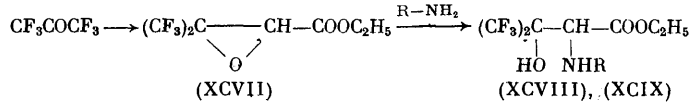
The diastereoselective synthesis of 4,4,4-trifluorothreonine (XXI) is carried out using as precursor ethyl 2-chloro-4,4,4-trifluoroacetoacetate (XCIV), which is readily obtained by the chlorination of 4,4,4-trifluoroacetoacetic ester.[91] The reduction of the carbonyl group of the ester (XCIV) leads to the formation of a mixture of diastereoisomers of ethyl 2-chloro-4,4,4-trifluoro-3-hydroxybutyrate (XCV) in a ratio of 7:4. Dehydrochlorination of hydroxyester (XCV) gives a single compound, the α-oxime (XCVI) to which the *trans*-configuration has been assigned.[91] Decomposition of the oxirane ring of the ester (XCVI) occurs mainly at the α-carbon atom leading to the formation of 4,4,4-trifluoro-*allo*-threonine as an ester or amide depending on the reaction conditions.



An alternative approach, comprising the condensation of ethyl *N,N*-dibenzylglycinate with ethyl trifluoroacetate under the action of sodium hydride and subsequent reduction of the carbonyl group and hydrogenolysis of the *N*-benzyl groups, gave a mixture of the diastereoisomers of trifluorothreonine (XXI) with a predominance of the *allo* form.[92]

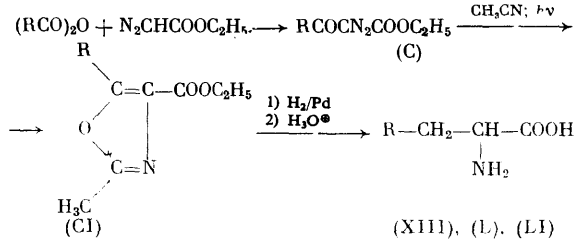


Opening of the oxirane ring with benzylamine or aniline in the bis(trifluoromethyl)glycidic ester (XCVII), obtained from hexafluoroacetone and diazoacetic ester,[93] leads to the formation of the ethyl esters of *N*-benzyl- and *N*-phenyl-4,4,4,4′,4′,4′-hexafluoro-3-hydroxyvaline (XCVIII) and (XCIX) respectively.[94]



R = $C_6H_5CH_2$ (XCVIII), C_6H_5 (XCIX)

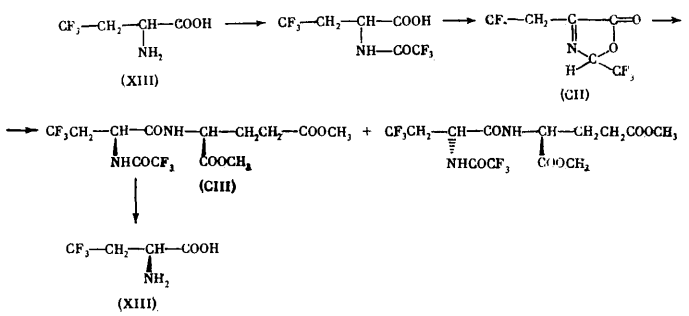
A general method has been developed for the synthesis of β-perfluoroalkylalanines based on the photochemical conversion of the perfluoroacyldiazoacetic esters (C).[34]



R = CF_3 (XIII), C_2F_5 (L), C_3F_7 (LI).

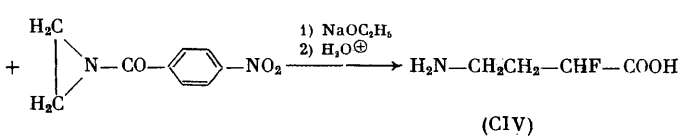
Irradiation of the compounds (C) leads to the formation of the ethyl esters of 2-methyl-5-perfluoroalkyloxazole-4-carboxylic acids (CI) the catalytic hydrogenation of which is accompanied by hydrogenolysis of the C—O bond giving the corresponding esters of *N*-acetyl-AA. Acid hydrolysis of the ethyl esters of *N*-acetyl-3-perfluoroalkylalanines gives 2-amino-4,4,4-trifluorobutyric acid (XIII), 4,4,5,5,5-pentafluoronorvaline (L) and 4,4,5,5,6,6,6-heptafluoronorleucine (LI).

An asymmetric process has been proposed to obtain the *L*-enantiomer of 2-amino-4,4,4-trifluorobutyric acid (XIII) using the racemic FAA (XIII) as starting material. *DL*-2-Amino-4,4,4-trifluorobutyric acid (XIII) was converted into 4-(2,2,2-trifluoroethyl)-2-trifluoromethyl-Δ^3-oxazolin-5-one (CII) by sequential trifluoroacetylation and dehydration by dicyclohexylcarbodiimide.[34]



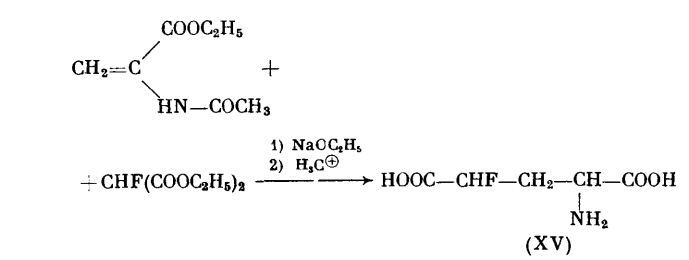
Opening of the oxazolinone ring of (CII) with dimethyl *L*-glutamate gives a mixture of the diastereoisomeric dipeptides (CIII) in a ratio $(L,L):(D,L) = 83:17$. Enantiomerically pure *L*-2-amino-4,4,4-trifluorobutyric acid (XIII) was obtained after numerous crystallisations of the mixture (CIII) with subsequent removal of the *L*-glutamic acid residue.

A convenient method of synthesising γ-amino-α-fluorobutyric acid (CIV) is based on the nucleophilic fission of the *N*-(4-nitrobenzoyl)aziridine anion with monofluoromalonic ester and subsequent saponification of the resulting condensation product.[95]

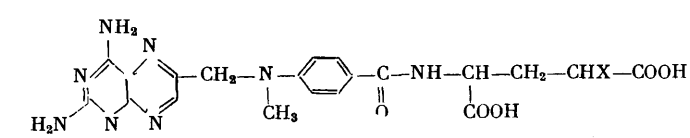


(CIV)

4-Fluoroglutamic acid (XV), obtained by the addition of fluoromalonic ester to ethyl 2-acetylaminoacrylate, has been used for the synthesis of the fluorinated analogue (CVI, X = F) of the known antitumour compound methotrexate (CVI, X = H) [35,38,96,97] which has been proposed for the treatment of leukaemia.[98]



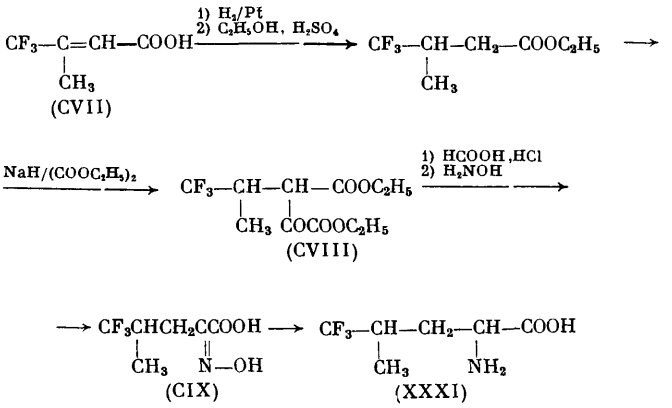
(XV)



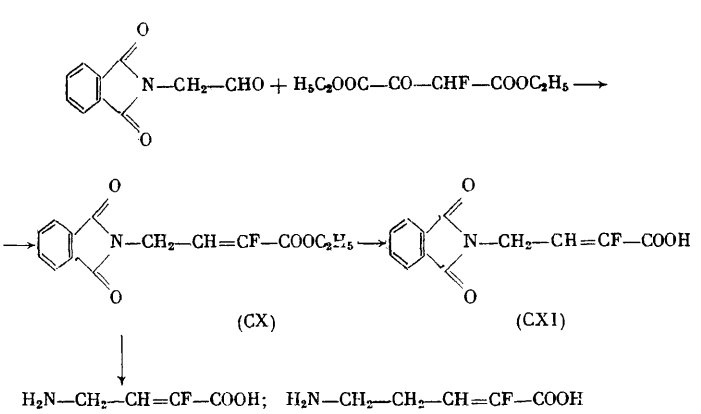
(CVI), X = H, F

It must be noted that this method gives a higher yield of FAA (XV) than the alternative Michael addition of ethyl 2-fluoroacrylate of acetamidomalonate.[35–37]

A multistage method has been proposed for obtaining 5,5,5-trifluoroleucine (XXXI) in which 4,4,4-trifluorocrotonic acid (CVII) is used as starting material.[99] The ketoester (CVIII) is synthesised from it by hydrogenation, esterification and condensation with diethyl oxalate. This is converted into the oxime (CIX) after hydrolysis of the ester groups and decarboxylation. Catalytic hydrogenation of the oxime (CIX) gives the desired AA, 5,5,5-trifluoroleucine (XXXI).



4-Amino-2-fluorocrotonic acid (LXIII) is obtained by boiling phthalimidoacetaldehyde with the sodium derivative of diethyl 2-fluoro-3-ketosuccinate in xylene, as a result of which compound (CX) is formed. Hydrolysis of it with dilute hydrochloric acid gives 2-fluoro-4-phthalimidocrotonic acid (CXI) but the use of concentrated HCl leads to the FAA hydrochloride (LXIII).



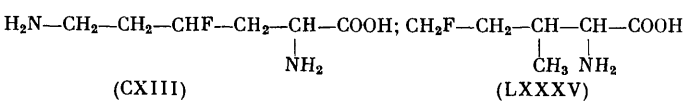
3-Phthalimidopropanal may be converted into 5-amino-2-fluoropent-2-enoic acid hydrochloride (CXII) in a similar manner.[100]

III. Application of methods of organofluorine chemistry to the synthesis of fluorine-containing amino acids

The application of the methods of organofluorine chemistry to the synthesis of aliphatic FAA is linked mainly with the possibility of introducing fluorine atoms and fluorine-containing groups directly into an already prepared AA and has certain advantages in some cases over the classical AA syntheses. For example replacement of hydrogen atoms by fluorine or fluoroalkyl groups in the side chain of an AA may be effected without affecting the chiral α-carbon atom of the AA. Consequently the use of enantiomerically pure AA in these syntheses enables optically active FAA to be obtained.

1. Replacement of hydrogen by fluorine

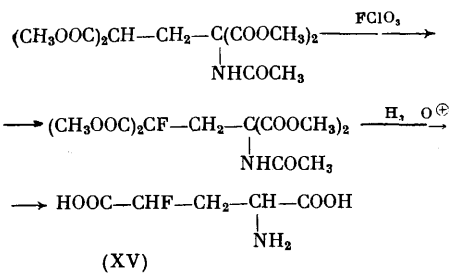
The use of methods for the direct fluorination of organic compounds to obtain aliphatic FAA is represented in the literature by only a few examples. This is evidently linked with the fact that aliphatic AA molecules are far less stable than aromatic AA towards the action of fluorine or its equivalents and also with the large quantity of reactive C–H bonds which is the reason for the very low regioselectivity of these processes. Thus after treatment of a solution of *L*-lysine in liquid HF with trifluoromethyl hypofluorite *L*-4-fluorolysine (CXIII) was isolated in low yield by ion exchange chromatography from the mixture of products. Compound (CXIII) has been used in a synthesis of a cyclic hexapeptide analogue of somatostatin.[101]



(CXIII) (LXXXV)

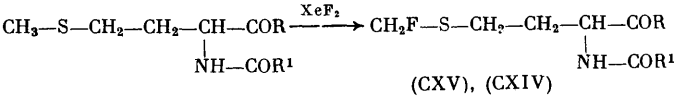
There are data on the formation of 5-fluoroisoleucine (LXXXV) by fluorinating isoleucine with trifluoromethyl hypofluorite. However its isolation was unsuccessful due to the ready heterocyclisation into 3-methylproline.[102]

4-Fluoroglutamic acid (XV) was obtained by replacing a hydrogen atom in the γ-position of tetramethyl 2-acetamido-2,4-dicarboxylglutarate with fluorine by reaction with perchloryl fluoride with subsequent hydrolysis and decarboxylation.[103–105]



(XV)

The differences in reactivity of the C–H bonds of methionine enabled the development of a preparative method for the monofluoro derivative of methionine (CXIV) and of the dipeptide methionyl-glycine (CXV) using XeF_2 as fluorinating agent.[106] It must be recorded that no products of more extensive fluorination, di- and trisubstituted compounds, were detected.

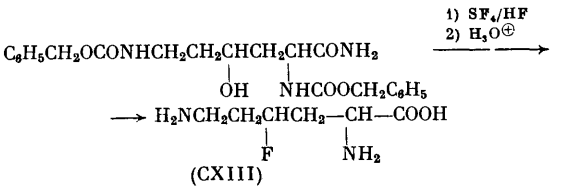


(CXV), (CXIV)

R = OCH_3, R^1 = CF_3 (CXIV); R = $NHCH_2COOC_2H_5$, R^1 = $OCH_2C_6H_5$ (CXV).

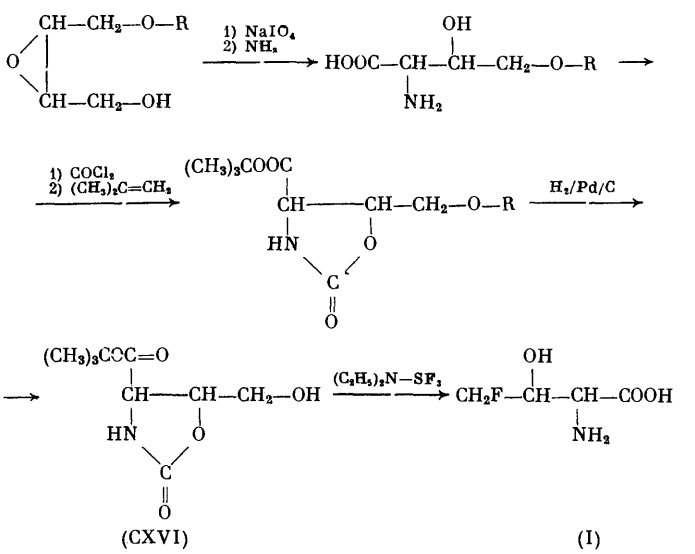
2. Replacement of a hydroxyl group by fluorine

The fluorodehydroxylation of protected 4-hydroxylysine by sulphur tetrafluoride in liquid HF proved to be a more efficient method of obtaining 4-fluorolysine (CXIII) than the direct fluorination of lysine with trifluoromethyl hypofluorite discussed above.[101]



(CXIII)

Optically pure (2*S*,3*S*)-4-fluorothreonine (I) is synthesised by the replacement of an OH group by fluorine by the reaction of diethylaminosulphur trifluoride (DAST) and the (4*S*,5*S*)-oxazolone (CXVI), which was obtained from (2*S*,3*R*)-3-benzyloxymethyl-2-hydroxymethyloxirane.[92]

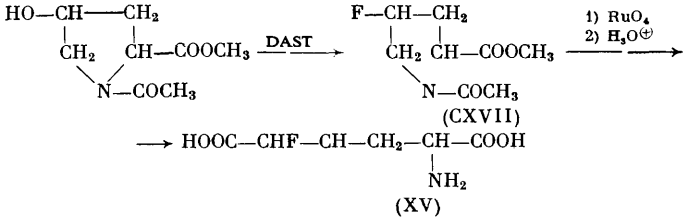


(CXVI) (I)

R = $CH_2C_6H_5$

The possibility of converting hydroxyproline into glutamic acid was used recently for the synthesis of optically pure (2*S*,4*S*)-4-fluoroglutamic acid (XV).[107] The fluorodehydroxylation of (–)-*N*-acetyl-*trans*-4-hydroxy-(*S*)-proline methyl ester by the action of DAST proceeds stereoselectively with the formation of a derivative of optically active 4-fluoroproline (CXVII). Compound

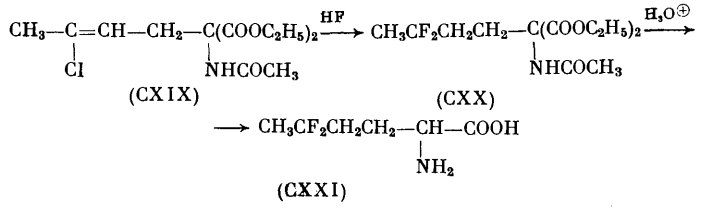
(CXVII) is oxidised regioselectively at the C(5) methylene group of the pyrrolidine ring and subsequent hydrolysis of the lactam (CXVIII) gives (2*S*,4*S*)-4-fluoroglutamic acid (XV).



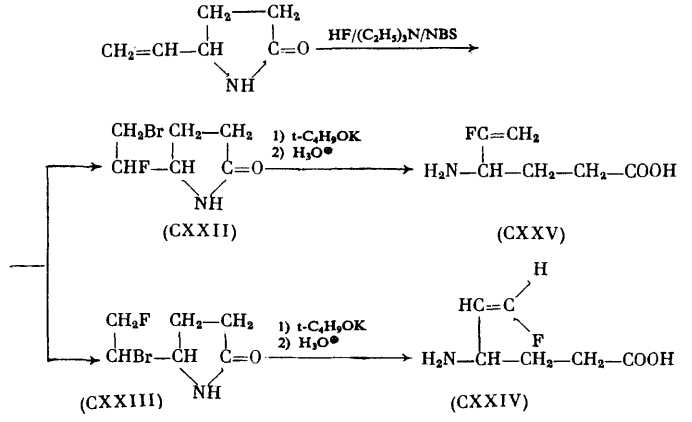
In view of the ease of *cis,trans*-isomerism of the 4-hydroxyprolines and the reduced cost of (+)-*cis*-4-hydroxy-*R*-proline it may be suggested that this method will be convenient for obtaining all four stereoisomers of 4-fluoroglutamic acid (XV).

3. Application of other methods of organofluorine chemistry to the synthesis of FAA

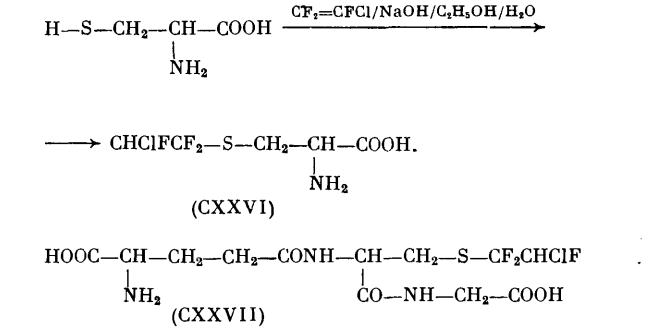
The action of hydrogen fluoride on the acetamidomalonic ester derivative (CXIX) leads to simultaneous addition of hydrogen fluoride to the C=C bond and replacement of the chlorine atom by fluorine. After hydrolysis of the product (CXX) a 50% yield of 5,5-difluoronorleucine (CXXI) is obtained.[108]



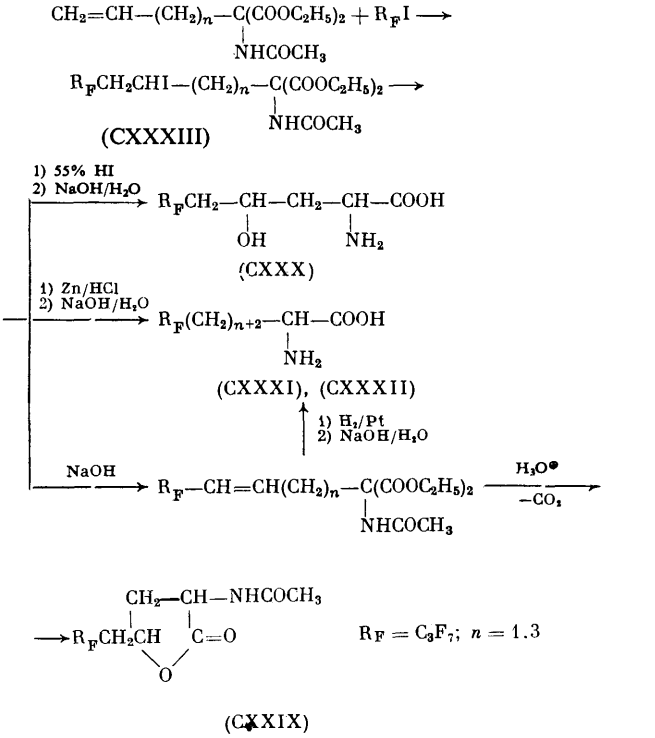
The combined addition of fluorine and bromine atoms to 5-vinylpyrrolid-2-one gives a mixture of the isomeric 5-(bromofluoroethyl)pyrrolidones (CXXIII), which is readily separated by chromatography. Dehydrobromination of compounds (CXXII) and (CXXIII) and subsequent hydrolysis leads to the formation of the γ-amino-γ-fluorovinylbutyric acids (CXXIV) and (CXXV). (*Z*)-γ-amino-γ-(2-fluoroethenyl)butyric acid (CXXIV) proved to be the strongest inhibitor of γ-aminobutyric acid (GABA) transaminase of the series of γ-fluorovinyl-substituted GABA (LXVI), (LXXVII), (CXXIV) and (CXXV).[71]



The direct chlorotrifluoroethylation of cysteine is effected by the reaction of chlorotrifluoroethylene and the disodium salt of *N*-t-butyloxycarbonyl-(*S*)-cysteine at 25 °C in aqueous ethanol.[109] (*S*)-*S*-Chlorotrifluoroethylcysteine (CXXVI) may be obtained by this reaction and from unsubstituted cysteine. The regioselectivity of the chlorotrifluoroethylation of the RS^- anion in the presence of RNH^- enables use of this approach for the direct chlorotrifluoroethylation of glutathione. The fluorinated analogues of cysteine (CXXVI) and of glutathione (CXXVII) proved to be nephrotoxic.



Progress in the area of free radical addition of perfluoroalkyl iodides to alkenic acids with a terminal C=C bond[110] has enabled development of a general method of synthesis of long chain FAA containing perfluoroalkyl groups.[111] The addition of perfluoropropyl iodide to diethyl 2-acetamido-2-allylmalonate ester or to diethyl 2-acetamido-2-(pent-4-enyl)malonate in the presence of the initiator azo-bis(isobutyronitrile) gives the products (CXXXVIII) in high yield.

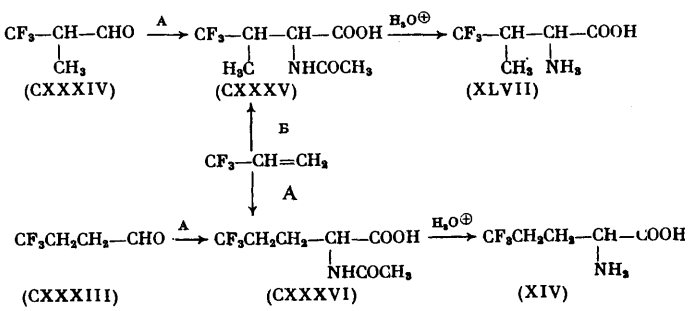


Subsequent hydrolysis of the acetamidomalonate (CXXVIII, $n = 1$) with 55% HI proceeds with simultaneous replacement of the iodine atom by hydroxyl, probably through the lactone (CXXIX), forming 2-amino-6,6,7,7,8,8,8-heptafluoro-4-hydroxyoctanoic acid (CXXX). In order to obtain free 2-amino-6,6,7,7,8,8,8-heptafluorooctanoic (CXXXI) and 2-amino-8,8,9,9,10,10,10-heptafluorodecanoic acids (CXXXII) the iodine atom is replaced by hydrogen, either directly in compound (CXXVIII) by the action of zinc and hydrochloric acid or by a two-stage process of dehydroiodination and catalytic hydrogenation, with subsequent removal of protecting groups and decarboxylation of one carboxyl group. This method is distinguished by high yields at each stage and by the availability of the starting materials. The FAA (CXXXI) and (CXXXII) may also be obtained from the corresponding α-bromocarboxylic acids.[111]

IV. Special methods of obtaining fluorine-containing amino acids

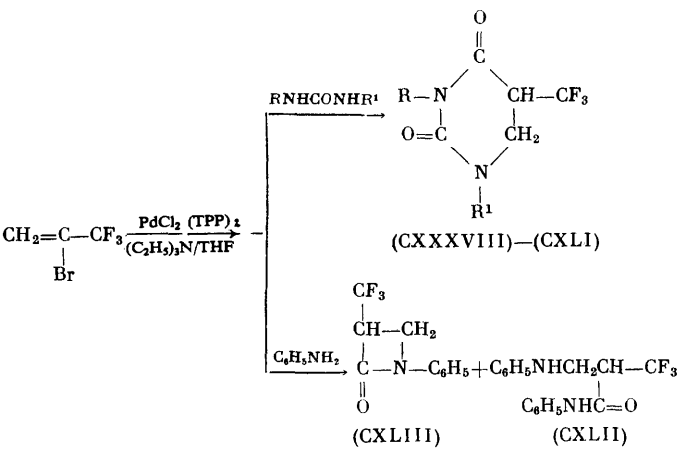
1. Amidocarbonylation of fluorine-containing amino acids

Trifluorovaline (XLVII) and trifluoronorvaline (XIV) are obtained by the amidocarbonylation of 4,4,4-trifluorobutyric (CXXXIII) and 3,3,3-trifluoroisobutyric (CXXXIV) aldehydes respectively. The amidocarbonylation of aldehydes (CXXXIII) and (CXXXIV) with acetamide in the presence of cobalt carbonyl and a mixture of carbon monoxide and hydrogen is carried under a pressure of about 100 atm on heating to 120 °C. Hydrolysis of the acetamides (CXXXV) and (CXXXVI) formed in high yield gives the free FAA (XLVII) and (XIV).[48,50,112] The trifluorovaline formed in this way is a mixture of two diastereoisomers in a ratio 38 : 62. Since the synthesis of the aldehyde (CXXXIII) from 3,3,3-trifluoropropene requires the same catalyst, viz. $Co_2(CO)_8$ and a CO/H_2 mixture,[47,113] the process of making trifluoronorvaline (XIV) in 94% purity may be effected directly from 3,3,3-trifluoropropene through the step of forming aldehyde (CXXXIII) *in situ*. Addition of small quantities of rhodium carbonyl to $Co_2(CO)_8$ leads to a change in the regioselectivity of the reaction giving *N*-acetyl-3,3,3-trifluorovaline (CXXXV) as the main reaction product (96% pure). Thus the regioselectivity of the preparation of trifluorovaline (CXXXV) or trifluoronorvaline (XIV) from trifluoropropene through the two steps of hydroformylation and amidocarbonylation is determined only by the nature of the catalyst.[114–116] The FAA (XLVII) and (XIV) are obtained in pure form by crystallisation of the crude product. Racemic trifluoronorvaline (XIV) has been separated into its (*S*)- and (*R*)-enantiomers by enzymic hydrolysis of its *N*-acetyl derivative.[50]



A = CO, H_2, CH_3CONH_2, $Co(CO)_8$; B = A + $Rh_6(CO)_{16}$.

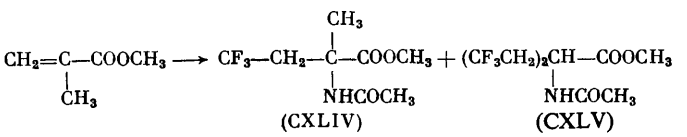
3,3,3-Trifluoropropene also proved to be a convenient starting material for the synthesis of α-trifluoromethyl-β-alanine derivatives. Trifluoropropene is converted in two stages (bromination, dehydrobromination) into 2-bromo-3,3,3-trifluoropropene (CXXXVII) in high yield.[117] Ureidocarbonylation of the propene (CXXXVII) with 1,3-dimethylurea and carbon monoxide on a catalyst consisting of the complex of palladium chloride with triphenylphosphine leads to the formation of 5-trifluoro-1,3-dimethyl-5,6-dihydrouracil (CXXXVIII) in 70% yield. The use of methylurea in this reaction gives a mixture of the 1-methyl- (CXXXIX) and 3-methyl-substituted (CXL) dihydrouracils in a ratio of 1 : 5. Unsubstituted urea forms 5-trifluormethyldihydrouracil (CXLI) (26%),[48,118,119] from which it is possible to obtain free α-trifluoromethyl-β-alanine (LXXVII) by hydrolysis. The use of aniline instead of urea enables the amide (CXLII) and β-lactam (CXLIII) of *N*-phenyl-α-trifluoromethyl-β-alanine to be obtained.[48]



TPP = $(C_6H_5)_3P$; R = R^1 = CH_3 (CXXXVIII); R = CH_3, R^1 = H (CXXXIX); R = H, R^1 = CH_3 (CXL); R = R^1 = H (CXLI)

2. The trifluoromethyl-acetamidation of olefins

The electrolysis of a mixture of trifluoroacetic acid and methyl methacrylate in aqueous acetonitrile leads to the formation of a complex mixture of products. From this the methyl esters of β-trifluoromethyl-α-methylalanine (CXLIV) and bis(trifluoroethyl)-glycine (CXLV) are isolated in 20 and 5% yield respectively.[120] As suggested, the electrochemical trifluoromethyl-acetamidation of methyl methacrylate may be used for the preparation of FAA (CXLIV).



At present the synthesis of fluorine-containing amino acids is a component of the approach to the solution of one of the basic problems of bio-organic chemistry, namely the purpose-directed modification of the natural bioregulators (mainly peptidic in nature)

to adjust their functions and properties (activities) in the required direction. Amino acids with one or more fluorine atoms on their carbon skeleton are required for the solution of this problem. As is seen from the literature data considered in this review the known methods of synthesis of aliphatic FAA enable practically any AA containing one fluorine atom or perfluoroalkyl groups to be obtained. However, the methods cited in the present review are not all of preparative value. Fluorine-containing amino acids, including the aliphatic AA, still remain difficultly accessible compounds, paticularly as pure diastereo- and/or enantiomers, for the majority of biochemical laboratories. The problem of the asymmetric synthesis of FAA must be taken separately and with certain exceptions has no optimal solution at present. Consequently it must be expected that further work in the area of FAA synthesis will be directed mainly to the creation of preparative methods of synthesis of these compounds from available organofluorine compounds using the latest achievements of organometallic chemistry, engineered enzymology and asymmetric synthesis.

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Translated from *Uspekhi Khimii* **60** 1708–1743 (1991)

U.D.C. 535.33.34.34:541.651:547.97

Structure and spectral-luminescent properties of polymethine dyes

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ABSTRACT. The review considers the influence of the length of the polymethine chain, the structures of the hetero-radicals, the nature of substituents, electronic asymmetry, interactions of chromophores, structures of ion-pairs, photochemical reactions with proton transfer, and concentration, on the spectral-luminescent properties of polymethine dyes. The characteristic features of these properties in low-polarity media, including polymeric matrices, are discussed. Solvatochroism and solvatofluorochroism of polymethines are considered. Major factors influencing changes in the spectral-luminescent properties of cyanines, in relation to their structure and the nature of the medium, are revealed. Possible applications of polymethines to the solution of various problems connected with the transformation of light energy are discussed.

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I. Introduction

Polymethine (cyanine) dyes (PD) are unique agents for the transformation of light energy in the visible and near infrared region of the spectrum.[1] They are able to strengthen and to weaken radiation, to change its wave length and to sensitise and desensitise various photo-processes,[2–6] and are thus suitable for wide application in various areas of science and technology.[7] In order to search effectively for PD that are specifically able to transform light energy, it became necessary to establish a relationship between their chemical structure and spectral-luminescent properties.

In the course of the long history of investigations of PD, fundamental relationships were obtained linking coloration with structure, making possible the synthesis of dyes with desired absorption maxima λ^{a}_{max}.[8–10] In spite of such a long history of investigation, interest in PD has revived strongly in recent times. This has been caused primarily by the fact, that in addition to their traditional application in the photographic industry,[10,11] PD have found wide application from the mid-seventies in other fields of technology, especially in the rapidly growing area of quantum electronics.[2,5,12,13] Only by the application of PD as passive locks has it been possible to obtain laser impulses of extremely short duration: femtoseconds (using jet dye lasers) in the visible region (487–508,[14] 553–570,[15] 576–615,[16] 652–694 nm[17]) and picoseconds (using solid state lasers) in the near infrared region (750–790,[18] 1060,[19] 1320,[20] and 1540 nm[21]). New possibilities have thereby been opened up for the investigation of ultra-fast photo-processes in chemistry and biology.[22] At the present time, PD are the only organic dyes which can be used as active laser media to provide generation (i.e. to change the wave length of laser radiation) in the region >1000 nm: 1080–1170,[23] 1150–1240,[24] 1200–1320,[25] 1425,[26] 1550, 1600, and 1800 nm.[27] The passive synchronisation and generation of radiation in this region are of great interest in the fields of optical fibres and medicine.[28,29]

However, the specific search for cyanines for use in quantum electronics cannot be carried out effectively on the basis of a relationship linking only λ^{a}_{max} and structure of the PD.[8–10]. It became necessary to establish an analogous relationship for luminescence. But this was also soon found to be insufficient in the effective search for PD with the required properties, since identical values of λ^{a}_{max} and of λ^{f}_{max} may be associated with different dyes, which differ distinctly in such spectral-luminescent properties as quantum yield of fluorescence, φ, life time of the excited state, τ, and shape of the bands (especially their width, σ). These differences determine the assignment of the PD to the solution of one or another problem. Thus, dyes with small values of σ, φ, and τ are used as passive locks for quality modulation and mode synchronisation of optical quantum generators.[30,31] On the other hand, dyes with large values of these parameters are applied as active media for frequency conversion in lasers.[2,12] New spheres of application for PD have stimulated the investigation of their spectral-luminescent properties and have led to the appearance of numerous publications in the literature. However, there are no reviews of this work†.

In the present review, a systematic analysis of literature data, including work of the author in the field of spectral-luminescent properties of PD, is first carried out. Considerable attention is given to problems of directional change of the Stokes shift (ΔS) and quantum yields of fluorescence of PD, the characteristics of their spectral-luminescent properties in low polarity media (including

† Reviews are available on analogous topics for aromatic[32] and heterocyclic compounds.[33]

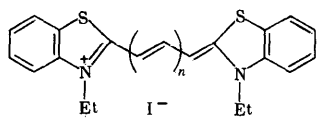
polymeric matrices), and the application of PD for the transformation of light energy. Prospects for future investigations of the spectral-luminescent properties of PD are considered.

II. Influence of the structure of the chromophore on the spectral-luminescent properties of polymethine dyes

Spectral-luminescent properties of polymethine dyes are due principally to their long-wave $\pi-\pi^*$ transition, the dipole moment of which is directed along the chain of conjugation from one heteroradical to the other. The probability of this transition is strongly dependent on structural changes in the chromophore. Therefore, the structure of the chromophore has an essential influence on the spectral-luminescent properties of PD.

1. Influence of the length of the polymethine chain on the spectral-luminescent properties of polymethine dyes

The polymethine chain (PC) is the major structural factor determining the spectral-luminescent properties of PD. In the example of the classical cyanine series of benzthiazoles, (I)–(V), it is seen that a change in chain length of only one vinylene group gives rise in symmetrical PD to a corresponding change in both λ^a_{max} [34] and λ^f_{max} [35] of about 100 nm. This agrees well with theoretical predictions of the change in position of electronic bands, with the length of the PC.[36,37]



(I) - (V)

Dye	n	λ^a_{max}, nm	λ^a_{max}, nm (CH_2Cl_2)
(I)	1	560	580
(II)	2	665	683
(III)	3	770	793
(IV)	4	895	918
(V)	5	1000	1023

The shapes of the bands in the absorption and fluorescence spectra, in contrast to their maxima, change in different ways with increase of n (Fig. 1*a*, *b*). Lengthening of the PC leads to a sharp fall in the selectivity of absorption (to a decrease in intensity and widening of the bands).[34] In addition, the dependence of the shape of the absorption bands on the nature of the solvent is increased (Fig. 1*a*). Conversely, the fluorescence bands become narrower with increase of n, and their shape is practically independent of the nature of the solvent[38] (Fig. 1*b*).

The shapes of the absorption and fluorescence bands of PD are determined mainly by vibrational and intermolecular interactions.[34,39] With increase of n in symmetrical cyanines, the former gradually become less, but the latter increase in strength.[34] A decrease in vibrational interactions leads to a narrowing of the bands, and an increase in intermolecular interaction leads, conversely, to broadening.[34] In the spectra of the thiocyanines (I)–(V), the described effects are explained by the dominant role of intermolecular interactions in absorption and of vibrational interactions in fluorescence.[38]

The length of the PC has a considerable effect on the quantum yield of fluorescence. Thus, for the symmetrical thiocyanines (I)–(V) and their analogues with benzoxazole and indolene radicals, the magnitude of φ increases with increase of n from 0 to 2–3.[35] For $n > 3$ the quantum yield for these PD decreases sharply.[35] For $n = 0$ and $n \geqslant 4$, the magnitude of φ is $< 1\%$. In the case of di- and tri-carbocyanines, φ varies within the range 25–58%.[35]

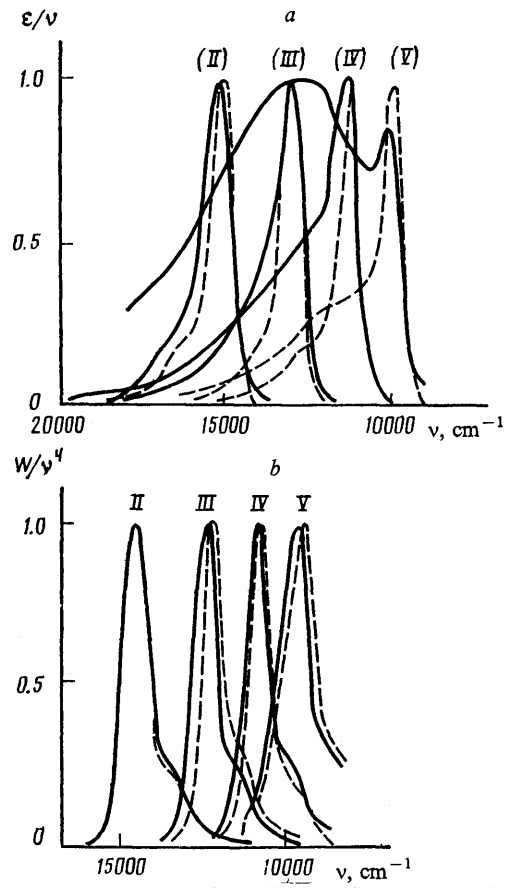
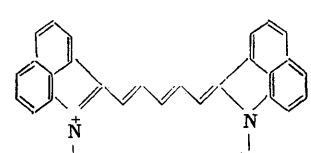
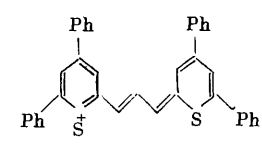


Figure 1. Absorption (*a*) and fluorescence (*b*) spectra for PD (II)–(V) in CH_2Cl_2 (dotted lines) and in DMF (continuous lines).

Small values of φ for the lower vinylogues are caused by effects arising from the close proximity of the nuclei, leading either to deviation from coplanarity,[40] or to interaction between the non-bonded heteroatoms.[41] The fall in the quantum yield of fluorescence with the higher vinylogues is caused, apparently, by the increased probability of internal conversion with increase of n, on account of a decrease in the energy difference between the ground (S_0) and first excited (S_1) states.[43,44] Such an assertion accords well with the fact that cyanines (VI) (λ^a_{max} = 876 nm, φ = 0.1%) and (VII) (λ^a_{max} = 865 nm, φ = 0.2%), with much shorter PC than the tetracarbocyanine (IV) whilst absorbing in practically the same region,[35] have almost the same values of φ.



(VI)



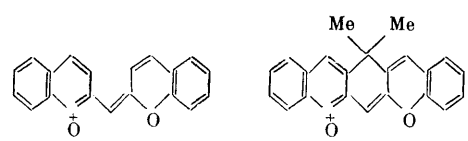
(VII)

The life times of the excited states of PD vary with increase in n in the same way as the quantum yields of fluorescence, since the change in τ[45–47] with lengthening of the PC results from the same causes as the change in φ.

Attention is drawn to the fact that for PD with an open PC, even in the optimum region of absorption in which internal conversion is a minimum, the quantum yields of fluorescence are mainly in the region of 20–40% and only in the case of oxatricarbocyanine, φ = 58%.[35] Moreover, it is possible that the latter value is overestimated, as are the values of φ for thio- and indotricarbocyanines, since later measurements on these PD by other authors[48] gave smaller magnitudes for φ on the second occasion. These facts indicate that low values of quantum yields for PD with open PC are linked not only with internal conversion but also with the nature of the chain.

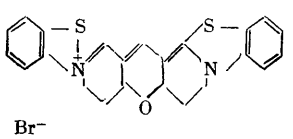
In symmetrical PD, the lengths of the carbon–carbon bonds are to a large extent equalised, as in aromatic compounds, and approximate to a bond order of one and a half.[49] Therefore rotation about these bonds is difficult by comparison with ordinary bonds. Nevertheless, the energy required is not large (33–63 kJ mol^{-1}).[40] In the ground state, dyes having no substituents in the PC and with $n \geqslant 1$ exist mainly as all-*trans* isomers.[4,40] With the introduction of bulky substituents into the PC, rotation about the bonds occurs, leading to the formation of various types of *cis*-isomer.[4,40]

With electronic excitation, the order of the carbon–carbon bonds decreases considerably,[50] so that rotation becomes easier. Therefore PD easily form photoisomers, which serve as basic "channels" for deactivation of the electronic excitation energy of cyanines.[4] The formation of photoisomers causes a sharp reduction in both the quantum yield and the life-time of the excited state.[3,51–53] Therefore, in spite of the fact that the oxygen analogue of PD (II), widely known as DODCI, possesses a nanosecond τ in its normal state, it is effective for passive mode synchronisation in dye lasers under pico- and even femto-second conditions[54] (it works as a short-life photoisomer[55,56]). It should be noted, that deactivation of the excited state will occur not only through rotations about the carbon–carbon bonds of the PC, but also through torsional vibrations about them.[3,4] If these rotations or vibrations are not hindered, then no structural changes whatever, which favour an increase in φ, wil be able to raise it to a value approaching 100%.



(VIII) (φ = 4%)

(IX) (φ = 97%)



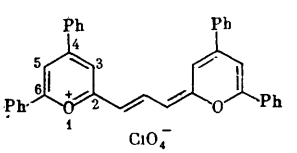
(X) (φ = 53%)

One way to solve this problem is by fixing the links of the PC rigidly with the aid of saturated bridging groups. Thus, for the monomethine cyanine (VIII), with an open PC, fluorescence is not visibly observed because of the low value of φ.[57] In the case of its analogue (IX), which has a rigidly fixed chromophore, such a strong golden-yellow luminescence is "kindled", that it masks the true crimsom colour of the dye which is like that of the compound (VIII). A sharp increase in φ is also observed by fixing the links of the PC of trimethine cyanines as, for example, in the case of PD (X).[58–60] In its benzoxazole analogues, φ = 80–90%.[58–60] Cyanines with completely fixed PC, containing five or more methine groups, are not known at present. There are certain PD with long PC, in which some of the groups form part of a saturated cyclic grouping,[61] but the fixing of separate parts of the PC only does not have such a significant effect on the value of φ,[62–65] as in the cases considered above.[58–60]

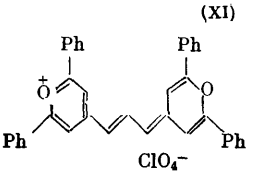
2. Influence of the structures of hetero-radicals on the spectro-luminescent properties of polymethine dyes

The structures of the hetero-radicals exert a very strong influence on the spectral-luminescent properties of PD. Thus, replacement of the benzthiazole nucleus in the dyes (I) and (II) with thiopyran or benz[*c*,*d*]indole groups [PD (VI) and (VII) respectively] gives rise to practically the same change in the absorption and fluorescence bands as does lengthening of the PC by two (*ca.* 200 nm) and three (*ca.* 300 nm) vinylene groups. In this way it is possible to obtain deeply coloured luminophores with short PC. Interest in such PD depends firstly on the fact that they are much more stable than dyes with long PC.[8,9]

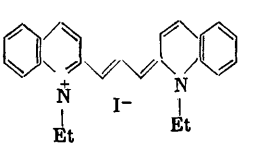
Isomeric change in the hetero-radicals has a significant effect on the spectral-luminescent properties of PD. Thus, cyanines in which the pyranyl or thiopyranyl heterocycles are linked to the chromophore by atom C(2) [PD (XI)], absorb or luminesce in a significantly longer wavelength region of the spectrum than their isomers, the pyran-4-yl (or thiopyran-4-yl) cyanines [PD (XII)].[41] For the nitrogen analogues of PD (XI) and (XII)[41] and the quinocyanine PD (XIII) and (XIV)[66] the opposite is true.



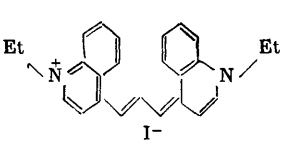
(XI)



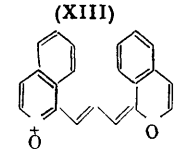
(XII)



(XIII)



(XIV)



(XV)

PD	λ^{a}_{max}, nm (CH_2Cl_2)	σ, cm^{-1}	φ, %	τ, ps	δ
(XI)	800	1176	1	—	0.176
(XII)	686	801	9	—	0.116
(XIII)	607	975	$\leqslant$0.01	9	0.182
(XIV)	713	769	2	37	0.083
(XV)	706	964	5	—	0.142

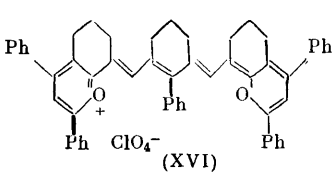
This is due to the fact that in pyran-2-yl- and thiopyran-2-yl-cyanines the carbon–carbon bonds in the hetero-radicals participate less in the general system of conjugation than in the pyrid-2-ylcyanines because of the smaller tendency to conjugation of atoms of oxygen and sulphur in comparison with atoms of nitrogen.[41]

Isomerism of the hetero-radicals is also strongly reflected in the shapes of the electronic bands of PD. The majority of symmetrical cyanines, including (XII) and (XIV) have characteristic spectral curves of similar shape, with vibrational maxima in their short-wave region.[67,68] For pyran-2-ylcyanines and their analogues there are anomalies. At room temperature the spectral curves of these compounds [for example, for (IX), (XI), and (XIII)] have four vibrational maxima[57,69,70] which is not uncommon for complex organic dyes.[71,72] For the 2-isomers, the absorption and luminescence bands are quite broad,[41,66,73–75] but the magnitudes of φ and of τ[76,77] are substantially less than for PD of types (XII) and (XIV).

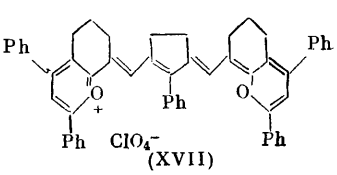
On the basis of quantum mechanical calculations using the squares of the changes in bond order (δ) on excitation[78] as a quantitative measure of the vibrational interactions in the PD chromophores, it was shown that there is an intensification of the vibrational structure, and a consequent widening of the bands, on going from the 4- to the 2-isomer in the pyranylcyanine series and their analogues.[79] Such an intensification is caused primarily by a sharp reduction in bond order between atoms C(3) and C(4) on excitation, a change which considerably exceeds that for all other bonds and which accounts for a significant contribution to the total magnitude of δ.[79]

Hence it follows that any structural modifications of the hetero-radicals of pyran-2-ylcyanines and their analogues, which hinder a change in the length of the bond between atoms C(3) and C(4), must lead to a weakening of the vibrational interactions. This can be achieved quite effectively as a result of annelation involving this bond, since a lowering of its order in the ground state decreases the extent to which it can change on excitation. Indeed, the bond between atoms C(3) and C(4) in cyanine (XV) contributes only 4% to the total magnitude of δ, whereas the analogous bond in the dye (XI) contributes 33%.[79] As a result, for PD (XV), a weakening of the vibrational interactions occurs, accompanied by a narrowing of the absorption bands in comparison to the analogous bands for compound (XI).

Vibrational interactions in molecules of PD are among the fundamental factors giving rise to a reduction in φ and τ.[80,81] It is very likely, therefore, that attenuation of their magnitude on going from the 4- to the 2-isomers is caused by an intensification of vibrational interactions. This assertion accords with the fact, that the excited states for pyran-2-yltricarbocyanines (XVI) and (XVII) have unusually short life times ($\leqslant 3$ ps).[19,77] Such small values of τ have made it possible to use PD (XVI) and (XVII) and their analogues as passive locks for lasers, with λ = 1060 nm, in order to generate impulses of extremely short duration.[19,77,82,83]



(XVI)



(XVII)

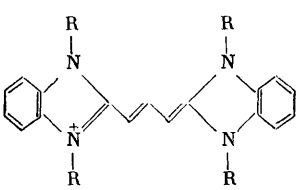
It should be noted, however, that the pyran-2-yl- and thiopyran-2-yl-cyanines are much more deeply coloured than the 4-isomers (by *ca.* 100–110 nm).[41] It can therefore be assumed that the reduction in φ and τ, on going from the latter to the former, is caused[43,44] by an increase in internal conversions. However, for the isomeric quinocyanines (XIII) and (XIV), the same tendency is observed in the changes in φ and in τ, in spite of the fact that pinacyanol (XIII) absorbs in a considerably more short-wave region (at 106 nm), than cryptocyanine (XIV). It can therefore be assumed that vibrational interactions play a dominant role in the reduction of φ and τ, on going from the 2- to the 4-isomer.

3. Influence of the nature of the substituents on the spectral-luminescent properties of polymethine dyes

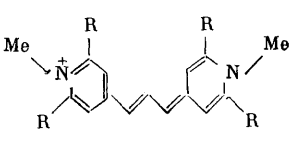
To regulate the extent of vibrational interactions in molecules of PD it is possible to introduce substituents with various electronic characteristics[84] into different positions of the heteroradicals[85–90] and into the PC.[91,92] For example, additional intensification of the vibrational interactions and a consequent shortening of the life time of the excited state of the pyran-2-yltricarbocyanines (XVI) and (XVII) is achieved on account of the electron-donating saturated cyclic groupings.[92]

Substituents containing heavy atoms, for example bromine and iodine,[4] have a considerable influence on the deactivation of electronically-excited states. They significantly increase the probability of intersystem crossing $S_1 \rightsquigarrow T$, because of the sharply decreasing values of φ and τ corresponding to the PD.[93] The role of such substituents in PC is more important than in the hetero-radicals.[93]

Substituents with their own conjugated electron system, such as those that are able to increase the Stokes shift of the PD molecules significantly, are of great interest.[93] Thus, the replacement of ethyl groups in the cyanine (XVIII) by phenyl [PD (XIX)], or better still by a heterocycle [PD (XX)], leads to an increase in ΔS and in φ.[94]



(XVIII)—(XX)



(XXI), (XXII)

PD	R	λ^a_{max}, nm	λ^f_{max}, nm	φ, % (ethanol)
(XVIII)	Et	500	515	0.5
(XIX)	Ph	519	563	5
(XX)	Py	530	593	25

PD	R	λ^a_{max}, nm	λ^f_{max}, nm (CH_2Cl_2)
(XXI)	Me	610	620
(XXII)	Ph	644	673

These effects have been shown to be associated with intramolecular processes. The increase in φ, by the introduction of substituents with their own π-system, is thought to be due to a decrease in the probability of the formation of stereoisomers, on account of "weighting" of the PD molecule with these substituents.[94] The increase of the Stokes shifts in the cited work is not explained. However, an explanation may easily be given on the basis of an analysis of the change in electronic structure of PD (XIX) and (XX) on excitation.

In the ground state of cyanine molecules (XIX) and (XX), the phenyl and pyridyl groups are displaced from the plane of the basic chromophore to a considerable extent, on account of steric hindrance by the atoms of hydrogen in positions 4,4′; 7,7′; and

8,8′. In the excited state, it follows from simple Hückel molecular orbital calculations for PD (XIX) (Fig. 2), that the bonds between N and C(2); C(4) and C(3*a*); C(7) and C(7*a*) are lengthened significantly. (In the calculations the parameters used were taken from Ref. 95, the angle of rotation of the phenyl group being represented by a value of $\beta_{C-Ph} = 0.7$). The steric hindrance to rotation of the phenyl groups is thereby reduced and they can therefore become much more nearly coplanar on excitation. Approach to coplanarity will also be favoured by the fact that in the excited state the N–Ph bond order is increased. A more planar structure for the phenyl (or pyridyl) substituted PD, (XIX) and (XX), in the excited state, compared with the ground state, leads to a larger bathochromic shift of the fluorescence bands than for the absorption bands. Therefore, a change from cyanine (XVIII) to (XIX) or (XX), is accompanied by an increase in ΔS.

On the basis of the above, it can be concluded that the introduction into a PD molecule of substituents with their own conjugated electron systems, capable of becoming more nearly coplanar on excitation, brings about an increase in the Stokes shift. Indeed, the replacement of methyl groups in the cyanine (XXI) by phenyl [PD (XXII)], increases ΔS. This arises from the fact that steric hindrance between the Ph and methyl groups in the ground state gives rise to a considerable departure from coplanarity with the chromophore,[96] but in the excited state, as a result of a decrease in the bond order of the bonds between the atoms of C and N and an increase in the order of the Ph–C bonds (Fig. 2), the groups becomes much more nearly coplanar.

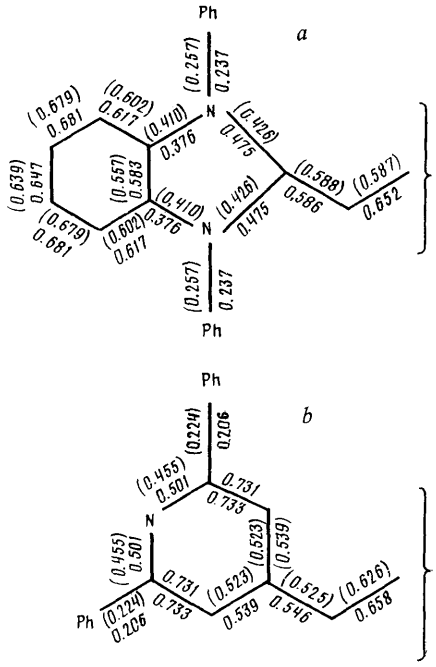
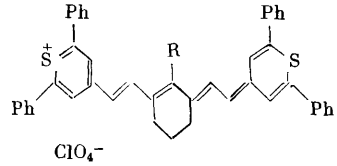


Figure 2. Orders of the π-bonds in the cations of PD (XIX) (*a*) and (XXII) (*b*) in the ground state and (in brackets) the excited state.

An analogous change in the conformation of the phenyl groups on excitation explains the anomalous Stokes shifts for 2,6-diphenyl substituted pyridine salts.[97–100]

In the *meso*-position of tricarbocyanines, the phenyl group also deviates considerably from the plane of the chromophore in the ground state.[101] However, replacement of the hydrogen atom in this position in the thiopyran-4-yltricarbocyanine (XXIII) with a phenyl group (compound XXIV) does not in practice increase ΔS.[102] The phenyl group in PD (XXIV) moves little towards coplanarity in the excited state.

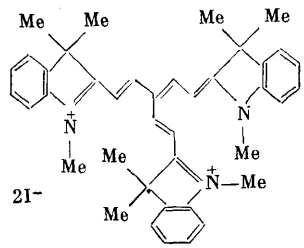


(XXIII), (XXIV)

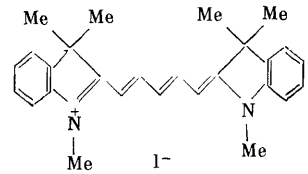
PD	R	λ^a_{max}, nm	λ^f_{max}, nm (CH_2Cl_2)
(XXIII)	H	1035	1090
(XXIV)	Ph	1040	1097

Especially large increases in Stokes shifts occur with the introduction into the *meso*-position of substituents that lead to branching of the PC, i.e. to the formation of tricyclic PD, for example (XXV), and its analogues.[103,104]

The magnitude of ΔS for the tricyclic dye (XXV) (1597 cm^{-1}) is almost twice that for the corresponding bicyclic PD (XXVI) (632 cm^{-1}).



(XXV): $\lambda^a_{max} = 636$ nm, $\lambda^f_{max} = 698$ nm



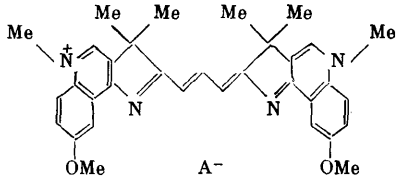
(XXVI): $\lambda^a_{max} = 640$ nm, $\lambda^f_{max} = 667$ nm.

Such a marked effect depends on the considerable change in geometry that occurs on excitation of the molecule (XXV) compared to (XXVI). In the ground state, tricyclic dyes have a propellor-like structure but in the excited state each of their nuclei in turn becomes perpendicular to the plane of the other two.[103,104] In bicyclic cyanines, excitation mainly brings about a change in bond lengths.

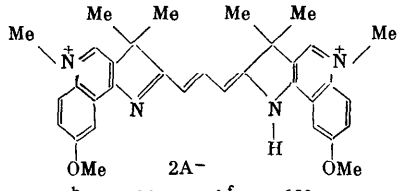
An increase in the Stokes shifts for PD (XXV) and its analogues is accompanied, in contrast to cyanines (XVIII)–(XX), by a marked lowering of φ.[104,105] This is linked with the fact that for tricyclic dyes the coplanarity is disturbed and there is a much more pronounced alternation of the bonds in the PC, than in the corresponding bicyclic dyes.[103,104] Consequently, the vibrational interactions and conformational processes are intensified in the former by comparison with the latter, with the result that PD (XXV) fluoresces much more weakly than (XXVI).

4. Photochemical reactions with proton transfer

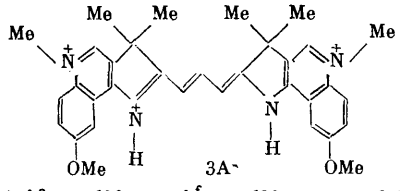
Large values of Stokes shifts and high quantum yields of fluorescence can be achieved for certain PD, for example (XXVII), through reversible photochemical reactions with proton transfer.[106,107] In absolute ethanol, this dye exists in the monocationic form (XXVII, a). On acidification with weak acids the protonated, dicationic form (XXVII, b), is produced. As a result, the electronic symmetry is disturbed and the conjugation of the chain is shortened, so that it absorbs in a considerably more short-wave region of the spectrum, than (XXVII, a). In strongly acidic solutions, compound (XXVII)



(XXVII, a): $\lambda^a_{max}=710$ nm; $\lambda^f_{max}=735$ nm; $\varphi=24\%$,



(XXVII, b): $\lambda^b_{max}=530$ nm; $\lambda^f_{max}=650$ nm; $\varphi=7\%$,



(XXVII, c): $\lambda^a_{max}=600$ nm; $\lambda^f_{max}=620$ nm; $\varphi=3.5\%$,

exists in the diprotonated, tricationic form, (XXVII, c). In this case the electronic symmetry of the molecule is restored, but the chain of conjugation becomes shorter. The absorption band of form (XVII, c) is therefore found in an intermediate region between the forms (XXVII, a) and (XXVII, b). For the PD (XVII) in the ground state there is an equilibrium (XXVII, a)$\rightleftharpoons$(XVII, b) or (XVII, b)$\rightleftharpoons$(XXVII, c), depending on the pH.

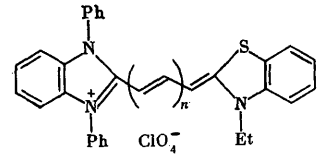
On excitation form (XXVII, b) results, with the loss of a proton, on account of redistribution of electron density in the chromophore. Therefore in the fluorescence spectra, in addition to the band of the dication (XXVII, c) the band responsible for the form (XXVII, a) appears, with a high value of φ, providing a large Stoke shift relative to the absorption of form (XXVII, b). This has made it possibe to use the equilibrium (XXVII, b)$\rightleftharpoons$(XXVII, a) for the generation of laser emission in the region of 720–810 nm, i.e. with a large shift relative to the wave length pumped, λ_P (λ_P = 530 nm).[106,107]

The form (XXVII, c) does not generate emission, most probably because of the low value of φ. In addition, it does not change on excitation into form (XXVII, b), or into form (XXVII, a). The first transformation does not occur because dissociation of the diprotonated form with formation of the excited monoprotonated form is energetically unfavourable, and the second is of low probability since it requires the simultaneous transfer of two protons.

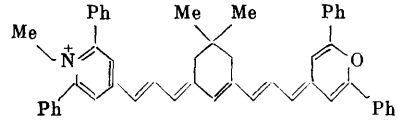
Photochemical reactions with proton transfer are highly sensitive to change in pH of the medium and are only characteristic of a small number of PD. These circumstances give rise to their wide application for the transformation of light energy.

5. Electronic asymmetry and spectral-luminescent properties of polymethine dyes

Asymmetrical PD are far more promising for the transformation of light energy.



(XXVIII) – (XXX)



(XXXI)

PD	n	Solvent	λ^a_{max}, nm	D^a_λ, nm	λ^f_{max}, nm	D^f_λ, nm
(XXVIII)	1	DMF	528	13	567	7.5
(XXIX)	2	DMF	618	22	670	2.5
(XXX)	3	DMF	645	95	779	5.0
(XXXI)	—	MeCN	610	387.5	1020	35.0

In the ground state of these cations the charge is mainly localised on the more electron-donating nucleus,[108–111] so that an alternation of single and double bonds arises in the PC leading, in the absorption spectra, to a rise in the deviation (D^a_λ), attenuation of the vinylenic shifts, and broadening of the bands.[108–111]

In the excited state, the nuclei of the hetero-radicals become equivalent to a considerable extent. For example, in the S_1-state of PD (XXX),[111] the total charges on the benzimidazole and benzthiazole radicals amount to 0.640 and 0.631, whereas in the S_0 state they are 0.858 and 0.388 respectively. Equalisation of the charges on the hetero-radicals and, consequently, equalisation of their electron-donating abilities, greatly reduces the alternation in the bond order in the PC of the cation in the excited state. Thus, for example, a measure of their alternation, calculated as described[57] for the dye (XXX) in the excited state, is 0.098 but in the ground state is 0.126. Consequently, typical electronically-asymmetric PD tend towards electronic symmetry in the excited state. This leads to a sharp decrease in the deviation in the fluorescence spectra (D^f_λ), a narrowing of their bands, and a rise in the vinylenic shifts of approximately 100 nm, i.e. to values characteristic of symmetrical PD. Asymmetric PD also retain high values of φ, at the level of the symmetrical PD.[112]

A marked difference in the electronic structure of asymmetric PD in the ground and excited states causes a large Stokes shift. Since this occurs for high values of φ, then highly effective generation of radiation was obtained for solutions of asymmetric cyanines in the near infrared region (650–900 nm).[112,113] It is significant, that in view of their wide absorption bands,[111-113] the generation of emission by PD of types (XXVIII)–(XXX) occurs with a pump of different

wave length from the most used sources of radiation in the visible range (510, 530, 578, 694 nm).[112,113] Asymmetric PD are advantageously different in this respect from the wide range of active media based on coumarins, rhodamines and oxazines.[112,114]

Variations between the absorption and fluorescence spectra of asymmetrical PD are more significant, the greater their electronic asymmetry. The latter increases regularly with increase in the difference in electron donating ability of the hetero-radicals and with the length of the PC.[109–111]

Pyrid-4-yl-pyran-4-yl-tetra- and -pentacarbocyanines have been described,[115] with the highest electronic asymmetry amongst organic dyes. In their absorption spectra, the deviation amounts to 545 nm (7450 cm^{-1}). However, these PD approach the symmetrical cyanines to a considerable extent in their luminescent properties in the excited state.[115] In the fluorescence spectra, the deviation falls to 35–65 nm (320–650 cm^{-1}).[115] The Stokes shift for PD (XXXI) amounts to 410 nm (6590 cm^{-1}), the highest value for all known dyes (Fig. 3). Unfortunately, the quantum yield of fluorescence is extremely small (< 0.01%) because, apparently, of strong vibrational interactions.[115]

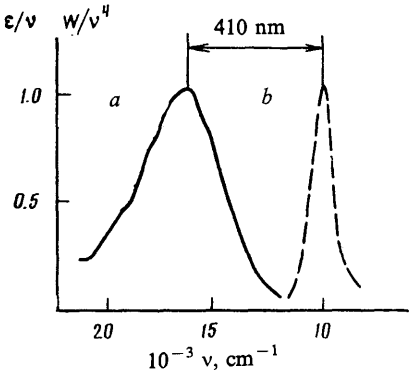
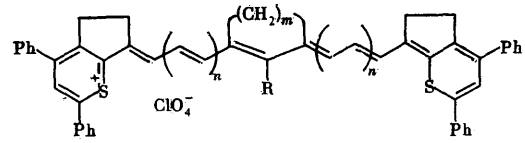


Figure 3. Absorption (*a*) and fluorescence (*b*) spectra of PD (XXXI) in MeCN.

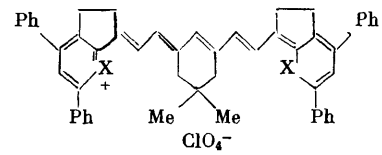
6. Spectral-luminescent properties of polymethine dyes in highly concentrated solutions

Highly concentrated solutions of the tri-, tetra-, and pentacarbocyanines (XXXII)–(XXXVI), absorbing in the region 1270–1500 nm, have interesting spectral-luminescent properties.[27,116,117] Thus, with increase in the concentration of the dye (XXXII) to 10^{-3} mol L^{-1} and above, in parallel with quenching of its principal fluorescence band at λ^{f}_{max} = 1283 nm, a new long-wave emission band is observed of approximately three times the intensity and with λ_{max} = 1613 nm.[116,117] The absorption spectrum of this compound remains unchanged for the whole working range of concentrations (10^{-5}–10^{-2} mol L^{-1}). On the basis of these data, longwave luminescence is explained by the formation and decomposition of associations of excited molecules.[116,117] In the ground state, molecules of PD (XXXII) are not associated, because the bulky phenyl groups that are present, displaced from the plane of the heteroradicals,[96] do not allow the molecules to approach sufficiently. On excitation of the pyran-2-ylcyanines and their hetero analogues, a considerable elongation of the carbon–heteroatom bonds occurs.[79,118] This decreases the steric hindrance between the heteroatoms and phenyl groups considerably. The orders of the C–C(Ph) bonds in the excited state are increased.[118] Both circumstances allow the phenyl groups to move into the plane significantly in the excited state and considerably facilitate the formation of associations.



(XXXII)–(XXXIV)

PD	*n*	*m*	R
(XXXII)	0	2	Ph
(XXXIII)	0	2	H
(XXXIV)	1	3	Ph



(XXXV), (XXXVI)

X = S (XXXV), X = Se (XXXVI).

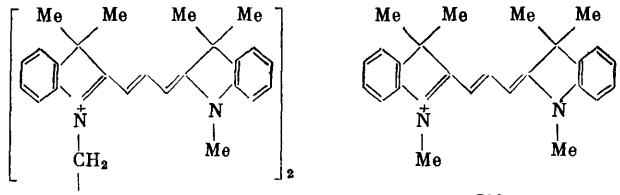
Highly concentrated solutions of PD (XXXII)–(XXXV) generate emission in the most longwave region 1400–1800 nm, with λ_P = 1060 nm.[27,117] This method should be promising for the generation of emission in the near infrared range, since it makes possible a considerable increase in both ΔS and φ. To bring about a significant increase in the quantum yield of fluorescence for monomeric organic dyes that absorb at more than 1200 nm, by means of structural changes, is highly problematical [for PD (XXXII)–(XXXVI), φ = 0.01–0.1%],[27] since small energy intervals and the effective promoting roles of high frequency CH-vibrations in this region, make internal conversion a powerful channel for the decay of electronic excitation.[44,119]

7. Spectral-luminescent properties of polymethine dyes with two chromophores

Much attention has been given recently to the investigation of spectral-luminescent properties of compounds with two chromophores,[120–123] since the intramolecular transfer of absorbed light energy from one chromophore to the other allows them to re-emit it effectively with a large red shift. Polymethine dyes with two chromophores (biscyanines) became known in 1965.[124] Fundamental relationships between the absorption spectra of PD and their chemical structure have been established.[125] Only the first steps have been taken towards the establishment of analogous relationships for the luminescence spectra of biscyanines.[126–129] Luminescence has previously been taken only as evidence for the structure of PD with two chromophores.[130,131]

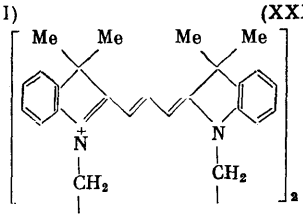
In the case of the biscyanines, resonance interaction of the chromophores, according to exciton theory,[132] causes splitting of the S_1-level into levels with higher energy S'_1 and lower energy S''_1.[125–128] In a number of cases, splitting into a *T*-level is also possible.[133] Electronic transitions $S_0 \rightarrow S'_1$ and $S_0 \rightarrow S''_1$ give rise to short- and long-wave bands respectively in the absorption spectra of biscyanines, compared to the bands associated with the $S_0 \rightarrow S_1$ transition in the monomeric (parent) dyes.[125–128] For illustration,

the spectra of the bisindocarbocyanine (XXXVII) and the parent indocarbocyanine (XXXVIII) can be compared.[128,134]



ClO_4^- (XXXVII)

ClO_4^- (XXXVIII)



ClO_4^- (XXXIX)

PD	λ^a_{max}, nm	λ^f_{max}, nm (CH_2Cl_2)
(XXXVII)	508, 570*	581
(XXXVIII)	550	570
(XXXIX)	506*, 590	662

*The more intense absorption band.

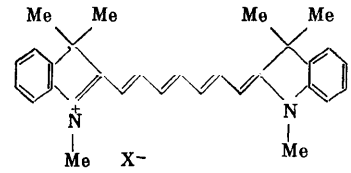
The transition $S'_1 \rightsquigarrow S''_1$ in the dimers is non-radiative.[135] Therefore, on excitation of the biscyanines, for both the short- and long-wave absorption bands, fluorescence is seen only from the S''_1-level. This situation gives rise to an increase in the shift of the emission bands relative to the shortwave absorption bands and the increase is greater, the more sharply the bands in the absorption spectra of the biscyanines move apart. According to exciton theory, the absorption bands move apart to a maximum for parallel orientations of the chromophores.[132] Therefore the change from the bis-dye (XXXVII) to (XXXIX) is accompanied by a sharp increase in the bathochromic shift of the fluorescence band relative to the short-wave absorption band.

It should, however, be borne in mind that long wave transition is forbidden for parallel orientations of the chromophores.[132–135] Luminescence occurs as a result of partial remission of the band, because of distortion of the "sandwich" structure (of the dye XXXIX) and slight displacement of the chromophores relative to each other, because they have a step-like form.[131] Therefore the luminescence of the dimers of such a structure is weak. It is also weak in the biscyanines with angular dispositions of the chromophores, for example in (XXXVII), by comparison with the monomeric PD (XXXVIII).[129] This, first of all, gives rise to an increase in the probability of intersystem crossing with change from the parent compounds to the bis-dyes.[136] This increase takes place on account of the decrease in energy difference between the S''_1 and T levels in the dimers in comparison with the S' and T levels in the monomers.

It appears to be possible to increase the luminescence of the dimers, as also of associations of some organic dyes, by the "kindling" of delayed luminescence.[137] In the dimers, it must in fact occur more easily than in the monomers, because of the increase in the probability of both $S_1 \rightsquigarrow T$ and the reverse $T \rightsquigarrow S_1$ transitions.[138]

III. The influence of the nature of the counter-ion on the spectral-luminescent properties of polymethine dyes

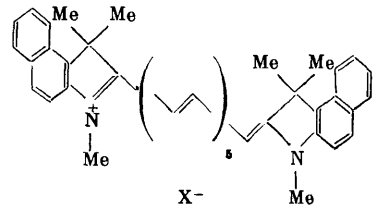
It has traditionally been thought that the spectral-luminescent properties of PD are not dependent on the nature of the colourless counter-ion but are determined only by the structure of the chromophore.[8–11] In the example of the caitonic indotricarbocyanines (XL) and (XLI) it has been shown[139] that in solvents of low polarity, as opposed to polar, the anion has a strong influence on the position, intensity and shape of the absorption bands.



(XL), (XLI)

PD	X	Solvent	λ^a_{max}, nm
(XL)	ClO_4	benzene	734*, 790
		ethanol	744
(XLI)	I	benzene	730, 790*
		ethanol	744

*The more intense band



(XLII)—(XLIV)

PD	X	λ^a_{max}, nm	λ^f_{max}, nm	τ, ps (dichloroethane)
(XLII)	I	1035	1075	97
(XLIII)	ClO_4	1035	1120	75
(XLIV)	BF_4	1035	1150	55

In the light of these published results, a wide range of investigations into the spectral-luminescent, nonlinear-optical, photophysical, and photochemical properties of cyanines in low polarity media, has subsequently been developed. On the basis of a study of ionic equilibria, the influence of salt addition, temperature, and the addition of polar ionising solvents, it was confirmed that solutions of indotricarbocyanines (XL) and (XLI) follow the Lambert-Beer law, and that the dependence of their absorption spectra on the nature of the counter-ion is caused by the formation of various types of ion pair. This conclusion was later confirmed by electroconductivity data.[140] Further investigations showed that the formation of such pairs can also give rise to marked changes in the spectral-luminescent properties of other types of salt-like PD.[141–144] A need arose to establish the structures of polymethine ion pairs.

The structures of ion pairs of dyes of the indolene and benz[*c,d*]indole series have been studied by means of ^1H, ^{14}N, and ^{15}N NMR spectroscopy[143,145,146] and by NMR with lanthanide shift reagents. It was shown for these PD that the anion is located in the

region of the nitrogen heteroradical, at which the maximum positive charge is shown, by quantum chemical calculations, to be concentrated.[143,144] On electronic excitation, a redistribution of charge occurs in the cations of the dye. Therefore the probabilities of formation of ion pairs in the ground and excited states are different. Thus, the positive charge on the cation of the pentacarbocyanines (XLII)–(XLIV) is more localised on the heteroradical in the S_1-state than in the S_0.[147] In the excited state, therefore, they form ion pairs more readily than in the ground state. Indeed, in dichloroethane, the position of the absorption band of PD (XLII)–(XLIV) does not depend on the nature of the anion. Conversely, the fluorescence band is displaced into the longwave region for the series of anions $I^- \rightarrow ClO_4^- \rightarrow BF_4^-$.[147] In this same series the values of φ and τ decrease regularly.[147]

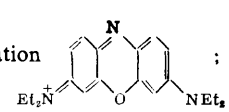
The described effects are caused by an intensification of electrostatic interactions and consequently, the formation of tighter ion pairs in the above mentioned sequence of anions in agreement with equivalent electroconductivity and dissociation constant data for pentacarbocyanines.[148] Intensification of electrostatic interactions on changing from I^- to ClO_4^- and BF_4^-, lowers the energy of the activated state,[147] and leads to a bathochromic shift of λ_{max}^{ϕ}.[147] In addition, the localisation of the anion at one of the heteroradicals gives rise to a disturbance of the electronic symmetry of the dye, leading to a displacement of the positive charge in this state. As a result, an alternation of bond order in the PC arises for the pentacarbocyanines (XLII)–(XLIV), and also for the asymmetric cyanines.[111] This, on the one hand, intensifies the vibrational interactions[110,111] but, on the other, increases the probability of isomerisation or, to a lesser extent, intensifies the critical vibrations around the bonds of the chain.[4] Both of these processes lead to an attenuation of the magnitude of φ and τ. Vibrational interactions and the probability of rotation about the bonds is greater, the tighter the ion-pairs that are formed. Therefore in the series of PD (XLII)–(XLIV) there is a regular decrease in the quantum yield of fluorescence and the life time of the excited state.[147]

A still greater effect on these values in low polarity media is caused by coloured organic anions, having their own system of π-bonds[149] as, for example, in the dyes (XLV), (XLVI) and (L).

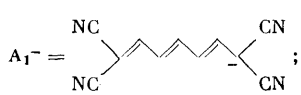
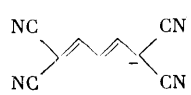
PD	Dye*	Solvent	λ_{max}^{a}, nm
(XLV)	$K_1^+A_1^+$	benzene	549, 763
(XLVI)	$K_2^+A_1^-$	,,	535, 663
(L)	$K_3^+A_2^-$	dichloroethane	448, 1030

PD	Dye*	Solvent	λ_{max}^{a}, nm
(XLVII)	$K^+{}_1C(CN)_3^-$	benzene	753
(XLVIII)	$K^+{}_2ClO_4^-$	,,	658
(XLIX)	$\overset{+}{N}(CH_3)_4A_1^-$	,,	551
(LI)	$Na^+A_2^-$	dichloroethane	448

*Designation adopted:

K_1^+ = cation of dye (XLI); K_2^+ = cation  ;

K_3^+ = cation of Pd (XLII)–(XLIV);

A_1^- =  ; A_2^- = 

Cation-anion dyes (XLV) and (XLVI) form ion-pairs in solvents of low polarity as do the corresponding cationic types.[149] In these ion-pairs, on account of the electrostatic forces of attraction, the two chromophores which have different electronic structures become "associated", in contrast to the chromophores of the biscyanines considered above. If the initial cationic and anionic dyes absorb in similar regions then the formation of a cationic-anionic compound will be accompanied by resonance interactions of the chromophores, leading to a change in the position of the electronic bands, as in the case of the biscyanines. For the cationic-anionic compounds (XLV) and (XLVI) in benzene, the absorption bands move apart: the longwave bands moving bathochromically and the shortwave bands hypsochromically, relative to the absorption bands of the corresponding cationic (XLVII), (XLVIII) and anionic (XLIX) dyes.[149]

For compound (XLVI) the absorption bands move apart to a greater extent than for (XLV), since (XLVIII) and (XLIX) absorb light at closer wave lengths than compounds (XLVII) and (XLIX).

For the cationic-anionic dye (L) there are also two absorption bands, but these do not move apart in comparison with those of the corresponding cationic and anionic cyanines.[150,151] This is due to the fact that the regions of absorption for the cationic and anionic chromophores differ sharply. Therefore resonance interactions, leading to splitting of the S_1-level and, consequently, to separation of the bands for PD (L), do not take place. Absorption bands for the cationic-anionic compound (L) are characterised by a significantly smaller integral intensity and greater width than the absorption bands of the corresponding cationic (XLII) and anionic (LI) dyes,[150,151] as the result of the formation of an ion pair, disturbing the electronic symmetry of the chromophore for the former more strongly than for the latter. Such a difference is due to the presence of a system of easily polarisable conjugated bonds and alternating positive and negative charges in the anions of cationic-anionic dyes, in contrast to the anions of the cationic types. It is able to increase the electronic asymmetry of the chromophores on account of non-resonance interactions with the analogous system of bonds of its cation and therefore cationic-anionic dyes have lower values of φ and τ than the corresponding cationic dyes.[150,151] For compound (L) in dichloroethane, τ = 49 ps, and for its analogue with the trimethineoxanine anion it falls to 24 ps.[150,151]

In polar solvents, the spectral-luminescent properties of PD (XL)–(LI) are independent of the nature of the anion, since these dyes are completely dissociated in these solvents.

Such a large reduction of τ in cationic-anionic compounds, with practically complete transparency at λ = 1060 nm, allows their use as effective passive locks for solid state lasers.[150] Cationic PD (XLII), widely known in the USSR under the number 3955 and having a large value of τ, works well in quality modulation.[152]

Cationic-anionic compounds, like mixtures of PD with other classes of dye, for example PD (II) plus rhodamine S[153] or PD (XLI) plus oxazine 750,[155] may also be used successfully for the transformation of light energy, with a large red shift. This shift, as in the case of the biscyanines, is achieved on account of the separation of the short- and long-wave bands of their ion pairs as a result of interaction of the chromophores. They are more promising than mixtures of dyes as transformers of light energy, since transfer of energy within ion pairs may occur in dilute solutions and is not dependent on the concentration of the dye, as is the case for the original components of mixtures. The latter circumstance may lead to undesirable concentration effects in mixtures of dyes.[156–158]

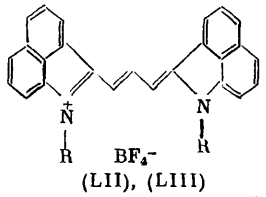
IV. Structure of associations of ion pairs of polymethine dyes

Salt-like cyanines with simple anions can also prove to be excellent transformers of light energy when they are associated. The association of PD in silver halide photographic emulsions has been widely investigated, since they have a considerable effect on the sensitising ability of cyanines in these emulsions.[10,159] Until recently, therefore, attention was given primarily to the problem of aggregation of dyes in aqueous solvents.[160] In these solutions, associations of cyanines are of low stability. They dissociate easily on warming.[161] In water and especially in other polar solvents aggregation of dyes occurs at high concentrations. This leads to concentration quenching of luminescence.[156]

Conversely, in low polarity media, cyanines easily associate in dilute solutions ($10^{-7}-10^{-5}$ molL^{-1}) at room temperature.[141,143] This is caused by the fact that the association of PD in low polarity media, in contrast to polar, comes about on account of both dispersion interactions and electrostatic interactions of different charges in the ion pairs according to the scheme $K^+A^-...K^+A^-$.[141-143]

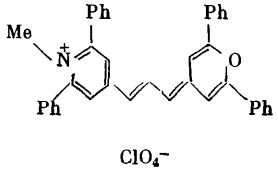
The study of association of salt-like dyes in low polarity solutions is frequently very difficult because of their low solubility. However for PD this problem can be solved by the introduction of aliphatic hydrocarbon radicals into their molecules.[143] Recently, interest in such PD has revived sharply in connection with their ability to form a Langmuir-Blodgett poly-layer,[162-170] which finds wide application in various fields of science and technology.[171]

The influence of processes of association in low polarity media on the spectral-luminescent properties of salt-like cyanines have been investigated in detail.[141-144]



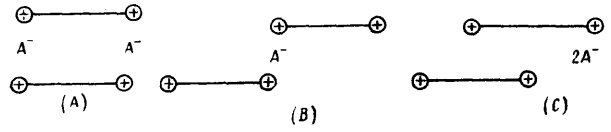
(LII), (LIII)

R = $C_{10}H_{21}$ (LII); R = $CH_2C_6H_4$ (LIII)



(LIV)

It has been shown that PD with a planar structure, not containing bulky substituents, for example (LII), easily form associations of ion pairs with a "sandwich" structure on lowering the polarity of the solution.[141-144] The formation of a "sandwich" structure favours the localisation of the anion in the region of the nitrogen heterocycle.[143] This is due to the fact that the terminal cations on both sides attach "rigidly" to the anions, because of the electrostatic attraction of the differing charges of the monomers of the ion pairs (Structure A).[143] Structure A is also advantageous from the point of view of dispersion interactions, since these are maximum for parallel orientations of the chromophores.[135] Therefore "sandwich" salt-like cyanines have high strength in low polarity media. They do not decompose on boiling even in high-boiling point, low polarity solvents,[143] in contrast to cyanines in polar, particularly aqueous, solvents.



(A) (B) (C)

The formation of associations with structure (A) is acompanied by a fall in the intensity of the absorption and luminescence bands of monomeric PD molecules to practically complete extinction and the appearance of new short-wave absorption bands (Fig. 4*a*, *b*). Thus for compound (LII) in low polarity media, the absorption band of its "sandwich" structure is shifted hypsochromically by 100 nm more than is the absorption band of the monomer.[141-144]

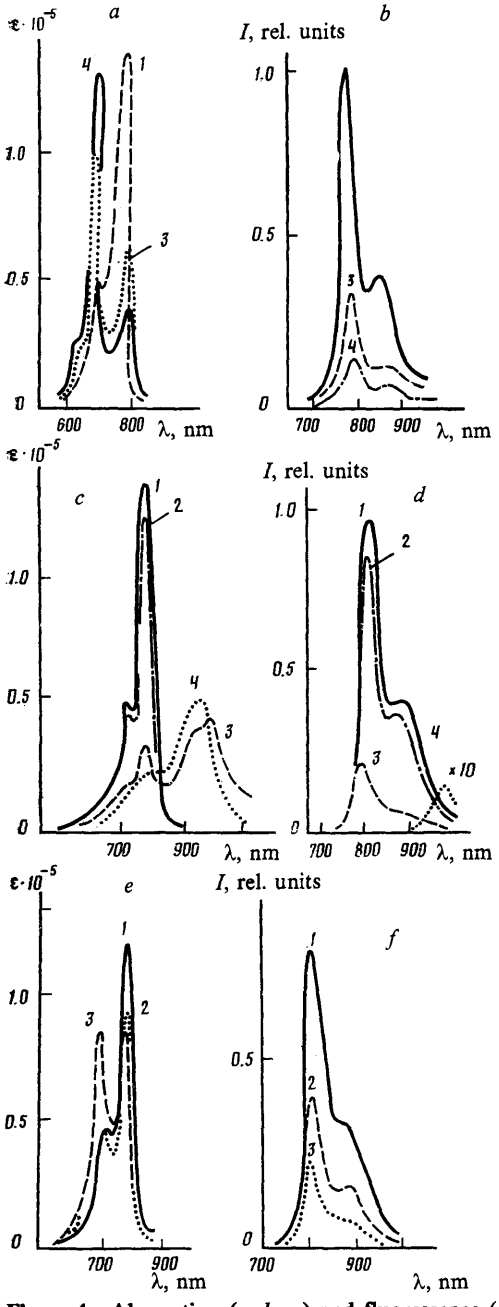


Figure 4. Absorption (*a*, *b*, *c*) and fluorescence (*d*, *e*, *f*) spectra of PD (LII) (*a*, *b*) and (LIII) (*c*–*f*) for $C = 10^{-5}$ mol L^{-1} in mixtures of CH_2Cl_2 and hexane (*a*–*d*) (CH_2Cl_2 content in %): *1*, 100; *2*, 50; *3*, 20; *4*, 10) and in DMF–water (*e*, *f*) (DMF content in %): *1*, 100; *2*, 20; *3*, 10. Fluorescence spectra standardised against the spectra of (LII) in CH_2Cl_2.

The introduction of bulky substituents hinders the formation of associations with structure (A). They are especially effective in the region of the heteroradicals, where the maximum positive charge is concentrated, since they hinder the "rigid" attachment of cations of dyes in the type (A) structure. However, in this case, it is possible for the cations to be attached at one end in a "head-to-tail" structure (Structure B), in which the angle between the direction of the chromophores is close to 180°.[143,144] The formation of associations with structure (B) is accompanied by the appearance of electronic spectra with new long-wave bands.[135,160] For example, replacement of the decyl groups in the hetero-radicals of the dye (LII) by tolyl groups (compound LIII), which deviate significantly from the plane of the chromophore, [as in the case of cyanine (XIX)] leads to the appearance of these bands (Fig. 4*c*) on reduction of the polarity of the medium (i.e. with increase in the content of hexane in the hexane–methylene chloride mixture).

The magnitude of the shift of the absorption and luminescence bands of associated molecules of PD, with respect to the corresponding bands of the unassociated molecules, deserves special attention. This magnitude is *ca.* 200 nm, which is equivalent to lengthening of the PC of the dye by two vinylene groups. Since dyes with long chains are much less photochemically stable than those with short chains, it may be hoped that associations of type (B) will be promising for the transformation of light energy from the visible into the near infrared region of the spectrum, especially as these large shifts of the electronic bands occur in even dilute solutions. This ease of association of salt-like cyanines in low polarity solutions depends on strong electrostatic attraction between the differing charges in the ion pairs of the monomers.[143,144]

It is significant, that association of the dye (LIII) in polar solutions is accompanied by opposite changes.[144] As for the cyanine (LII), in parallel with a drop in absorption ability and quenching of the luminescence, there is a characteristic appearance of a new short-wave absorption band at a distance >100 nm from the absorption band of the monomer (Fig. 4*e*, *f*). This difference depends on the fact that in polar solutions the anion does not take part in association. Under these conditions, therefore, the chromophore does not need to be so precisely fixed in the "sandwich" structure as in low polarity media. In this connection, the PD (LIII) in the DMF–water system is able to form some deformed "sandwich" structures in which the chromophores are displaced with respect to each other (structure C), on account of dispersion interactions,[144] allowing a reduction in steric hindrance between the $N-C_6H_4CH_3$ groups. Deformation of the "sandwich" structure in a DMF–water mixture is associated with greater intensity of the forbidden long-wave absorption band (Fig. 4*e*, *f*) by comparison with a solution of the same dye in a methylene chloride–hexane mixture (Fig. 4*c*, *d*).[144]

Changes in spectral-luminescent properties according to the polarity of the medium, as observed for the associated forms of compound (LIII), occur also for other PD.[172]

In low polarity media, various types of salt-like cyanines are able to associate, in particular to form dimers.[141–144] It is convenient to take advantage of this fact in those cases in which chemically bonded dimers—biscyanines—cannot be synthesised. The latter are interesting targets for use in the study of problems of chromaticity and luminescence in organic dyes, but they are frequently difficult to obtain. This is due firstly to the fact that their synthesis is accompanied by the formation of traces of monomeric dyes which are difficult to separate, especially in terms of luminescent purity. Furthermore, not all heterocycles yield bi-quaternary salts for use as starting materials in the synthesis of biscyanines.

The bis-dyes themselves associated considerably more easily than the parent dyes in low polarity solutions.[126,128] This is due to the presence of two anions in the biscyanines, so that the probability of association of their ion pairs is increased by comparison with monomeric PD.[126,128]

In polar solutions the anion does not take part in aggregation. Nevertheless, in this case, as also in low polarity solvents, biscyanines associate more easily than the parent dyes. This is due to the fact that aggregation occurs in polar solutions on account of dispersion interactions of the π-systems of the PD. For compounds with two chromophores, these systems are more extended than in those with one chromophore. The former, therefore, associate more easily than the latter.[126,127]

V. Spectral-luminescent properties of polymethine dyes in polymeric matrices

Polymeric matrices also can be regarded as low polarity media. Coloured polymeric materials are especially widely used at present in quantum electronics,[173–175] helioenergetics,[176,177] and as agents for recording information.[178,179] Polymeric matrices have a number of operational advantages by comparison with liquid media,[173–175] although these advantages may only be realised if, in addition, the spectral-luminescent properties of the dye do not deteriorate under these conditions.

The first attempt to introduce PD into polymeric matrices led to a marked distortion of their spectral-luminescent properties.[180,181] In addition, a new band appears for many PD at the short-wave end of the absorption spectrum and the intensity of the long-wave band decreases, for example in the case of thiopyranyltricarbocyanine (XXIII) when dichloroethane is replaced by poly(methyl methacrylate) (PMMA).[181–184] These changes are accompanied by the quenching of luminescence.[185] It has been shown[182–185] that the described spectral-luminescent effects are caused by the formation of ion pairs and by their association in the type (A) "sandwich" structure, in the same way as in low polarity liquid solutions.[141–143] It has also been shown that such association leads to a fall in the photochemical stability of coloured polymeric matrices.[181,183]

It is difficult to avoid the association of PD in polymers, as it is in low polarity liquids, since association occurs at even low concentrations of cyanines.[183,184] The situation is also complicated by the fact that for a number of purposes highly delicate films are required, for example for passive laser locks.[186] For achieving the required degree of transmission of such films it is necessary to use a concentration of dye that is some orders of magnitude higher than that used for measurement of the absorption spectra in a 1 cm cell.

In order to reduce the tendency of salt-like PD to the formation of ion pairs, and also therefore association, it is necessary to use polymers with high values of dielectric permeability, ε. However, the preparation of such polymers is difficult. For the majority of polymeric materials ε is <10,[187] and dyes are therefore not completely dissociated in these materials. It is possible to facilitate the dissociation of PD in matrices which have low values of ε by the use of polymers containing polar groups. The role of such groups is to solvate the charges of the chromophore of the dye, separating them from the counterions, and to some extent hinder the formation of tight ion pairs.[147] Solvent separated ion pairs have practically the same electronic spectra as the solvated ions.[148] Therefore the formation of such pairs in a polymer does not cause a substantial

change in the spectro-luminescent properties of salt-like PD from those found in liquids, even if the cyanines are fully dissociated in liquids. Specific solvation of the charges of PD by polar groups of the polymer also reduces the electrostatic and dispersion interactions between the chromophores of the dye, making association of the latter more difficult.[126,142]

For cationic PD, which undergo mainly nucleophilic solvation,[188] it is necessary to use polymeric matrices that contain strongly nucleophilic groups, for example polyvinylbutyral, polyepoxides, and polyurethanes. The latter are especially promising, since they not only have strongly nucleophilic groups (comparable in nucleophilicity to DMF), but also they also have some of the highest values of ε for polymeric media.[187] The absorption spectra of thiopyranyltricarbocyanine (XXIII) in these polymers, in contrast to PMMA which has a lower value of ε, have the same form as in liquid solvents (Fig. 5).[183,184] Conversely, in polystyrene, which is characterised by minimum values of ε and nucleophilicity *B* (both of which are comparable to those of toluene) the form of the spectral curve of the same dye is altered considerably more than it is in PMMA (Fig. 5).

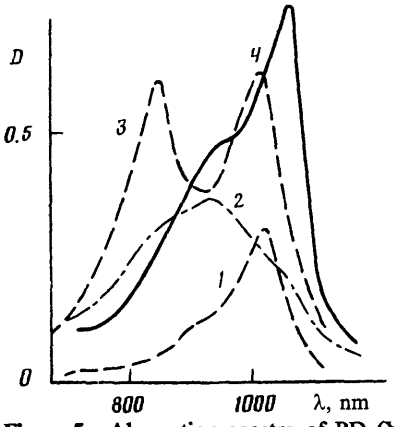


Figure 5. Absorption spectra of PD (XXIII). *1*, in dichloroethane ($C = 10^{-4}$ mol L^{-1}, *1* = 69 mm); *2*, in polystyrene; *3*, in poly(methyl methacrylate); *4*, in polyurethane (*2*–*4*, $C = 5 \times 10^{-7}$ mol g^{-1}, *1* - 70 mm).

However, a change in the nature of the matrix is not always justified. Thus, for example, for use in luminescent solar concentrators (LSC) the most preferred polymer is PMMA, which possesses excellent optico-mechanical properties[189] and is also extremely accessible and cheap.

In order to avoid the association of polymethines in PMMA, it is therefore necessary to modify them. For example, in the molecule of thiopyranyltricarbocyanine (XXIII) it is possible to introduce bulky substituents in order to prevent the formation of associations with structure (A).[185] Thus, if a hydrogen atom in the *meso*-position [dye (XXIII)] is replaced by a phenyl group [dye (XXIV)], the shape of the spectral curve remains the same in both dichloroethane and PMMA. An analogous result is also obtained with the introduction of other bulky substituents, such as CH_3, Cl, or *iso*-C_3H_7 into the *meso*-positon.[183] The formation of "sandwich" structures can be prevented, not only by the introduction of bulky groups into the polymethine chain, but also by their introduction into the heteroradicals.[183]

The above-mentioned substituents, having decreased the tendency to association of thiopyranylcyanines in polymers, substantially increased the photochemical and radiation stability of coloured matrices.[185] It allowed them to be used as the basis for the production of highy effective passive film locks, working in synchronised mode and guaranteeing the generation of ultra-short impulses of picosecond duration.[185,190]

If the association of PD in polymeric matrices is reduced to a minimum, it is possible to increase their quantum yields of fluorescence substantially. This is due to the fact that the polymer, being a "rigid" medium, impedes isomerisation processes which reduce the magnitude of φ significantly.[4] It has been shown that the quantum yields of fluorescence for a series of PD are increased more strongly by their introduction into a polymeric matrix, than by complete cyclisation of their PC. For example, on going from thiacarbocyanine (I) with an open chain to its analogue (X) with a rigidly fixed PC chain the value of φ is increased from 5 to 53%, whereas with the introduction of PD (I) into a polymer this value increases to 72%.[191]

A greater increase in the quantum yield of fluorescence of the thiacarbocyanine (I) by its introduction into a matrix, than by "chemical" fixing of its chain, is most probably due to the fact that not only are isomerisation processes hindered in "rigid" media, but also the quenching of luminescence, due to diffusion-controlled collision with molecules of oxygen and other quenching impurities, is decreased.[192–194] This fact also leads to a significant rise in the photochemical stability of coloured polymeric matrices based on PD. The latter are, in fact, able to sensitise the formation of singlet oxygen,[192–194] which is one of the basic factors in the photochemical destruction of cyanines.[195–197] In a polymer, because of weak diffusion, the generation of singlet oxygen is of low probability and cyanines are therefore more stable in these than in liquid solutions.

In luminescent ability and photochemical stability many PD in polymeric matrices are comparable with a wide range of luminophores, such as rhodamine 6G, POPOP, and various coumarins, etc.[198] In matrices, therefore, even those cyanines which are unsuitable as active laser media in liquid solutions can be used for the highly effective generation of emission.[199] In a polymer, the effectiveness of generation of emission is increased not only because of the increase in φ, but also as the result of a decrease in the losses that are caused by the induced absorption of the isomer in the intensified band.[200]

It should be noted that in "rigid" media the Stokes shift frequently falls. Thus, for the pyridylpyranyltetracarbocyanine (XXXI), which has one of the highest ΔS values, the Stokes shift decreases by 820 cm^{-1} on going from acetonitrile solution to polyurethane film, although its magnitude nevertheless remains rather significant. In general, if a decrease in ΔS occurs in polymers, then it does not decrease to the same extent as for completely fixed PC, with saturated cyclic groupings.[191] Small values of ΔS are also characteristic of other classes of structurally rigid luminophores.[198]

The possibility of achieving large Stokes shifts and quantum yields of fluorescence, together with high photochemical stability, makes coloured matrices based on PD more promising than the above named luminophores for the solution of problems connected with the transformation of light energy. One of these is helioenergetics.[191,201] The use of PD as LSC has been proposed.[191,201] It was shown that cyanines, that are not even the most suitable, can have larger coefficients of energy concentration than the widely used rhodamine 6G.[191,202]

It should be emphasised that a considerable increase in φ can be achieved, not only by the introduction of PD into polymeric matrices but also by increasing the viscosity of the medium.[59,60,203,204] It has therefore been possible to produce highly effective fluorescent probes, based on polymethines, for the determination of the microviscosity of phospholipid membranes.[205]

It was recently found that a sharp increase in the quantum yield of fluorescence of PD can also occur in low viscosity aqueous solutions in the presence of DNA.[206] This fact is of particular interest, since quenching of luminescence normally occurs in water because of the high tendency of PD to aggregation especially with the formation of "sandwich" structures, under these conditions.[156,160] Furthermore, the concentration of DNA employed does not increase the viscosity of the solution sufficiently for this be the cause of an appreciable increase in φ. The role of DNA in the case decribed is different. On the one hand, DNAs are surface active substances which hinder the association of dyes in aqueous solutions,[207] but on the other they form complexes with molecules of PD, most probably on account of electrostatic interactions which fix the dye rigidly in one isomeric form only. If this form is the *trans*-isomer, which usually has good luminescence, then fluorscence of the cyanine is enhanced in the presence of DNA. Conversely, in the case of the *cis*-isomer, quenching occurs.[4] Depending on the type of DNA and PD the formation of one or other of isomer occurs and, consequently, the enhancement or quenching of luminescence. Polymethines can therefore be used successfully in aqueous solutions as fluorescent probes for the recognition of types of DNA.[206]

VI. Influence of the nature of the solvent on the spectral-luminescent properties of polymethine dyes

It has been generally accepted that the solvent cannot have a significant effect on the spectral-luminescent properties of salt-like PD, since in contrast to intraionic (merocyanine) dyes, their dipole moment should change little on excitation.[208,209] It has been shown[34,110,111,188] that cyanines, depending on their chemical structure, may undergo strong solvation that becomes distinctly apparent from the position, intensity, and form of the electronic bands. For the exact quantitative estimation of these changes the moments method is applied,[210,211] as used in probability theory for the determination of functional parameters of various distributions, for example intensities in absorption and luminescence spectra.[210,211]

This method was used to calculate the mean frequencies (centres of gravity) of the bands ($\bar{\nu}$), oscillator strengths (f), band widths (σ), coefficients of asymmetry (γ_1), excess (γ_2), and fine structure (F). The magnitude of $\bar{\nu}$ has an advantage over the band maximum, in that its position in the series becomes determined more precisely and it more strictly characterises the vertical change in energy.[210] The magnitude of σ, being proportional to the dispersion of the band, allows an objective comparison of the widths of curves of different shapes to be made, in contrast to the half-widths (widths at half height) that are traditionally used for these purposes. The coefficients γ_1, γ_2, and F give additional information relating to changes in symmetry, steepness, and the degree of fine structure that is observed with widening or narrowing of the spectral curves. It has been shown possible to use these coefficients for analysis of the mechanisms of broading (uniform or otherwise) of the electronic bands.[211]

Moments of the absorption bands are determined by the coordinates ε/ν, and of the fluorescence bands by the coordinates W/ν^4, since these coordinates follow the law of mirror symmetry for the named spectra most exactly.[212]

1. Solvatochroism

In the examples of the dyes (XL) and (LIV), which differ sharply in chemical properties and in the regions of absorption and shape of their spectral curves, a study was made of the influence of various parameters of solvent polarity on the position, intensity, and shape of the absorption bands.[188] For this purpose the same range of solvents were used, that made it possible to obtain objective information on the influence of intermolecular interactions on the spectroluminescent properties of dyes. For a series of solvents with similar properties it was concluded[213] that a change in the position of the absorption band maximum for symmetrical cyanines correlates well with the Bayliss refractive index function: $(n_D^2-1)/(2n_D^2+1)$. However the inclusion of even a small number of solvents of other types at once led to a breakdown of the relationship,[214] i.e. the correlation is only satisfactory for a series of solvents of the same type.[214] Indeed, as seen for the example of the indotricarbocyanine (XL) (Fig. 6) neither ν^a_{max} (correlation coefficient $r = 0.912$) nor $\bar{\nu}^a$ ($r = 0.807$) correlate with the mentioned Bayliss function if different classes of solvent are used. The picture is not improved substantially by the use of the two-paramter function $f(n_D, \varepsilon)$.

Hence it follows, that solvation of the PD cations depends not only on macro- but also on microscopic properties of the medium. It has been shown for cyanines of the types (XL) and (LIV), and in general for polymethines that do not contain functional groups able to form hydrogen bonds, that the microscopic properties are determined by specific electrostatic interactions of the charges of the PD molecules and the solvent.[188] On the basis of an analysis of solvatochroism effects for cyanines (XL) and (LIV) and their dependence on empirical parameters of solvent polarity. viz. nucleophilicity (B) and electrophilicity (E), it was established for cationic PD that these interactions are significantly more sensitive to changes in parameter B than E. In other words, specific solvation of these dyes is determined mainly by nucleophilic solvation of the positive charges of their cations with the negative charges of the solvent molecules. Specific solvation becomes stronger with increasing unevenness in the distribution of charge in the cyanine molecules[34] and this in its turn increases with lengthening of the PC, deviation of the electron-donating abilities of the terminal heterocyclic groups from average values,[34,215] and increase in the electronic asymmetry.[111] Thus, for thiapentacarbocyanine (V), containing two benzthiazole nuclei, the electron-donating ability of which is above average, replacement of weakly nucleophilic methylene chloride by strongly nucleophilic DMF gives rise to such marked changes in the absorption spectra, that they do not appear to be caused by the change in the nature of the solvent but by the presence of two different dyes (see Fig. 1*a*). Equally strong effects, with change in the nucleophilicity of the medium, are observed for cyanines having weakly electron-donating radicals.[216] In both cases these effects are shown more distinctly for PD with longer PC (see Fig. 1).

It has been established that the nucleophilicity of a solvent has a significantly greater influence on the shape of the band (especially width), than on its position. The latter is more sensitive to change in the refractive index of the medium.

On the basis of an analysis of the moments of the absorption bands of PD in pairs of solvents, for which one parameter of

polarity was the same but the other different, the following law was formulated[188] concerning the influence of the solvent on the characteristics of the absorption bands of these dyes: in order to maximally deepen the coloration, to narrow the band and to increase the peak intensity, it is necessary to use, as media, solvents which have as large refractive indices as possible (a necessary condition for deepening of the coloration) and as low nucleophilicities as possible. Conversely, the largest increase in coloration, widening of the bands, and decrease in their extinction occurs in solvents with maximum B (a necessary condition for the creation of wide bands) and minimum n_D.

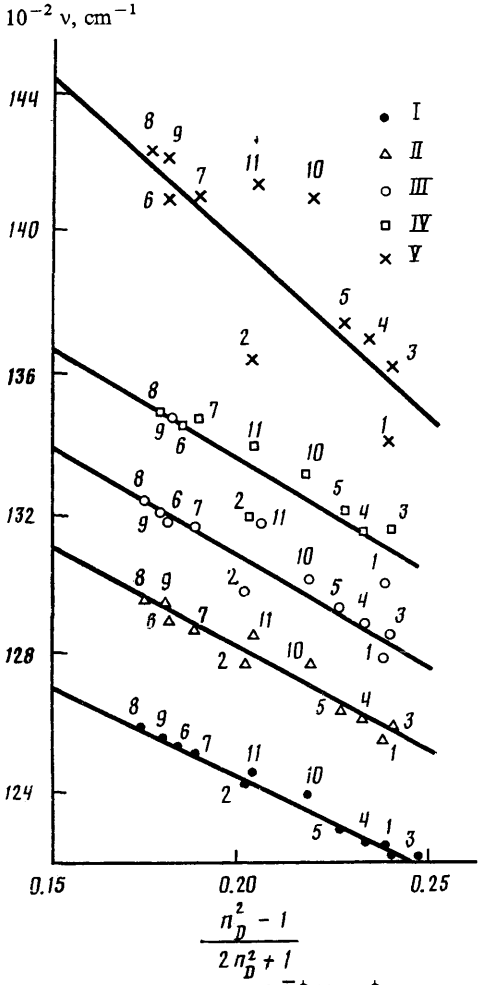


Figure 6. Dependence of $\bar{\nu}^{\Phi}$(I), ν^{Φ}_{max}(II), ν_{00}(III), ν^{a}_{max}(IV), and $\bar{\nu}^{a}$(V) for the dye (XL) on the Bayliss function. *1*, *o*-dichlorobenzene; *2*, methylene chloride; *3*, nitrobenzene; *4*, benzonitrile; *5*, pyridine; *6*, ethanol; *7*, nitromethane; *8*, acetonitrile; *9*, acetone; *10*, DMSO; *11*, DMF.

2. Solvatofluorochroism

The first report of the solvatofluorochroism of cyanines appeared only in 1987.[217] In this publication, and subsequently in others,[38,211] the influence of the nature of the solvent on the moments of the fluorescence bands of PD (XXVI), (XXXVIII) and (XL) was investigated. It was shown that the magnitudes of solvatofluorochroism effects were significantly less than those of solvatochroism. For example, the replacement of *o*-dichlorobenzene by DMF (these solvents differ considerably in the magnitude of n_D and B)[188] leads to a hypsochromic shift of the maximum and mean frequencies of the fluorescence bands of indotricarbocyanine (XL) of 400 and 361 cm^{-1} respectively, whereas the analogous values for absorption are 470 and 818 cm^{-1}. Still more contrasting is the influence of the solvent on the magnitudes of α^a and σ^f. Thus, in the above mentioned pair of solvents, the change in band width in the emission spectra amounts to only 58 cm^{-1} but in the absorption spectra to 414 cm^{-1}.[38,217] It was shown that the solvent has very little effect on the shape of the fluorescence band, in contrast to that of absorption, even for the strongly solvatochromic thia- (see Fig. 1*b*) and thio-pyranylcyanines with log PC. It has been found that the magnitudes of σ, γ_1, γ_2 and F for fluorescence bands are significantly less than the corresponding values for the absorption bands (especially σ).[211,217] This shows that the law of mirror symmetry for absorption and emission spectra is not observed. This conclusion is fairly important, since it was traditionally considered from the appearance of the spectral curves, that the above mentioned law is observed for the cyanine (XL) and for many other PD.[68,69] Only the application of the moments method revealed the considerable deviation from this law.

Deviation from mirror symmetry, and also a decrease in the magnitude of solvatofluorochromic effects by comparison with solvatochromic, witnesses to a weakening of the solvation of dyes in the excited state by comparison with the ground state.

From the data obtained by quantum chemical calculations for the molecule of indotricarbocyanine (XL), it follows[217] that the charges in the S_1-state have, as a rule, smaller numerical values than in the S_0-state. The total positive charge responsible for nucleophilic solvation also decreases with excitation (in the ground state it is 1.616 and in the excited state, 1.324).[217] In the excited state, therefore, electrostatic interactions (nucleophilic solvation), in contrast to dispersion interactions, must become significantly weaker, causing a decrease in the solvatofluorochromic effects by comparison with the solvatochromic.

With electronic excitation of the cyanine cations a marked redistribution of charge occurs. Specifically solvated forms of the dyes (SSFD), which are formed on account of nucleophilic solvation in the ground state, will therefore become unstable in the excited state and will seek to undergo reorganisation, with some dissociating completely. The probability of formation of SSFD in the excited state also falls because of a decrease in the absolute magnitude of the majority of the charges in this state by comparison with the ground state. As a result, the solvent will have a smaller effect on the shape of the absorption band than on the fluorescence band. Weakening of nucleophilic solvation leads also to a large decrease in the magnitudes of σ^{Φ}, γ_1^{Φ}, γ_2^{Φ} and F^{Φ}, by comparison with σ^a, γ_1^a, γ_2^a and F^a,[211] giving rise to deviation from mirror symmetry.

Additional narrowing of the fluorescence bands, by comparison with the absorption bands and a decrease in the influence of the solvent on the magnitudes of σ^{Φ}, γ_1^{Φ}, γ_2^{Φ} and F^{Φ}, occurs because of radiationless, directed transfer of light energy from the "blue" to the "red" solvate.[218,219] As a result, not all SSFD take part in such a transfer in emission in contrast to absorption, but mainly long-wave and non-specific solvates, absorbing in the still more "red" region than SSFD.[38,217]

The occurrence of radiationless directed transfer of energy also accords with the fact that quantum yields of fluorescence and life-

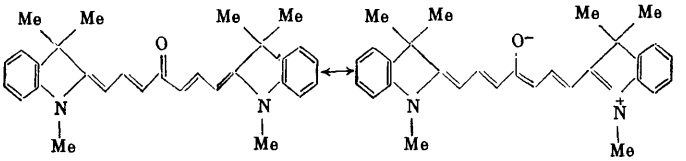
times of the excited states in a group of strongly nucleophilic solvents are, as a rule, lower than in weakly nucleophilic solvents,[38] since the probability of the formation of SSFD and, consequently, degradation of the excitation energy of the former is higher. This is due to the fact that the quantum yield and life time depend not only on the nucleophilicity of the medium, but also on its other properties, for example on viscosity. Therefore, in the highly viscous DMSO, in spite of its high nucleophilicity, a fairly high quantum yield of fluorescence is achieved.[38]

In alcohols, for PD absorbing in the region >1000 nm, the value of τ is minimal.[220] This is because there are additional routes of degradation for the energy, as a result of an overlap of the long-wave absorption bands of the cyanines with the overtone bands of the valence vibrations of the alcoholic OH groups. By deuteriation of these alcoholic groups, the magnitude of τ increases. Thus, for thiopyranylcyanine (XXIV), the values of τ in C_2H_5OH and C_2H_5OD are 14 and 23 ps respectively.

The Stokes shifts increase in almost the same way in a series of solvents, as the band widths. This is explained by the fact that ΔS is caused by an increase in hypsochromic band shifts, which result from a large reduction in the energy of the ground state of the dye, by comparison with the excited state, on account of an increase in nucleophilic solvation of the former.

This solvation is so significant, that the characteristic positions of the absorption bands, as already noted, do not correlate satisfactorily with the Bayliss function of refractive index (Fig. 6). This is specially clear for $\bar{\nu}^a$ since the average frequency, being at the centre of gravity of the band, is extremely sensitive to changes in band shape. A change in the latter, under the influence of solvent, is due mainly to specific rather than general electrostatic interactions, leading to a breakdown of the correlation mentioned above. Solvatochromic shift of the band maxima is more dependent on the polarisability of the solvent, than on its nucleophilicity. There is therefore an approximate correlation ($r = 0.912$) between ν^a_{max} and the Bayliss function. The picture is improved to some extent by the closeness of the $0-0$ transition, ν_{00} (Fig. 6). This is because the vibrational transition corresponding to the band maximum, is partially removed under the influence of solvent because of the formation of SSFD.[221] The extent of this removal changes according to the nature of the solvent. Therefore the band maximum, in contrast to the magnitude of ν_{00}, may be dependent in different solvents on various vibrational transitions in a sub-level of the excited state of the SSFD. But in spite of the advantage of the closeness of the $0-0$ transition, a satisfactory correlation between this and the refractive index function is not acheived ($r = 0.942$). This once again shows the significant contribution of specific interactions in solvated cationic dyes. Indeed, a satisfactory relationship of the above mentioned characteristics of the electronic bands and refractive index is only obtained for uncharged compounds.[222,223] The excellent correlation shown between $\bar{\nu}^\Phi$ and the refractive index ($r = 0.993$) for fluorescence of the dye (XL) is therefore striking; it is better than for ν^a_{max} ($r = 0.974$), although the latter is extremely satisfactory. These facts convincingly confirm the conclusion that nucleophilic solvation is significantly weakened in the exicted state, in comparison with the ground state.

The opposite is true of the analogue of dye (XL), indotricarbo-ketocyanine (LV).[224,225]

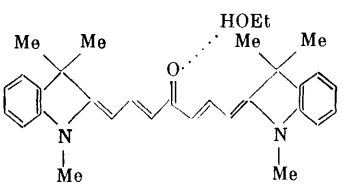


(LV)

(LV): $\lambda^a_{max} = 465$ nm; $\lambda^f_{max} = 475$ nm (heptane).

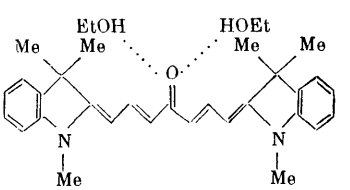
Compound (LV), being intra-ionic, is shown as a nonpolar-bipolar borderline structure. The latter predominates in the excited state. Therefore in the molecule (LV) in the S_1-state, in contrast to the cationic indotricarbocyanine (XL), the specific electrostatic interactions are intensified. This is shown by the fact that an increase in the nucleophilicity of the medium does not give rise to a bathochromic shift rather than a hypsochromic shift, as takes place for compound (XL).[224] Such changes in the spectra are caused by the fact that nucleophilic solvation of the ketocyanine (LV) increases in the excited state and reduces its energy more than for the ground state.

In the S_1-state of compound (LV), electrophilic solvation is also increased. This becomes especially apparent in protic solvents, in which the ketocyanine (LV) forms two types of complex (LVa) and (LVb).[224,225]



(LVa)

(LVa): $\lambda^a_{max} = 487$ nm; $\lambda^f_{max} = 540$ nm



(LV6)

(LVb): $\lambda^a_{max} = 565$ nm; $\lambda^f_{max} = 620$ nm.

The probability of their formation is increased in the excited state, since the negative charge on the oxygen atom increases on excitation. This leads to a rise in ΔS in protic solvents by comparison with aprotic. In addition, there is an excellent increase in the order of the quantum yield. This is caused by saturation of the carbonyl with hydrogen bonds, leading to an increase in rigidity of the complexes, fixed in the all *trans*-conformation.[225]

Owing to the high values of ΔS and φ, alcoholic solutions of ketocyanines generate emission effectively with both laser[226] and lamp[227] pumping.

VII. Conclusion

PD are seen to possess unique and widely ranging spectral-luminescent properties.

Depending on structure, cyanines may absorb and luminesce in the whole visible and near infrared regions of the spectrum. At the present time, PD have the most interesting long-wave (1600 nm)[1] $\pi-\pi^*$ transitions among all the dyes investigated, with extinction reaching 5.10^5 l mol^{-1} cm^{-1}.[126]

Band shape may change from being strongly structured to being completely diffuse, from the most narrow ($\sigma \leqslant 700$ cm^{-1})[126,215] to the most wide (σ 3000 cm^{-1}).[115]

The quantum yield of fluorescence and the life-time lie within the limits 0.01–100% and $10^{-12}-10^{-9}$ s respectively.[3,4] Stokes shifts change from unity to 100 nm (from 200 to 7000 cm^{-1}).[112,115]

The spectral-luminescent properties of some PD are strongly sensitive to change in the nature of the medium, and others significantly so.[34,216]

No one class of organic dyes possesses such contrasting properties. Furthermore, a change from one class to another, is not always accompanied by such strong effects. PD are therefore ideal subjects for answering the main question of photoluminescence, formulated by S I Vavilov as follows: "...why does one molecule luminesce and others not?".[228] Further investigations of the spectral-luminescent properties of cyanines and the factors which determine them, should answer this question to a large extent. Special attention will be given to non-radiative processes in the region > 1000 nm, since only PD show interesting absorptions in this region. It will assist in the simple resolution of the question of the roles of internal conversion and high frequency vibrations in processes of deactivation of the excited states of the molecules.

Their solution may be most facilitated by the preparation of fully deuteriated PD with $\lambda^{a}_{max} > 1000$ nm. Since, in this region, the gap between the S_1- and T-levels decreases, an increase in the role of triplets in deactivation of the excited state can be expected. Elucidation of their role in deactivation is very necessary for the creation of stable PD which absorb and luminesce in the near infrared region. Singlet oxygen luminesces in this region (λ^{ϕ}_{max} = 1270 and 1590 nm).[119] PD with $\lambda_{max} > 1000$ nm should therefore occupy a fundamental place in the study of problems of energy transfer from themselves to singlet oxygen and *vice versa*. As a result of such a study, effective quenchers and sensitisers for singlet oxygen may be discovered.

In future, much greater attention will apparently be given to the investigation of the spectral-luminescent properties of the highly excited state of PD. Practical applications of cyanines are, in fact, frequently based on interactions of their molecules with intensive light fields. Such interactions give rise to non-linear optical effects in molecules of PD, with the participation of highly excited states.[229] Until recent times, the study of the latter was very difficult because of their very short life times. However, with the appearance of multi-photon laser spectrosocpy[230] this aim has become practicable for PD.[231]

Investigations in all these areas will make it possible to search still more effectively and purposefully for cyanines that are suitable for the solution of the problems of the transformation of light energy.

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Translated from *Uspekhi Khimii* **60** 1744–1776 (1991) U.D.C. 577.1

S-alkynyl esters of phosphorus thioacids as inhibitors of cholinesterases and as promising physiologically active compounds

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ABSTRACT. Data are given in the review on the anticholinesterase activity of 58 specially synthesised esters of phosphorus thioacids containing an actylenic bond in the thioester group. It was established that compounds containing an acetylenic group in the β and especially in the α position of the thioester residue display an inhibitory action many times greater than that of their saturated analogues. A phosphorylated enzyme is formed by the reaction of the actylenic organophosphorus inhibitors (OPIs) with the enzymes as in the case of reaction with the saturated analogues. It was shown that the acetylenic organophosphorus inhibitors possess high biological activity both for mammals and for arthropods. On replacing the phosphoryl oxygen (P=O) by sulphur (P=S) the toxicity of the acetylenic organophosphorus inhibitors for mammals was sharply reduced but was little changed for arthropods. This raises the possibility of obtaining highly selective insecto-acaricides. The mechanism of the antienzymic action of the acetylenic OPIs and the mechanism of detoxication of diethyl *S*-hexynyl dithiophosphate are considered.

The bibliography includes 44 references.

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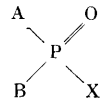
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I. Introduction

Among the substances influencing the transmission of nervous excitation in cholinergic synapses a significant place is occupied by derivatives (esters, amides, etc.) of phosphorus acids, many of which are used as insectoacaricides. Their bioligical action consists mainly of the inhibition of acetylcholinesterase (ACE), the enzyme causing the hydrolysis of acetylcholine (AC), the mediator of nervous excitation. It is well known[1] that under the stimulus of a nervous impulse, AC enters the synaptic gap and is reversily adsorbed onto a receptor which leads to excitation of the innervated cell. Due to the hydrolytic action of ACE the receptor is freed from AC and is transformed into its initial state acquiring the ability to take up a further portion of mediator. When ACE is inhibited the removal of AC from the receptor occurs very slowly, by diffusion alone, and the transmission of nervous impulses is disturbed which gives rise to serious disorders in the vital activity of organisms.

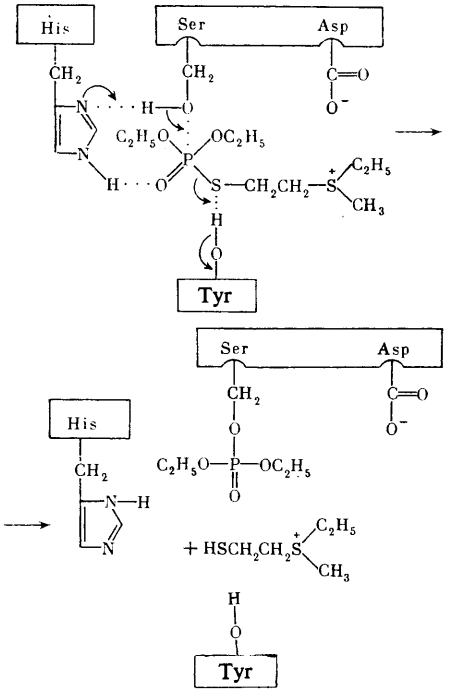
In addition to nervous tissue there are cholinesterases (CE) in erythrocytes and in the serum of many animals, in muscular tissue, etc. There are several varieties of CE which differ from one another not only in substrate specificity, i.e. the ability to hydrolyse choline esters of carboxylic acids, but also in sensitivity to inhibitors.[2,3]

Many derivatives of phosphoric, phosphonic and phosphinic acids of the following general formula are organophosphorus inhibitors (OPI) of cholinesterase.



where A and B are the same or different substituents at the phosphorus atom (alkyl, alkoxyl, amide, aryl, etc.) and X is a residue of an organic or inorganic acid (fluoride, cyano, phenol, mercaptan, etc.).

It has been demonstrated[4] that on reaction with cholinesterase these inhibitors phosphorylate the hydroxyl group of a serine residue which forms part of the catalytic centre of the enzyme. According to current ideas[5] the activation of the serine hydroxyl required to carry out this process occurs with the direct participation of the OPI by the following scheme.



The above scheme explains why thione OPI do not phosphorylate these enzymes. Unlike oxygen the sulphur atom is unable to form a stable hydrogen bond.[1,5]

The phosphorylated enzyme formed is a fairly stable compound. Spontaneous dephosphorylation takes place extremely slowly. Significant dephosphorylation occasionally leading to almost complete restoration of the cholinesterase catalytic activity (reactivation) is effected only by aromatic or aliphatic oximes.[6]

There is an anionic site in the active centre of the cholinesterases at a distance of 4–5 Å from the esterase site which interacts with the onium groups of substrates and of organophosphorus inhibitors increasing their adsorption to the active surface of the enzyme. Presumably[1] the anionic site is a carboxylate ion of a dibasic amino acid, such as aspartic or glutamic acid, forming part of the polypeptide chain of the enzyme. Both the esterase and the anionic sites are surrounded by hydrophobic regions on which hydrophobic adsorption of hydrocarbon radicals of substrates or inhibitors is effected thereby enabling the appropriate processes to occur at a higher rate.[7]

The anticholinesterase (anti-CE) activity of an OPI is characterised quantitatively by the bimolecular rate constant for the inhibition of the enzyme (k_{II}). In addition to the reaction conditions (pH, ionic strength, temperature and composition of the reaction medium) this activity depends on the nature of the enzyme and also on the structure of the substituents A and B and the fissile grouping.[7,8]

The presence of an onium atom in the β position of a thioalkyl radical, as in the compound Gd-42, viz. $(C_2H_5O)CH_3P(O)SCH_2CH_2\overset{+}{S}(C_2H_5)CH_3$, causes extremely high anti-CE activity sometimes exceeding the activity of its non-ionic analogue $(C_2H_5O)CH_3P(O).SCH_2CH_2SC_2H_5$ by a thousandfold.[1,2] Hydrophobic adsorption exerts a large effect on anti-CE activity. The value of k_{II} for the inhibition of human erythrocyte ACE by the compounds $(C_2H_5O).CH_3P(O)SC_nH_{2n+1}$ and $(C_nH_{2n+1}O)CH_3P(O)SC_4H_9$ is raised a hundredfold on increasing n from 1 to 7.[7]

Table 1. ω-Chlorobutynyl esters of phosphorus thioacids $RR'P(O)SCH_2C{\equiv}CCH_2Cl$.[18,19]

R	R′	Yield, %	Bp, °C (1.10^{-1} mm Hg)	d_4^{20}	n_D^{20}	Empirical formula
CH_3	C_2H_5O	72.5	122–123	1.2605	1.5283	$C_7H_{12}ClO_2PS$
CH_3	C_3H_7O	71.3	131–133	1.1918	1.5233	$C_8H_{14}ClO_2PS$
CH_3O	CH_3O	45.5	128–130	1.3015	1.5163	$C_6H_{10}ClO_3PS$
C_2H_5O	C_2H_5O	56.5	127–130	1.2441	1.5080	$C_8H_{12}ClO_2PS$
iso-C_3H_7O	iso-C_3H_7O	52	118–120	1.1635	1.4940	$C_{10}H_{18}ClO_3PS$
C_6H_5	C_2H_5O	48	162–163	1.2593	1.5721	$C_{12}H_{14}ClO_2PS$

It was shown recently[9,10] that a significant increase in the anti-CE activity of an OPI may be achieved by introducing an acetylenic grouping into the thioester residue. In some cases such phosphorus thioacid *S*-alkynyl esters supersede their saturated analogues in inhibitory activity by thousands and millions of times. Some of them inhibit the CE of arthropods more strongly than the CE of mammals, which is one source of selective toxicity. There is considerable practical interest in the *S*-alkynyl esters of dialkyl dithiophosphoric acids which acquire anti-CE activity by conversion into esters of monothiophosphoric acids by microsomal monooxidases. Such dithiophosphates display very high selective toxicity for arthropods and therefore are promising insecto-acaricides.[11]

To date a relatively large quantity of experimental data has been accumulated on the acetylenic OPIs which may be used for further study of the anti-CE activity and toxicity of this new and extremely intersting class of biologically active compounds.[9–17] The data presented in this review indicate the route for a purpose-directed search for highly selective insecto-acaricides. They are also of interest for the clarification of the mechanism of the interaction of the acetylenic OPIs with CEs.

II. Methods of synthesis of acetylenic organophosphorus inhibitors

The *S*-alkynyl esters of thiophosphoric and dithiophosphoric acids were synthesised by methods developed specially for this investigation.[13–15,18–28]

***S*-Butynyl esters of phosphorus thioacids** containing a triple bond in the β-position and a functional group in the ω-position of the thioester residue were obtained in the following way. The ω-chlorobutynyl esters of these acids were obtained initially by the reaction of the sodium or potassium salts of the appropriate phosphorus monothioacids with a 5-fold excess of 1,4-dichlorobutyne in alcohol (Table 1).[18]

$$RR'PSOM+ClCH_2C{\equiv}CCH_2Cl \rightarrow RR'P(O)SCH_2C{\equiv}CCH_2Cl,$$

R = CH_3, C_6H_5, CH_3O, C_2H_5, iso-C_3H_7O; R′ = CH_3O, C_2H_5O. iso-C_3H_7O, M = K or Na.

The products were subsequently converted by reaction with various nucleophilic reagents into ω-substituted *S*-butynyl esters of phsophorus monothioacids (Table 2). Sodium alkylmercaptides, dimethyl sulphide, dimethylamine, trimethylamine, triphenylphosphine and potassium dialkyl thiophosphate or thioacetate were used as nucleophilic reagents.[19]

$RR'P(O)SCH_2C{\equiv}CCH_2Cl \rightarrow$

- $\xrightarrow{R''SNa}$ $RR'P(O)SCH_2C{\equiv}CCH_2SR''$
- $\xrightarrow{S(CH_3)_2}$ $RR'P(O)SCH_2C{\equiv}CCH_2\overset{+}{S}(CH_3)_2Cl^-$
- $\xrightarrow{HN(CH_3)_2}$ $RR'P(O)SCH_2C{\equiv}CCH_2N(CH_3)_2$
- $\xrightarrow{N(CH_3)_3}$ $RR'P(O)SCH_2C{\equiv}CCH_2\overset{+}{N}(CH_3)_3Cl^-$
- $\xrightarrow{(C_6H_5)_3P}$ $RR'(O)SCH_2C{\equiv}CCH_2\overset{+}{P}(C_6H_5)_3Cl^-$
- $\xrightarrow{(iso\text{-}C_3H_7O)_2PSOK}$ $(iso\text{-}C_3H_7O)_2P(O)SCH_2C{=}CH_2S(iso\text{-}C_3H_7O)_2P(O)$
- $\xrightarrow{CH_3C(O)SK}$ $RR'P(O)SCH_2C{\equiv}CCH_2SC(O)CH_3$

O,O-Dimethyl and *O,O*-diethyl *S*-(4-acetoxybut-2-ynyl) thiophosphates (Table 2) were obtained by the reaction of 4-chlorobut-2-ynyl acetate with potassium dimethyl or diethyl thiophosphate.[20]

$$(RO)_2PSOK+ClCH_2C{\equiv}CCH_2OC(O)CH_3 \rightarrow$$
$$\rightarrow (RO)_2P(O)SCH_2C{\equiv}CCH_2OC(O)CH_3.$$

S-Propargyl esters of diethyl thiophosphoric acid were obtained by the reaction of the *O,O*-diethyl thiophosphates of potassium or monovalent copper with the appropriate propargyl halides.[12,21]

$$(C_2H_5O)_2PSOM + XCH_2C{\equiv}CR \rightarrow (C_2H_5O)_2P(O)SCH_2C{\equiv}CR,$$

R=H, Pr, Br; M=K, Cu; X=Cl, Br.

Table 2. ω-Substituted *S*-butynyl esters of phosphorus thioacids $RR'P(O)SCH_2C{\equiv}CCH_2R''$.[19,20]

R	R′	R″	Yield, %	Bp, °C (1.10^{-3} mm Hg)	d_4^{20}	n_D^{20}	Empirical formula
CH_3	C_2H_5O	C_2H_5S	24	125–130	1.1538	1.5335	$C_9H_{17}O_2PS_2$
CH_3	C_3H_7O	C_2H_5S	21	136–137	1.1319	1.5260	$C_{10}H_{19}O_2PS_2$
CH_3	C_4H_9O	C_2H_5S	20	140–145	1.1018	1.5198	$C_{11}H_{21}O_2PS_2$
CH_3	C_2H_5O	$CH_3C(O)S$	65	resin*	1.1993	1.5248	$C_9H_{19}O_3PS_2$
CH_3	C_2H_5O	$[(CH_3)_2\overset{+}{S}]Cl^-$	81	viscous oil	–	–	$C_9H_{18}O_2ClPS_2$
CH_3	C_2H_5O	$[(CH_3)_3\overset{+}{N}]Cl^-$	90	155–157	–	–	$C_{10}H_{21}O_2NClSP$
CH_3O	CH_3O	C_2H_5S	25	122–124	1.2005	1.5245	$C_8H_{15}O_3PS_2$
CH_3O	CH_3O	$CH_3C(O)S$	65	resin*	1.2552	1.5260	$C_8H_{13}O_4PS_2$
C_2H_5O	C_2H_5O	C_2H_5S	31	135–137	1.1548	1.5162	$C_{10}H_{19}O_3PS_2$
C_2H_5O	C_2H_5O	C_4H_9S	90	resin*	1.1110	1.5012	$C_{12}H_{23}O_3PS_2$
C_2H_5O	C_2H_5O	$[(CH_3)_2\overset{+}{S}]Cl^-$	75	glass	–	–	$C_{10}H_{20}O_3ClPS_2$
C_2H_5O	C_2H_5O	$[(CH_3)_2N]$	25	120–121	1.1045	1.4927	$C_{10}H_{20}O_3NPS$
C_2H_5O	C_2H_5O	$[(CH_3)_3\overset{+}{N}]Cl^-$	88	189–190 **	–	–	$C_{11}H_{23}ClO_3NPS$
C_2H_5O	C_2H_5O	$CH_3C(O)S$	71	resin*	1.1994	1.5195	$C_{10}H_{27}O_4PS_2$
CH_3O	CH_3O	$CH_3C(O)O$	60	resin*	1.2206	1.4970	$C_8H_{13}O_5PS$
C_2H_5O	C_2H_5O	$CH_3C(O)O$	75	resin*	1.1744	1.4860	$C_{10}H_{17}O_5PS$

*Purified by column chromatography on silica gel.
**MP.

Sterically hindered *S*-propargyl esters of diethyl thiophosphoric acid were obtained by the reaction of the copper(I) salt of diethyl phosphoric acid with the sterically hindered propargyl chlorides.

$$(C_2H_5O)_2PSOCu + HC{\equiv}CCR'R''Cl \rightarrow (C_2H_5O)_2P(O)SCR'R''C{\equiv}CH,$$

$$R'=R''=CH_3, \quad R'+R''=(CH_2)_5.$$

S-Ethynyl esters of dialkyl thiophosphates were obtained by three methods:

a) by the reaction of the potassium salts of *O,O*-dialkyl thiophosphates with substituted ethynyl bromides in the presence of equimolar quantities of copper(I) chloride (Table 3).[22]

$$(RO)_2PSOK + BrC{\equiv}CR' \xrightarrow{CuCl} (RO)_2P(O)SC{\equiv}CR',$$

R=CH_3, C_2H_5, C_3H_7 and R′=C_4H_9, $CH_2SC_2H_5$, $CH_2OC_2H_5$, $CH_2OC(O)CH_3$, C_6H_5, cyclo-C_6H_{11}, cyclohex-1-enyl.

b) by the reaction of the copper(I) salts of *O,O*-dialkyl thiophosphates with substituted ethynyl bromides (Table 4).[23]

$$(RO)_2PSOCu + BrC{\equiv}CR' \rightarrow (RO)_2P(O)SC{\equiv}CR',$$

R = C_2H_5 and R′ = C_4H_9, t-C_4Hh_9, $CH_2CH_2SC_2H_5$, cyclo-C_6H_{11}, 1-hydroxycyclohexyl, 1-acetoxycyclohexyl.

c) by the reaction of dialky phosphorylsulphenyl chlorides with substituted ethynyl magnesium bromides (Table 5).[24]

$$(RO)_2P(O)SCl + BrMgC{\equiv}CR' \rightarrow (RO)_2P(O)SC{\equiv}CR',$$

R = C_2H_5, C_3H_7 and R′ = H, C_4H_9, $CH_2SC_2H_5$, $CH_2SC_4H_9$.

Table 3. *S*-Ethynyl esters of dialkyl thiophosphoric acids $(RO)_2P(O)SC{\equiv}C-R'$.[22,23]

R	R′	Yield, %	d_4^{20}	n_D^{20}	Empirical formula
CH_3	$CH_2SC_2H_5$	75	1.3365	1.5130	$C_7H_{13}O_3PS_2$
CH_3	C_4H_9	78	1.1175	1.4845	$C_8H_{15}O_3PS$
CH_3	$CH_2OC_2H_5$	80	1.0575	1.4940	$C_7H_{13}O_4PS$
CH_3	$CH_2OC(O)CH_3$	75	1.3091	1.4989	$C_7H_{11}O_5PS$
CH_3	C_6H_5	70	1.2667	1.5780	$C_{10}H_{11}O_3PS$
CH_3	cyclo-C_6H_{11}	71	1.1279	1.5002	$C_{10}H_{17}O_3PS$
CH_3		75	1.2078	1.5425	$C_{10}H_{15}O_3PS$
C_2H_5	$CH_2SC_2H_5$	70	1.1648	1.4980	$C_9H_{17}O_3PS_2$
C_2H_5	C_4H_9	76	1.0758	1.4705	$C_{10}H_{19}O_3PS$
C_2H_5	$CH_2SC_4H_9$	81	1.1925	1.5155	$C_{11}H_{21}O_3PS_2$
C_2H_5	$CH_2OC_2H_5$	85	1.1482	1.4820	$C_9H_{17}O_4PS$
C_2H_5	$CH_2OC(O)CH_3$	81	1.2190	1.4859	$C_9H_{15}O_5PS$
C_2H_5	C_6H_5	72	1.2123	1.5640	$C_{12}H_{15}O_3PS$
C_2H_5		80	1.1235	1.5225	$C_{12}H_{19}O_3PS$
C_3H_7	$CH_2OC(O)CH_3$	82	1.1860	1.4904	$C_{11}H_{19}O_5PS$
C_3H_7	C_6H_5	71	1.1515	1.5370	$C_{14}H_{19}O_3PS$

Table 4. *S*-Ethynyl esters of diethyl thiophosphoric acids $(C_2H_5O)_2P(O)SC{\equiv}C-X$.[23]

X	Yield, %	d_4^{20}	n_D^{20}	Empirical formula
C_4H_9	60	1.0750	1.4700	$C_{10}H_{19}O_3PS$
t-C_4H_9	70	1.0432	1.4860	$C_{10}H_{19}O_3PS$
$CH_2CH_2SC_2H_5$	60	1.1470	1.5120	$C_{10}H_{19}O_3PS_2$
cyclo-C_6H_{11}	80	1.1063	1.4965	$C_{12}H_{21}O_3PS$
	81	1.1595	1.5055	$C_{12}H_{21}O_4PS$
	76	1.1394	1.4900	$C_{14}H_{23}O_5PS$

***S*-Alkynyl esters of diethyl phosphoric acid** containing an acetylenic bond in the γ-position of the thioester residue were synthesised by the alkylation of potassium diethyl thiophosphate with the appropriate bromoalkynes.

$$(C_2H_5O)_2PSOK + RC{\equiv}C(CH_2)_2Br \rightarrow (C_2H_5O)_2P(O)S(CH_2)_2C{\equiv}CR,$$

R=H, C_2H_5;

Alkylthio-substituted *S*-butynyl esters of *O,O*-dialkyl thiophosphoric acids containing a triple bond in the β-position of the thioester residue were obtained analogously to the corresponding esters of the phosphorus monothioacids through the intermediate ω-chlorobutynyl esters of these acids.[25,26]

$$(RO)_2P(S)SK+ClCH_2C{\equiv}CCH_2Cl \rightarrow (RO)_2P(S)SCH_2C{\equiv}CCH_2Cl,$$

$$(RO)_2P(S)SCH_2C{\equiv}CCH_2Cl+R'SNa \rightarrow (RO)_2P(S)SCH_2C{\equiv}CCH_2SR',$$

$R=CH_3$, C_2H_5 and $R'=C_2H_5$, C_4H_9.

Table 5. ***S*-Ethynyl esters of thiophosphoric acids $(RO)_2P(O)SC{\equiv}CX$.**[12,24]

R	X	Yield, %	Bp, °C (1.10^{-3} mm Hg)	d_4^{20}	n_D^{20}	Empirical formula
C_2H_5	H	21	72–76	1.2108	1.4683	$C_6H_{11}O_3PS$
C_3H_7	H	25	85–87	1.1273	1.4650	$C_8H_{15}O_3PS$
C_4H_9	H	20	98–100	1.0337	1.4580	$C_{10}H_{19}O_3PS$
C_2H_5	C_4H_9	30	100–104	1.0750	1.4688	$C_{10}H_{19}O_3PS$
C_2H_5	$CH_2SC_2H_5$	22	105–108	1.1639	1.4912	$C_9H_{17}O_3PS_2$
C_2H_5	$CH_2SC_4H_9$	19	–	1.1925	1.5150	$C_{11}H_{21}O_3PS_2$
C_2H_5	$S(O)P(OC_2H_5)_2$	18	–	1.1344	1.4892	$C_{14}H_{28}O_6P_2S_2$

Table 6. ***S*-Ethynyl esters of dialkyl dithiophosphoric acids $(RO)_2P(S)SC{\equiv}C-X$.**[27,28]

R	X	Yield, %	d_4^{20}	n_D^{20}	Empirical formula
CH_3	C_4H_9	78	1.1540	1.5215	$C_8H_{15}O_2PS_2$
CH_3	$CH_2SC_2H_5$	75	1.2384	1.5670	$C_7H_{13}O_2PS_3$
C_2H_5	C_4H_9	81	1.0797	1.5140	$C_{10}H_{19}O_2PS_2$
C_2H_5	$CH_2SC_2H_5$	85	1.0271	1.5486	$C_9H_{17}O_2PS_3$
C_2H_5	$CH_2SC_4H_9$	70	1.1545	1.5426	$C_{11}H_{22}O_2PS_3$

O,O-Diethyl *S*-(4-acetoxybut-2-ynyl) dithiophosphate was obtained by the reaction of 4-chlorobut-2-ynyl acetate with potassium *O,O*-diethyl dithiophosphate.[20]

$$(C_2H_5O)_2P(S)SK+CH_3C(O)OCH_2C{\equiv}CCH_2Cl \rightarrow$$
$$\rightarrow (C_2H_5O)P(S)SCH_2C{\equiv}CCH_2OCOCH_3.$$

***S*-Ethynyl esters of dialkyl dithiophosphoric acids** were obtained by two methods:

a) by the reaction of dialkyl thiophosphoryl disulphides with lithium acetylides (Table 6),[27]

$$(RO)_2P(S)S-SP(S)(OR)_2+LiC{\equiv}CR' \rightarrow (RO)_2P(S)SC{\equiv}CR';$$

b) by the reaction of copper(I) salts of *O,O*-dialkyl dithiophosphoric acids with substituted ethynyl bromides (Table 7),[28]

$$(RO)_2P(S)SCu+BrC{\equiv}CR' \rightarrow (RO)_2P(S)SC{\equiv}CR',$$

$R'=C_4H_9$, C_6H_5, cyclo-C_6H_{11}, cyclohex-1-enyl,

$R=CH_3$, C_2H_5, C_3H_7, C_4H_9.

***S*-Alkynyl esters of diethyl dithiophosphoric acid** containing a triple bond at various distances from the phosphorus atom were obtained by the reaction of potassium *O,O*-diethyl dithiophosphate with the appropriate bromoalkynes.[28]

$$(RO)_2P(S)SK+Br(CH_2)_nC{\equiv}CR' \rightarrow (RO)_2P(S)S(CH_2)_nC{\equiv}CR',$$

$R'=H$, C_2H_5, C_3H_7, C_4H_9; $n=0, 1, 2$.

Table 7. Ethynyl esters of dialkyl dithiophosphoric acids $(RO)_2P(S)SC{\equiv}C-X$.[27,28]

R	X	Yield, %	d_4^{20}	n_D^{20}	Empirical formula
CH_3	C_4H_9	80	1.1540	1.5225	$C_{19}H_{15}O_2PS_2$
CH_3	C_6H_5	80	1.2920	1.6215	$C_{10}H_{11}O_2PS_2$
CH_3	cyclo-C_6H_{11}	68	1.1638	1.5460	$C_{10}H_{17}O_2PS_2$
CH_3		85	1.2306	1.5840	$C_{10}H_{15}O_2PS_2$
C_2H_5	C_4H_9	85	1.0790	1.5140	$C_{10}H_{19}O_2PS_2$
C_2H_5	C_6H_5	78	–	1.5925	$C_{12}H_{15}O_2PS_2$
C_2H_5	cyclo-C_6H_{11}	71	1.1191	1.5335	$C_{12}H_{21}O_2PS_2$
C_2H_5		90	1.1764	1.5635	$C_{12}H_{19}O_2PS_2$
C_3H_7	C_6H_5	80	1.1695	1.5735	$C_{14}H_{19}O_2PS_2$
C_4H_9	C_6H_5	90	1.1498	1.5700	$C_{16}H_{23}O_2PS_2$

***S*-Alkyl esters of *O,O*-dialkyl thio- and dithiophosphoric acids** were obtained by the reaction of the appropriate alkyl halides with the potassium salts of these acids (Table 8).

$$(RO)_2P(S)YK+BrCH_2CH_2R' \rightarrow (RO)_2P(Y)SCH_2CH_2R',$$

$R'=CH_2SC_2H_5$, CH_2OCOCH_3, t-C_4H_9, CH_2Br, C_6H_5,

cyclo-C_6H_{11}, cyclohex-1-enyl and Y = O or S.

The synthesis of *O,O*-diethyl *S*-(3-ethylthiopropyl) thio- and dithiophosphates was effected in the following way. First *O,O*-diethyl *S*-(3-bromopropyl) thio- or dithiophosphates were obtained by the reaction of the potassium salts of diethyl thio- and dithiophosphoric acid with 1,3-dibromopropane. The corresponding *S*-ethylthiopropyl thioesters were then obtained from them by the action of sodium ethylmercaptide.

$$(C_2H_5O)_2PSYK+BrCH_2CH_2CH_2Br \rightarrow (C_2H_5O)_2P(Y)SCH_2CH_2CH_2Br,$$
$$(C_2H_5O)_2P(Y)SCH_2CH_2CH_2Br+C_2H_5SNa \rightarrow$$
$$\rightarrow (C_2H_5O)_2P(Y)S(CH_2)_3SC_2H_5,$$

Y = O or S.

***S*-Propargyl thioacetate** was obtained by the reaction of propargyl bromide or chloride with potassium thioacetate.[29]

$$CH_3C(O)SK+XCH_2C{\equiv}CH\rightarrow CH_3C(O)SCH_2C{\equiv}CH+KX,$$

X = Cl or Br.

4-Chlorobut-2-ynyl acetate was obtained in one step in 65% yield by the reaction of 1,4-butynediol with acetyl chloride and then with thionyl chloride.[20]

$$CH_3C(O)Cl+HOCH_2C{\equiv}CCH_2OH+SOCl_2\rightarrow$$
$$\rightarrow CH_3C(O)OCH_2O{\equiv}CCH_2Cl.$$

Table 8. *S*-Alkyl esters of diethyl thio- and dithiophosphoric acids $(C_2H_5O)_2P(Y)SCH_2CH_2-X$.[28]

X	Y	Yield, %	d_4^{20}	n_D^{20}	Empirical formula
$CH_2SC_2H_5$	O	80	1.1378	1.4920	$C_9H_{21}O_3PS_2$
CH_2OCOCH_3	O	70	1.1440	1.4620	$C_9H_{19}O_5PS$
t-C_4H_9	O	90	1.0058	1.4610	$C_{10}H_{23}O_3PS$
CH_2Br	O	71	1.3420	1.4930	$C_7H_{16}O_3PSBr$
C_6H_5	O	78	1.1097	1.5170	$C_{12}H_{19}O_3PS$
cyclo-C_6H_{11}	O	70	1.0462	1.4802	$C_{12}H_{25}O_3PS$
	O	70	1.0677	1.4925	$C_{12}H_{23}O_3PS$
$CH_2SC_2H_5$	S	80	1.1161	1.5212	$C_9H_{21}O_2PS_3$
CH_2OCOCH_3	S	70	1.1570	1.4995	$C_9H_{19}O_4PS_2$

***S*-Hex-1-ynyl thioacetate** was obtained in one stage in the following way.[30] Hex-1-ynyllithium was obtained by the reaction of a freshly prepared soluton of butyllithium in ether with 1-hexyne and was then converted into the corresponding lithium mercaptide by reaction with sulphur.

$$C_4H_9C{\equiv}CH \xrightarrow{C_4H_9Li} C_4H_9C{\equiv}CLi,$$
$$C_4H_9C{\equiv}CLi \xrightarrow{S} C_4H_9C{\equiv}CSLi.$$

Reaction with acetyl bromide then gives *S*-hex-1-ynyl thioacetate.

$$C_4H_9C{\equiv}CSLi+CH_3C(O)Br\rightarrow CH_3C(O)SC{\equiv}CC_4H_9.$$

III. Anticholinesterase activity of acetylenic organophosphorus inhibitors

Partially purified water-soluble preparations of acetylcholinesterase of human erythrocytes (ACE) and butyrylcholinesterase of horse serum (BuCE) served as enzyme sources. In addition a brain homogenate from white mice (mouse CE), a homogenate of the heads of the fly *Musca domestica L.* (fly CE), homogenates of whole beet aphids *Aphis fabae Scop.* and grass aphids *Schizaphis gramina Rond.* (aphid CE) and spider mites *Tetranychus urticae Koch* (mite CE) were also used. The rates of cholinesterase hydrolysis of acetylthiocholine (ATC) before (v_0) and after (v_i) reaction with the various inhibitors were determined at 25 °C and pH 7.5 by Ellman's method.[31] Ellman's reagent was added after stopping the enzymic reaction in experiments with aphid CE.[32] The bimolecular rate constant (k_{II}) for the reaction of a cholinesterase with an OPI was determined at 25 °C and pH 7.5 by known methods[7,8] and was calculated from the formula:

$$k_{II}=\frac{2.303}{t[I]}\lg\frac{v_0}{v_i}(M^{-1}\,min^{-1}),$$

where v_i is the rate of enzymic hydrolysis of ATC after t min incubation of the CE with the OPI at a concentration [I] many times greater than the concentration of enzyme active centres; v_0 is the rate of enzymic hydrolysis of ATC in the absence of the OPI. The rate constant for the alkaline hyrolysis of the OPI (k_{OH}) was determined at 25 °C and pH 9.2 by a known method.[14]

Table 9. Anticholinesterase activity (k_{II}, M^{-1} min^{-1}) of acetylenic OPI $(RO)_2P(O)SCH_2C{\equiv}CCH_2R'$ and their saturated analogues $(RO)_2P(O)SCH_2CH_2CH_2CH_2R'$ (compounds numbered 'a').[8,9]

Compound No.	OPI		Anticholinesterase activity of OPI					
	R	R'	ACE	BuCE	mouse CE	fly CE	beet aphid CE	mite CE
(I)	CH_3	Cl	$2.8\cdot10^5$ (28)	$7.2\cdot10^5$ (36)	$6.2\cdot10^4$ (8)	$1.3\cdot10^6$ (19)	$4.8\cdot10^5$ (23)	$3.5\cdot10^5$ (125)
(II)	C_2H_5	Cl	$2.6\cdot10^5$ (10)	$5.8\cdot10^5$ (3)	$8.9\cdot10^4$ (12)	$2.5\cdot10^6$ (37)	$1.0\cdot10^5$ (3)	$6.5\cdot10^4$ (1.6)
(III)	CH_3	SC_2H_5	$3.2\cdot10^5$ (270)	$1.0\cdot10^6$ (1000)	$3.3\cdot10^5$ (140)	$7.0\cdot10^6$ (580)	$2.9\cdot10^6$ (2000)	$3.8\cdot10^6$ (7600)
(IV)	C_2H_5	SC_2H_5	$2.1\cdot10^5$ (260)	$2.9\cdot10^6$ (60)	$1.1\cdot10^5$ (48)	$3.2\cdot10^6$ (640)	$1.5\cdot10^4$ (7)	$6.5\cdot10^5$ (810)
(V)	C_2H_5	SC_4H_9	$3.6\cdot10^6$	$2.1\cdot10^7$	$2.8\cdot10^5$	–	–	$2.5\cdot10^5$
(VI)	CH_3	$OC(O)CH_3$	$1.4\cdot10^5$	$1.4\cdot10^5$	$1.0\cdot10^5$	$3.0\cdot10^5$	$1.8\cdot10^5$ $1.4\cdot10^2$	$2.8\cdot10^5$
(VII)	C_2H_5	$OC(O)CH_3$	$1.4\cdot10^5$	$3.3\cdot10^5$	$1.5\cdot10^5$	$4.5\cdot10^5$	$6.5\cdot10^5$	$2.7\cdot10^5$
(VIII)	CH_3	$SC(O)CH_3$	$4.4\cdot10^5$	$5.0\cdot10^5$	$2.9\cdot10^5$	$5.5\cdot10^6$	$1.8\cdot10^5$	$1.7\cdot10^6$
(IX)	C_2H_5	$SC(O)CH_3$	$6.8\cdot10^5$	$5.2\cdot10^6$	$3.8\cdot10^5$	$1.5\cdot10^7$	$1.3\cdot10^5$	$1.2\cdot10^6$
(X)	C_3H_7	$SC(O)CH_3$	$3.0\cdot10^6$	$3.8\cdot10^7$	$3.2\cdot10^6$	$4.0\cdot10^6$	$6.0\cdot10^5$	$1.3\cdot10^3$
(XI)	C_2H_5	OH	$2.9\cdot10^4$	$2.9\cdot10^5$	$2.0\cdot10^5$	$2.2\cdot10^6$	$4.8\cdot10^6$	$4.0\cdot10^5$
(XII)	C_2H_5	$\overset{+}{N}(CH_3)_3Cl^-$	$1.5\cdot10^6$	$1.0\cdot10^7$	$1.8\cdot10^6$	–	–	$1.7\cdot10^7$
(Ia)	CH_3	Cl	$1.0\cdot10^4$	$2.0\cdot10^4$	$7.8\cdot10^3$	$7.7\cdot10^4$	$2.1\cdot10^4$	$2.8\cdot10^3$
(IIa)	C_2H_5	Cl	$2.7\cdot10^4$	$1.7\cdot10^5$	$7.7\cdot10^3$	$6.7\cdot10^4$	$3.4\cdot10^4$	$4.0\cdot10^4$
(IIIa)	CH_3	SC_2H_5	$1.2\cdot10^3$	$1.0\cdot10^3$	$2.3\cdot10^3$	$1.2\cdot10^4$	$1.3\cdot10^3$	$5.0\cdot10^2$
(IVa)	C_2H_5	SC_2H_5	$8.0\cdot10^2$	$4.8\cdot10^4$	$2.3\cdot10^3$	$5.0\cdot10^3$	$2.2\cdot10^3$	$8.0\cdot10^2$

Footnote. Values of the acetylene effect q are given in parentheses (q = k_{II} acetylenic OPI/k_{II} saturated analogue).

1. *S*-Butynyl esters of phosphorus thioacids containing an acetylenic bond in the β-position of the thioester residue

The esters investigated were of *O,O*-dialkyl thiophosphoric acid, viz $(RO)_2P(O)SCH_2C{\equiv}CCH_2R'$, where R = CH_3, C_2H_5, C_3H_7, and R' = Cl, OH, SC_2H_5, SC_4H_9, $OC(O)CH_3$, $SC(O)CH_3$, and $\overset{+}{N}(CH_3)_3Cl^-$ (Table 9) and of *O*-ethyl thiophosphoric acids, viz. $(C_2H_5O)RP(O)SCH_2C{\equiv}CCH_2R'$, where R = CH_3, C_6H_5, and R' = Cl, SC_2H_5, $SC(O)CH_3$, $\overset{+}{N}(CH_3)_3Cl^-$ (Table 10). In these compounds the acetylenic group is at approximately the same distance from the

phosphorus atom as the sulphonium sulphur atom in the preparation Gd-42 (see above for formula). It was assumed that this highly reactive group may react with the anionic centre in cholinesterases and thereby affect the inhibitory activity of these compounds.

Table 10. Anticholinesterase activity (k_{II}, M^{-1} min^{-1}) of acetylenic OPI $R(C_2H_5O)P(O)SCH_2C{\equiv}CCH_2R'$ and their saturated analogues $R(C_2H_5O)P(O)SCH_2CH_2CH_2CH_2R'$ (compounds numbered 'a').[9]

Compound No.	OPI		Anticholinesterase activity of OPIs					
	R	R'	ACE	BuCE	mouse CE	fly CE	beet aphid CE	mite CE
(XIII)	CH_3	Cl	$3.1\cdot10^6$ (62)	$2.1\cdot10^6$ (1500)	$9.3\cdot10^6$ (140)	$1.0\cdot10^9$ (21 000)	$6.6\cdot10^6$ (51)	$9.0\cdot10^5$ (4.5)
(XIV)	C_6H_5	Cl	$4.0\cdot10^5$ (50)	$2.2\cdot10^5$ (8)	$4.7\cdot10^4$ (9)	$1.0\cdot10^5$ (31)	$9.0\cdot10^6$ (310)	$2.7\cdot10^4$ (11)
(XV)	CH_3	SC_2H_5	$6.6\cdot10^6$ (41)	$1.3\cdot10^6$ (20)	$2.9\cdot10^7$ (260)	$1.1\cdot10^9$ (38 000)	$5.3\cdot10^7$ (590)	$2.5\cdot10^7$ (1200)
(XVI)	C_6H_5	SC_2H_5	$6.2\cdot10^5$ (31)	$1.8\cdot10^6$ (8)	$4.6\cdot10^4$ (38)	$4.4\cdot10^5$ (44)	$5.6\cdot10^6$ (670)	$1.1\cdot10^5$ (85)
(XIIIa)	CH_3	Cl	$5.0\cdot10^4$	$1.4\cdot10^3$	$6.7\cdot10^4$	$4.8\cdot10^4$	$1.3\cdot10^5$	$2.2\cdot10^5$
(XIVa)	C_6H_5	Cl	$8.0\cdot10^3$	$2.7\cdot10^4$	$5.4\cdot10^3$	$3.2\cdot10^3$	$2.9\cdot10^4$	$2.4\cdot10^3$
(XVa)	CH_3	SC_2H_5	$1.6\cdot10^5$	$6.4\cdot10^4$	$1.1\cdot10^5$	$2.9\cdot10^4$	$9.0\cdot10^4$	$2.1\cdot10^4$
(XVIa)	C_6H_5	SC_2H_5	$2.0\cdot10^4$	$2.2\cdot10^5$	$1.2\cdot10^3$	$1.0\cdot10^4$	$8.4\cdot10^3$	$1.3\cdot10^3$

Footnote. Values of the acetylene effect q are given in parentheses.

Parallel experiments were carried out with saturated analogues of some of the acetylenic inhibitors in order to assess objectively the effect of the acetylenic group on the anticholinesterase (anti-CE) activity of the compounds. This effect was assessed quantitatively by the size of the 'acetylene effect' (q) which shows how many times the bimolecular rate constant for cholinesterase inhibition by the acetylenic compound was greater than the same inhibition constant of its saturated analogue.

It follows from the data of Tables 9 and 10 that the acetylenic compounds (I)–(IV) and (XIII)–(XVI) possess higher anti-CE activity than their saturated analogues. This is observed for all compounds without exception but varies within very wide limits depending on the nature of the enzyme and the structure of the inhibitor. The ethylmercapto-substituted thiophosphates (III) and (IV) exceed the chloro-substituted compounds (I) and (II) in the size of the acetylenic effect. This is linked with the fact that the inhibitory activity of an acetylenic OPI is practically independent of the nature of the substituent but for the saturated analogues the chloro-substituted compounds possess a higher anti-CE activity than the ethylmercapto-substituted compounds. It is characteristic that the structure of the phosphoryl portion of the inhibitor molecule shows a smaller influence on the acetylenic effect. Relatively close values of q were observed for mouse CE, fly CE and ACE both for the chloro-substituted esters of dimethyl and diethyl thiophosphoric acids (I) and (II) and for the ethylmercapto-subtituted derivatives of these acids (III) and (IV). The dimethyl thiophosphates surpassed by a little the corresponding diethyl thiophosphates in the size of q for the other CE.

There were no saturated analogues for compounds (V)–(XII). Experiments with them gave additional information on the link between the structure of the acetylenic OPI and their anti-CE activity. Dimethyl and diethyl esters of thiophosphoric acids with an $OC(O)CH_3$ substituent (VI) and (VII) displayed close inhibitory activity towards each of the CE investigated as was also seen in experiments with chloro- and ethylmercapto-substituted derivatives of these acids. Appreciable differences were also not observed in their anti-CE activity for various CE. For example the size of the inhibition constant for compound (VI) for fly CE, the most sensitive, was 3.0×10^5 M^{-1} min^{-1}, and for mouse CE, the least sensitive, was 1.0×10^5 M^{-1} min^{-1}, i.e. a threefold difference.

On the other hand a clearly marked dependence of inhibitory activity was shown by the acetylenic OPIs with a $SC(O)CH_3$ substituent (VIII)–(X) on the structure of the phosphoryl portion of the molecule for each CE and on the nature of the CE for each compound. Thus mammalian and aphid CE proved to be the most sensitive to the ester of dipropyl thiophosphoric acid and fly CE to the ester of diethyl thiophosphoric acid. In difference to the other enzymes mite CE displayed an extremely low sensitivity towards the ester of dipropyl thiophosphoric acid (X) $k_{II} = 1.3 \times 10^3$ M^{-1} min^{-1} which is 30 000 times less than k_{II} for BuCE, 3.8×10^7 M^{-1} min^{-1}. A large difference was detected in the sensitivity of the CEs investigated towards a diethyl thiophosphate with an OH susbtituent (XI). In the inhibition of ACE $k_{II} = 2.9 \times 10^4$ M^{-1} min^{-1} but in the inhibition of aphid CE $k_{II} = 4.8 \times 10^6$ M^{-1} min^{-1}.

The butylmercapto derivative (V) possesses a higher anti-CE activity than the methylmercapto derivative (IV) in relation to mammalian CE. Consequently in addition to the acetylenic group, the length of the hydrocarbon chain, which provides hydrophobic adsorption to the corresponding portion of the catalytic centre of the enzyme, enhances the anti-CE activity. Compound (XII), having a trimethylammonium group, surpasses all the other compounds, except for compound (X), in its anti-CE activity on reaction with mouse CE. The sensitivity of the other CEs to compound (XII) differed little from their sensitivity to certain uncharged actylenic OPIs.

Two general regularities must be mentioned in relation to the selectivity of the inhibitory action of the actylenic OPIs investigated. a) Among the mammalian enzymes BuCE proved to be the most sensitive to each of the OPIs investigated which is in agreement with numerous literature data on the higher inhibitory activity of phosphates in relation to BuCE than to ACE.[2] b) Among the arthropod enzymes, fly CE possesses the highest sensitivity towards the OPIs investigated with few exceptions.

It follows from the data of Table 10 that a sharp increase in anti-CE activity is also observed for the thiophosphonates on introducing an acetylenic group into the OPI molecule. Thus for the methyl esters (XIII) and (XV) the size of k_{II} in relation to fly CE proved to be exceptionally high (10^9 M^{-1} min^{-1}) and these compounds may be considered to be highly selective inhibitors of this enzyme. Such an enormous increase in anti-CE activity over the saturated analogues (XIIIa) and (XVa) cannot be explained by the higher phosphorylating ability of the acetylenic compounds since the introduction of an acetylenic group into the β-position of the thioalkyl residue increases the rate constant for alkaline hydrolysis by only 5–6 times. It must be noted that the saturated methylthiophosphonates strongly inhibit not fly CE but the other CEs, compound (XIIIa) inhibits the aphid CE and mite CE and compound (XVa) inhibits mouse CE and ACE.

In contrast to the thiophosphates, the nature of the substituent for the methylthiophosphonates (XIII) and (XV) showed a less clear influence on the acetylene effect. On reacting these compounds with ACE, fly CE and mouse CE the size of q varied little with the nature of the substituent. For aphid CE and mite CE the size of q was greater than when reacting these enzymes with ethylmercapto-substituted derivatives, and for BuCE than with chloro-substituted compounds.

With few exceptions the *S*-butyl esters of phenylthiophosphonic acid (XIV) and (XVI), in comparison with similar esters of methylphosphonic acid (XIII) and (XV), proved to be less strong inhibitors of the CEs investigated. For example, a large difference was observed towards esters of these acids for mite CE for all three substituents. There was a particularly large difference in the sensitivity of fly CE to compounds with substituents Cl and SC_2H_5. For the chloro-substituted derivatives (XIII) and (XIV) this difference was 10000 times and for the ethylmercapto-substituted derivatives (XV) and (XVI) 2500 times.

The thioesters of phenylthiophosphonic acid were surpassed by the corresponding methylthiophosphonates in the size of the acetylene effect. For the majority of the CEs investigated the size of q did not exceed 50 (Table 10), and only for aphid CE were they relatively large, viz. 310 for chloro-substituted and 670 for ethylmercapto-substituted compounds. As for the methylthiophosphonates, the influence of the substituent on the acetylene effect for phenylthiophosphonates is displayed in different ways for the investigated CEs. For arthropod and mouse CE the size of q is greater for ethylmercapto-substituted compounds [(XIV) and (XV)], on the other hand for ACE the size of q is greater for chloro-substituted compounds and for BuCE there is no difference in the values of q for these compounds.

From the experimental data given in this section the problem arises as to which position of the acetylenic bond in the *S*-butynyl group provides the greatest anti-CE activity. The acetylenic group, with its high π-electron density, may react by forming a type of π-complex not only with the carboxyl group of the anionic site of the CE, but also with other groups such as alcohols, amino groups, etc. Consequently the optimum effect of the acetylenic grouping may not necessarily be displayed at the β-position.

2. *S*-Alkynyl esters of diethyl phosphoric acid with the acetylenic group at various positions in the thioester residue

The anti-CE activity of two sets of compounds of general formula $(C_2H_5O)_2P(O)SX$ has been investigated (Table 11). In compounds (XVII)–(XIX), the first set, the group X is a hexynyl group C_6H_9 in which the acetylenic bond is found in the α-, β- or γ-positions relative to the sulphur atom, i.e. X = $-C\equiv CC_4H_9$, $-CH_2.C\equiv CC_3H_7$, $-CH_2CH_2C\equiv CC_2H_5$. In compounds (XX)–(XXII), the second set, the position of the acetylenic bond and the length of the *S*-alkynyl chain are chained. i.e. X = $-C\equiv CH$, $-CH_2C\equiv CH$, $-CH_2CH_2C\equiv CH$. The anti-CE activity of the saturated analogues of these compounds was studied. Compound $(C_2H_5O)_2P(O)SC_6H_{13}$ is the saturated analogue for the three compounds of the first set, each compound of the second set has its own analogue.

It follows from the data of Table 11 that inhibitors with an actylenic bond in the α-position possess the greatest anti-CE activity. In their ability to inhibit CEs they surpassed such strong OPIs as the onium compounds, such as the methylsulphomethylate of *O,O*-diethyl S-[β-(phenylmethylamino)ethyl] thiophosphate.[35] The k_{II} for this compound when inhibiting ACE was 2.5×10^7 M^{-1} min^{-1}, and when inhibiting BuCE was 6.8×10^7 M^{-1} min^{-1}. Compound (XX) gave the same value for the constant when inhibiting ACE, viz. 2.3×10^7 M^{-1} min^{-1}, but compound (XVII) gave the even larger value of 1.0×10^8 M^{-1} min^{-1} when inhibiting BuCE (Table 11).

Table 11. Anticholinesterase activity (k_{II}, M^{-1} min^{-1}) of OPIs of structure $(C_2H_5O)_2P(O)SX$ with various positions of the acetylenic group in the thioether residue.[10,12]

Compound No.	OPI	Anticholinesterase activity of OPIs					
	X	ACE	BuCE	mouse CE	fly GE	beet aphid CE	mite CE
(XVII)	$C\equiv CC_4H_9$	$9.5\cdot10^8$ (2500)	$1.0\cdot10^8$ (3100)	$7.1\cdot10^6$ (7100)	$1.5\cdot10^8$ (169 000)	$4.6\cdot10^7$ (6600)	$6.0\cdot10^7$ (8600)
(XVIII)	$CH_2C\equiv CC_3H_7$	$1.4\cdot10^4$ (3.7)	$1.0\cdot10^6$ (30)	$7.0\cdot10^3$ (7.0)	$3.0\cdot10^5$ (34)	$1.7\cdot10^4$ (2.4)	$4.0\cdot10^4$ (5.7)
(XIX)	$CH_2CH_2C\equiv CC_2H_5$	$4.0\cdot10^3$ (1)	$1.2\cdot10^5$ (3.6)	$6.6\cdot10^3$ (6.6)	$1.1\cdot10^5$ (12.3)	$1.7\cdot10^4$ (2.4)	$3.0\cdot10^4$ (4.3)
(XX)	$C\equiv CH$	$2.3\cdot10^7$ (82 000)	$5.6\cdot10^7$ (210 000)	$2.2\cdot10^7$ (220 000)	$3.8\cdot10^8$ (2 700 000)	$1.4\cdot10^7$ (140 000)	$4.8\cdot10^7$ (480 000)
(XXI)	$CH_2C\equiv CH$	$2.2\cdot10^5$ (3000)	$4.0\cdot10^5$ (600)	$7.0\cdot10^4$ (1400)	$1.2\cdot10^5$ (3000)	$1.5\cdot10^4$ (500)	$6.3\cdot10^4$ (300)
(XXII)	$CH_2CH_2C\equiv CH$	$4.0\cdot10^3$ (6.3)	$2.4\cdot10^4$ (4.9)	$1.7\cdot10^3$ (5.0)	$1.1\cdot10^4$ (0.6)	$2.0\cdot10^3$ (0.7)	$2.6\cdot10^3$ (0.09)
(XXIII)	$C(CH_3)_2C\equiv CH$	$6.6\cdot10^4$	$2.4\cdot10^5$	$5.9\cdot10^4$	$8.5\cdot10^5$	$9.0\cdot10^4$ *	–
(XVIIa)	C_6H_{13}	$3.8\cdot10^3$	$3.3\cdot10^4$	$1.0\cdot10^3$	$8.9\cdot10^3$	$7.0\cdot10^3$	$7.0\cdot10^3$
(XXa)	C_2H_5	$2.7\cdot10^2$	$2.7\cdot10^2$	$1.0\cdot10^2$	$1.1\cdot10^2$	$1.0\cdot10^2$	$1.0\cdot10^2$
(XXIa)	C_3H_7	$0.7\cdot10^2$	$0.7\cdot10^3$	$0.5\cdot10^2$	$0.4\cdot10^2$	$0.3\cdot10^2$	$2.0\cdot10^2$
(XXIIa)	C_4H_9	$6.4\cdot10^2$	$4.9\cdot10^3$	$2.9\cdot10^2$	$1.8\cdot10^4$	$3.0\cdot10^3$	$3.0\cdot10^4$

*Grass aphid CE was used in this experiment.
Footnote. Values of the acetylene effect q are given in parentheses.

Moving the acetylenic bond in the thioalkynyl group from the α- to the β-position leads to a sharp fall in the inhibition rate constant for the CE investigated extending to two to three orders of magnitude (Table 11). In line with this the sizes of the acetylene effect were also sharply reduced. The values of q for compound (XVII) of the first series with the acetylenic bond in the α-position were in the thousands but with the acetylenic bond in the β-position [compound (XVIII)] q was in the range 2.4–34.

A large difference in values of q was also observed for the corresponding compounds of the second series. Thus for compound (XX) the size of q when inhibiting fly CE ws 2.7×10^6 but for compound (XXI) with the acetylenic bond in the β-position q was 3000. Further movement of the triple bond to the γ-position of the thioester residue showed a less marked effect in the compounds of both the first and second series.

It seemed of interest to compare the anti-CE activity of compounds (XVII) and (XX) and also compounds (XVIII) and (XXI). Replacement of a hydrogen atom in compound (XX) by a C_4H_9 group [(compound (XVII)] leads to an increase in the inhibitory activity in relation to arthropod CE and BuCE and caused a small reduction in this activity in relation to mouse CE and ACE. Replacement of the acetylenic hydrogen in compound (XXI) by a C_3H_7 group [compound (XVIII)] and replacement of two other hydrogen atoms in the alkylthio residue of this compound by methyl groups [compound (XXIII)] proved to have a weak effect. Here also

Table 12. Anticholinesterase activity (k_{II} M^{-1} min^{-1}) of acetylenic OPIs $(RO)_2P(O)SC{\equiv}CR'$ and their saturated analogues $(RO)_2P(O)SCH_2CH_2R'$ (compounds numbered 'a').[10,11,15]

Compound	OPI		Anticholinesterase activity of OPIs					
	R	R'	ACE	BuCE	mouse CE	fly CE	beet aphid CE	mite CE
(XX)	C_2H_5	H	$2.3\cdot10^7$ (820 000)	$5.6\cdot10^7$ (210 000)	$2.2\cdot10^7$ (220 000)	$3.0\cdot10^8$ (2 700 000)	$1.4\cdot10^7$ (140 000)	$4.8\cdot10^7$ (480 000)
(XXIV)	C_3H_7	H	$1.5\cdot10^7$	$4.0\cdot10^8$	$1.4\cdot10^8$	–	–	–
(XXV)	C_4H_9	H	$6.2\cdot10^5$	$5.7\cdot10^7$	$1.4\cdot10^6$	–	–	–
(XXVI)	CH_3	$CH_2OC(O)CH_3$	$9.3\cdot10^6$	$1.1\cdot10^8$	$3.4\cdot10^6$	$1.3\cdot10^7$	$1.4\cdot10^7$ *	$4.8\cdot10^7$
(XXVII)	C_2H_5	$CH_2OC(O)CH_3$	$1.7\cdot10^7$ (68 000)	$8.5\cdot10^8$ (610 000)	$5.0\cdot10^7$ (500 000)	$2.1\cdot10^8$ (210 000)	$3.0\cdot10^9$ * (30 000 000)	$1.6\cdot10^9$ (10 000 000)
(XXVIII)	C_3H_7	$CH_2OC(O)CH_3$	$1.9\cdot10^7$	$3.6\cdot10^8$	$2.3\cdot10^7$	$5.7\cdot10^7$	$1.5\cdot10^7$ *	$8.0\cdot10^4$
(XXIX)	CH_3	$CH_2SC_2H_5$	$2.0\cdot10^7$	$5.1\cdot10^7$	–	–	–	–
(XXX)	CH_3	$CH_2OC_2H_5$	$7.3\cdot10^6$	$3.7\cdot10^7$	–	–	–	–
(XXXI)	C_2H_5	$CH_2OC_2H_5$	$1.0\cdot10^9$	$3.4\cdot10^9$	–	–	–	–
(XXXII)	C_2H_5	$CH_2OC_3H_7$	$2.1\cdot10^7$	$2.2\cdot10^8$	$1.2\cdot10^7$	$1.7\cdot10^8$	$2.5\cdot10^8$	$1.6\cdot10^7$
(XXXIII)	C_2H_5	$CH_2OC_4H_9$	$5.7\cdot10^7$	$2.4\cdot10^8$	$6.1\cdot10^7$	$2.6\cdot10^9$	$1.7\cdot10^8$	$1.3\cdot10^7$
(XXXIV)	C_3H_7	$CH_2OC_4H_9$	$6.5\cdot10^7$	$9.8\cdot10^8$	$6.7\cdot10^7$	$1.7\cdot19^9$	$4.8\cdot10^8$	$2.1\cdot10^6$
(XXXV)	C_2H_5	$CH_2CH(COOC_2H_5)_2$	$4.5\cdot10^6$	$3.0\cdot10^7$	$5.0\cdot10^6$	–	$3.5\cdot10^7$ *	–
(XVII)	C_2H_5	C_4H_9	$9.5\cdot10^6$ (2 500)	$1.0\cdot10^8$ (3 000)	$7.1\cdot10^6$ (7 100)	$1.5\cdot10^9$ (169 000)	$4.6\cdot10^7$ (6 600)	$6.0\cdot10^7$ (86 000)
(XXXVI)	C_2H_5	$CH_2SC_2H_5$	$7.3\cdot10^6$ (4 000)	$2.1\cdot10^8$ (5 200)	$5.0\cdot10^6$ (7 100)	$5.2\cdot10^8$ (55 000)	$5.0\cdot10^7$ (500 000)	$5.0\cdot10^7$ (50 000)
(XXXVII)	C_2H_5	$CH_2SC_4H_9$	$2.3\cdot10^7$	$1.0\cdot10^7$	$1.0\cdot10^7$	$1.0\cdot10^9$	$7.5\cdot10^7$	$2.0\cdot10^7$
(XXXVIII)	C_2H_5	$C(CH_3)_3$	$1.7\cdot10^7$ (14 000)	$2.8\cdot10^8$ (80 000)	$2.0\cdot10^6$ (5 000)	$7.0\cdot10^6$ (11 000)	$1.8\cdot10^7$ * (11 000)	–
(XXXIX)	C_2H_5	$CH_2CH_2SC_2H_5$	$1.7\cdot10^7$ (21 000)	$6.3\cdot10^7$ –	$2.0\cdot10^7$ (8 700)	$1.5\cdot10^8$ (30 000)	$1.3\cdot10^7$ * (6 000)	–
(XL)	C_2H_5	$CH_2CH_2\overset{+}{S}(CH_3)C_2H_5$	$4.0\cdot10^6$ (220)	$4.5\cdot10^7$ –	$1.2\cdot10^7$ (520)	$3.0\cdot10^8$ (3 300)	$4.8\cdot10^7$ * (900)	–
(XXa)	C_2H_5	H	$2.7\cdot10^2$	$2.7\cdot10^2$	$1.0\cdot10^2$	$1.1\cdot10^2$	$1.0\cdot10^2$	$1.0\cdot10^2$
(XXVIIa)	C_2H_5	$CH_2OC(O)CH_3$	$2.5\cdot10^1$	$1.4\cdot10^3$	$1.0\cdot10^2$	$1.0\cdot10^3$	$1.0\cdot10^2$ *	$1.0\cdot10^2$
(XVIIa)	C_2H_5	C_4H_9	$3.8\cdot10^3$	$3.3\cdot10^4$	$1.0\cdot10^3$	$8.9\cdot10^3$	$7.0\cdot10^2$	$8.0\cdot10^2$
(XXXVIa)	C_2H_5	$CH_2SC_2H_5$	$1.8\cdot10^3$	$4.0\cdot10^3$	$7.0\cdot10^2$	$9.6\cdot10^3$	$1.0\cdot10^2$	$1.0\cdot10^3$
(XXXVIIIa)	C_2H_5	$C(CH_3)_3$	$8.0\cdot10^2$	$3.5\cdot10^3$	$4.0\cdot10^2$	$6.2\cdot10^2$	$1.6\cdot10^2$ *	–
(XXXIXa)	C_2H_5	$CH_2CH_2SC_2H_5$	$8.0\cdot10^2$	–	$2.3\cdot10^3$	$5.0\cdot10^3$	$2.2\cdot10^3$ *	–
(XLa)	C_2H_5	$CH_2CH_2\overset{+}{S}(CH_3)C_2H_5$	$1.8\cdot10^4$	–	$2.3\cdot10^4$	$9.0\cdot10^4$	$5.3\cdot10^4$ *	–

*Grass aphid CE was used in experiments.
Footnote. Values of the acetylene effect q are given in parentheses.

a small reduction was observed in the anti-CE activity in relation to ACE. It is characteristic that compound (XXII) with the acetylenic bond in the γ-position is a weaker inhibitor than its saturated analogue in relation to arthropod CEs, giving a value of $q < 1$.

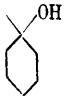
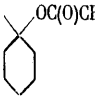
3. *S*-Alkynyl esters of dialkyl thiophosphoric acids containing hydrophobic or onium groups in the alkylthio residue

OPIs of general formula $(RO)_2P(O)SC{\equiv}CR'$ have been investigated where the acyclic hydrophobic group R' = C_4H_9, $CH_2SC_2H_5$, $CH_2SC_4H_9$, $CH_2CH_2SC_2H_5$, $CH_2SC(O)CH_3$, $CH_2OC(O)CH_3$, $CH_2OC_2H_5$, $CH_2OC_3H_7$, $CH_2OC_4H_9$, $CH_2CH(COOC_2H_5)_2$, and R = CH_3, C_2H_5, C_3H_7, C_4H_9 (Table 12). In the experiments with these compounds a study was made of the dependence of their anti-CE activity on the structure of the group R' which is capable of hydrophobic adsorption onto appropriate portions of the enzyme active surface. In addition, comparison of the anti-CE activity of compounds with various R but with the same R' made it possible to assess the effect of the structure of the phosphoryl group of the OPIs. These same problems were also investigated in experiments with compounds containing cyclic hydrophobic groups R', such as phenyl, cyclohexenyl and cyclohexyl and groups R = CH_3 and C_2H_5 (Table 13). The influence of onium groups was investigated in experiments with the inhibitor $(C_2H_5O)_2P(O)SC{\equiv}CCH_2CH_2\overset{+}{S}(CH_3)C_2H_5$ (Table 12).

It follows from the data of Table 12 that replacement of the hydrogen atom of the acetylenic group in the alkylthio residue of compound (XX) with various acyclic hydrophobic groups leads to a significant increase in the anti-CE activity in relation to BuCE. Only the substituents $-CH_2CH(COOC_2H_5)_2$ and $-CH_2SC_4H_9$ did not increase it but reduced the inhibitory action on this CE a little [compounds (XXXV) and (XXXVII)]. In the majority of cases the substituent reduced or did not change the anti-CE activity in relation to the other CE.

For example, compound (XXXVIII) inhibits these CE more weakly than compound (XX). In this case the hydrophobic t-butyl group does not aid but seemingly hinders absorption of the acetylenic inhibitor molecule to the active surface of the enzyme. Only a few substituents increased the anti-CE activity of an inhibitor for certain CE. Thus compound (XX) is surpassed in anti-CE activity by compounds (XVII) and (XXXVII) in experiments with fly, beet aphid and spider mite CE, by compound (XXVII) in experiments with aphid and mite CE and by compound (XXXVIII) in experiments with fly and aphid CE.

Table 13. Anticholinesterase activity (k_{II}, M^{-1} min^{-1}) of acetylenic OPI $(RO)_2P(O)SC{\equiv}CR'$ and their saturated analogues $(RO)_2P(O)SCH_2CH_2R'$ (compounds numbered 'a').[9,12]

Compound No.	OPI		Anticholinesterase activity of OPIs				
	R	R'	ACE	BuCE	mouse CE	fly CE	grass aphid CE
(XLI)	CH_3	C_6H_5	$1.8\cdot10^5$ (1 800)	$1.3\cdot10^7$ (16 000)	$5.5\cdot10^5$ (5 500)	$7.3\cdot10^7$ (20 000)	$5.0\cdot10^5$ (5 000)
(XLII)	CH_3		$6.4\cdot10^5$ (1 500)	$1.9\cdot10^7$ (240)	$6.4\cdot10^5$ (4 300)	$1.6\cdot10^8$ (3 900)	$2.3\cdot10^5$ (300)
(XLIII)	CH_3	*цикло*-C_6H_{11}	$2.0\cdot10^8$ (2 000 000)	$2.2\cdot10^9$ (1 500 000)	$1.0\cdot10^8$ (1 000 000)	$2.3\cdot10^9$ (300 000)	$1.5\cdot10^8$ (1 500 000)
(XX)	C_2H_5	H	$2.3\cdot10^7$ (82 000)	$5.6\cdot10^7$ (210 000)	$2.2\cdot10^7$ (220 000)	$3.0\cdot10^8$ (2 700 000)	$1.4\cdot10^7$ * (140 000)
(XLIV)	C_2H_5	C_6H_5	$9.0\cdot10^6$ (2 100)	$1.3\cdot10^8$ (10 000)	$7.9\cdot10^6$ (10 000)	$1.4\cdot10^8$ (14 000)	$8.0\cdot10^6$ (27 000)
(XLV)	C_2H_5		$8.5\cdot10^6$ (450)	$4.3\cdot10^8$ (1 400)	$3.3\cdot10^6$ (400)	$7.0\cdot10^8$ (1 300)	$9.5\cdot10^5$ (53)
(XLVI)	C_2H_5	cyclo-C_6H_{11}	$3.1\cdot10^8$ (18 000)	$1.2\cdot10^9$ (19 000)	$8.0\cdot10^8$ (670 000)	$8.0\cdot10^8$ (24 000)	$1.4\cdot10^9$ (400 000)
(XLVII)	C_2H_5		$8.0\cdot10^6$	$2.3\cdot10^8$	$9.0\cdot10^5$	$1.2\cdot10^8$	$9.0\cdot10^7$
(XLVIII)	C_2H_5		$3.0\cdot10^6$	$4.8\cdot10^7$	$4.1\cdot10^6$	$7.5\cdot10^8$	$5.2\cdot10^6$
(XLIX)	C_3H_7	C_6H_5	$1.8\cdot10^7$	$1.8\cdot10^8$	$1.3\cdot10^7$	$3.6\cdot10^8$	$4.4\cdot10^7$ *
(XLIa)	CH_3	C_6H_5	$1.0\cdot10^2$	$8.0\cdot10^2$	$1.0\cdot10^2$	$3.7\cdot10^3$	$1.0\cdot10^2$
(XLIIa)	CH_3		$4.3\cdot10^2$	$8.0\cdot10^4$	$1.3\cdot10^2$	$4.3\cdot10^4$	$7.7\cdot10^2$
(XLIIIa)	CH_3	*цикло*-C_6H_{11}	$1.0\cdot10^2$	$1.5\cdot10^3$	$1.0\cdot10^2$	$8.0\cdot10^3$	$1.0\cdot10^2$
(XXa)	C_2H_5	H	$2.7\cdot10^2$	$2.7\cdot10^2$	$1.0\cdot10^2$	$1.1\cdot10^2$	$1.0\cdot10^2$ *
(XLIVa)	C_2H_5	C_6H_5	$4.3\cdot10^3$	$1.3\cdot10^4$	$8.0\cdot10^2$	$1.0\cdot10^4$	$3.0\cdot10^2$
(XLVa)	C_2H_5		$1.9\cdot10^4$	$3.1\cdot10^5$	$1.5\cdot10^4$	$5.5\cdot10^5$	$1.8\cdot10^4$
(XLVIa)	C_2H_5	cyclo-C_6H_{11}	$1.7\cdot10^4$	$6.3\cdot10^4$	$1.2\cdot10^3$	$3.3\cdot10^4$	$3.3\cdot10^3$

*Beet aphid CE was used in experiments.

Footnote. Values of the acetylene effect q are given in parentheses.

Replacement of a hydrogen atom in compound (XX) by phenyl [compound (XLIV)] and cyclohexenyl [compound (XLV)] residues led to an increase in the anti-CE activity for BuCE and to a decrease for mouse CE, aphid CE and ACE (Table 13). Compound (XLIV) proved to be less strong in relation to fly CE, but compound (XLV) was a stronger inhibitor than compound (XX). Again, replacement of hydrogen on the acetylenic bond in compound (XX) by a cyclohexenyl group [compound (XLVI)] is accompanied by a significant strengthening of the inhibitory activity in relation to all the CE investigated. For aphid CE the size of k_{II} for this compound was 1.4×10^9 M^{-1} min^{-1}, which is two orders of magnitude greater than for compound (XX). It is characteristic that compounds (XLVII) and (XLVIII), into the cyclohexyl residue of which OH and $OC(O)CH_3$ groups respectively have been introduced, possess many times lower anti-CE activity than compound (XLVI).

A reduction in k_{II} is observed in many cases on replacing the acetylenic hydrogen atom by hydrophobic susbtituents but an appreciable increase always occurred in the value of k_{II} on analogous replacement of hydrogen in the saturated analogue (XXa) [i.e. compounds (XVIIa), (XXXVa), (XXXVIIIa), (XXXIXa), (XLa), (XLIVa), (XLVa), (XLVIa)], seemingly as a result of the increase in the adsorption rate of inhibitors onto the active surface of the CE caused by the hydrophobic adsorption of substituents onto the correpsonding hydrophobic portions of this surface. The cyclohexenyl derivative (XLVa), and not the cyclohexyl compound (XLVIa), was the strongest inhibitor, in relation to all the CE, of the saturated analogues with cyclic substituents [Table 13, compounds

(XXIVa), (XLVa), (XLVIa)] in contrast to the acetylenic compounds. This occurred in spite of the high hydrophobicity of cyclohexyl groups.

It is possible that the difference noted in the effectiveness of substituents is explained by the fact that when many acetylenic compounds are adsorbed onto the enzymes these substituents do not make contact with the hydrophobic portions of the active surface. The linear acetylenic group orients the acetylenic compound on the enzyme differently from the orientation of the saturated analogue. Overall the impression is created that the interaction with the anionic centre of the CE active site does not play a major role in the inhibition process in the case of the acetylenic OPIs.

It is seen from the data shown in Tables 12 and 13 that the values of the acetylenic effect vary between very wide limits and depend on both the structure of the compound and on the source of the enzyme. As already mentioned above the value of q for compound (XX) was very high. Replacement of the hydrogen atom on the acetylenic bond of this compound by groups of various structure led, as a rule, to a reduction in the size of q. Only on replacing the hydrogen atom by a cyclohexyl group [compound (XLVI)] was there an increase in q for the inhibition of mouse and aphid CE. The absence of a correlation between the change in the size of k_{II} and q for an acetylenic analogue is worthy of attention. For example on replacing the hydrogen atom in compound (XX) by a cyclohexyl group [compound (XLVI)] the size of k_{II} for fly CE was increased almost threefold (3×10^8 M^{-1} min^{-1} and 8×10^8 M^{-1} min^{-1} respectively) but the size of q was reduced by more than 100 times (2 700 000 and 24 000 respectively). The same picture was observed on replacing the hydrogen atom in compound (XX) by a butyl group [compound (XVII)] when inhibiting BuCE and arthropod CE. These divergences between the changes of k_{II} and q are explained by the fact that replacement of the hydrogen atom by certain groups in the saturated analogue (XXa) causes an increase in k_{II} several times greater than the analogous replacement in the acetylenic compound (XX). For example, replacement by a cyclohexyl group [compound (XLVI)] in the acetylenic compound (XX) leads to an increase in k_{II} for fly CE of less than threefold but replacement of hydrogen by this group [compound (XLVIa)] in the saturated compound (XXa) leads to an increase of k_{II} for the same enzyme of 300-fold.

The dependence of inhibiting ability on the length of the alkyl chain in the phosphoryl portion of the OPI molecule has been investigated for certain compounds. It must be noted first that the esters of dimethyl thiophosphoric acid, both acetylenic [(XXVI), (XXX), (XLI)–(XLIII)] and saturated [(XLIa), (XLIIa), (XLIIIa)], display in the majority of cases a lower anti-CE activity than their diethyl homologues (XXVII), (XXXI), (XLIV), (XLV), (XLVI), (XLIVa), (XLVa) and (XLVIa). Only in the case of the cyclohexyl derivatives (XLIII) and (XLVI) and only for fly CE and BuCE was the ratio reversed. These two compounds surpass significantly all the known acetylenic OPIs in anti-CE activity. Further lengthening of the alkyl chain in the phosphoryl portion of the OPI molecule leads to a different result depending on the enzyme and on the structure of the group R′ on the acetylene. On investigating a series of acetylenic OPIs with R′ = H [compounds (XX), (XXIV), (XXV)] it was discovered that the diethyl thiophosphate possesses the greatest activity in relation to mouse CE and ACE but the dipropyl thiophosphate possessed the greatest in relation to BuCE. This agrees with the results obtained previously for ACE and BuCE in experiments with $(RO)_2P(O)SC_2H_4\overset{+}{N}(CH_3)_2C_6H_{11}$, where R = C_2H_5, C_3H_7, C_4H_9 and $(RO)_2P(O)SC_2H_4\overset{+}{S}(CH_3)C_2H_5$, where R = C_2H_5, C_3H_7.[34] It was characteristic that grass aphid CE proved to be the more sensitive to the diethyl thiophosphate.[35]

However, in the series of OPIs with R′ = $CH_2OC(O)CH_3$ the diethyl thiophosphate (XXVII) was a more active inhibitor of all the CE, except for ACE, than the dimethyl thiophosphate (XXVI) and the dipropyl thiophosphate (XXIII). Among the compounds with R′ = $CH_2OC_4H_9$ the ester of diethyl thiophsophoric acid [compound (XXXIII)] inhibits mite CE more strongly, the ester of dipropyl thiophosphoric acid [compound (XXXIV)] BuCE and aphid CE, but mouse and fly CE and ACE were equally sensitive to both OPIs. The dipropyl derivative [compound (XLIX)] of the OPI series with R′ = C_6H_5 was a stronger CE inhibitor than the diethyl derivative (XLIV) in all cases.

The anti-CE activity of compounds therefore depends on the nature of the enzyme and on the structure of the OPI in both the phosphoryl and the cleavable portions of the molecule.

The change in anti-CE activity on converting the acetylenic compound (XXXIX) with a sulphide sulphur atom into the derivative (XL) with a sulphonium sulphur atom was unusual. In this case the cationic group provides a reduction in the size of k_{II} for warm-blooded CE and an insignificant increase (2–4 times) for fly CE and aphid CE while the rate constant for alkaline hydrolysis of the sulphonium derivative was many times greater than that for the sulphide (2.9×10^{-1} and 4.4×10^{-4} min^{-1} respectively).

It was characteristic that the acetylenic effect for compounds with a sulphide sulphur atom (XXXIX) was significantly greater than for the derivative with sulphonium sulphur atom (XL) for all CEs. This is linked with the fact that replacement of sulphide sulphur atom in the saturated prototype [compound (XXXIXa)] by sulphonium [compound (XLa)] leads to a strengthening of the anti-CE activity in relation to each CE. The k_{II} constants are increased 10–25 times, the alkaline hydrolysis constant is increased 75 times.

The low effect on introducing an onium grouping is explained to a significant extent by the fact that in compounds (XL) and (XLa) the onium atom is placed at a significantly large distance from the phosphorylmercapto group ($-CH_2CH_2CH_2CH_2\overset{+}{S}=$), compared with the optimum distance ($-CH_2CH_2\overset{+}{S}=$) for example in preparation Gd-42 mentioned above. The rigidity of the *S*-alkynyl residue also plays a particular role in the case of the acetylenic OPIs. It is possible that the hypothesis on the absence or small extent of reaction with the anionic site of a CE for all groups of acetylenic OPIs is correct.

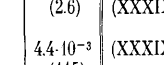
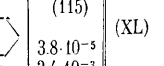
4. Analysis of the mechanism of the anticholinesterase action of acetylenic OPIs

a) Alkaline hydrolysis

The mechanism of the interaction of acetylenic OPIs with the cholinesterases is an extremely important problem. It might have been thought that the acetylenic group, which shows an electron-accepting effect, increases the electrophilicity of the phosphorus atom and thereby increases the phosphorylating ability of a compound. The rate constant for alkaline hydrolysis (k_{OH}) of the organophosphorus inhibitors is a fairly reliable measure of this ability. Experiments have shown that the values of k_{OH} for the acetylenic OPIs are in reality higher than the values for their saturated analogues (Table 14). They are particularly high for compounds with an acetylenic bond in the α-position. For compound (XX) $k_{OH} = 2.2 \times 10^{-3}$ min^{-1} but for its saturated analogue (XXa) this constant was 290 times smaller.

Such a strengthening of the phosphorylating ability does not agree quantitatively in any way with the enormous size of the acetylene effect which ranges from 82 000 for ACE to 2 700 000 for fly CE for the same compound (XX) (Table 11). In addition the colossal difference observed in the values of the acetylene effect for a single compound against several CEs cannot be explained by the change in k_{OH}.

Table 14. Rate constants for the alkaline hydrolysis (k_{OH}, min^{-1}) of the acetylenic OPIs $(C_2H_5O)_2P(O)SR$ and their saturated analogues (compounds number 'a').[12–14]

OPI		k_{OH}, min^{-1}	OPI		k_{OH}, min^{-1}
Compound No.	R		Compound No.	R	
(XVII)	$C\equiv CC_4H_9$	$1.2\cdot10^{-3}$ (150)	(XX)	$C\equiv CH$	$2.2\cdot10^{-3}$ (290)
(XVIIa)	C_6H_{13}	$8.0\cdot10^{6}$	(XXa)	CH_2CH_3	$7.7\cdot10^{-6}$
(XVIII)	$CH_2C\equiv CC_3H_7$	$2.2\cdot10^{-5}$ (2.7)	(XXXVI)	$C\equiv CCH_2SC_2H_5$	$2.9\cdot10^{-4}$ (17)
(XIX)	$C_2H_4C\equiv CC_2H_5$	$2.0\cdot10^{-5}$ (2.6)	(XXXVIa)	$CH_2CH_2CH_2SC_2H_5$	$1.7\cdot10^{-5}$
			(XXXIX)	$C\equiv CCH_2CH_2SC_2H_5$	$4.4\cdot10^{-4}$ (81)
(XLV)		$4.4\cdot10^{-3}$ (115)	(XXXIXa)	$CH_2CH_2CH_2CH_2SC_2H_5$	$5.4\cdot10^{-6}$
(XLVa)		$3.8\cdot10^{-5}$	(XL)	$C\equiv CCH_2CH_2\overset{+}{S}(CH_3)C_2H_5$	$2.9\cdot10^{-4}$ (740)
(XLVI)	$C\equiv CC_6H_{11}$-cyclo	$2.4\cdot10^{-3}$ (70)	(XLa)	$CH_2CH_2CH_2CH_2\overset{+}{S}(CH_3)C_2H_5$	$3.9\cdot10^{-4}$
(XLVIa)	$CH_2CH_2C_6H_{11}$-cyclo	$3.4\cdot10^{-5}$			

Footnote. Values of the acetylene effect q are given in parentheses.

At first glance the non-correspondence between the acetylene effects in the alkaline hydrolysis reaction and in the reaction with CE may be a reason to propose a different mechanism for the irreversible inhibition of enzymes by acetylenic OPIs, for example not phosphorylation but alkylation of the active site. It is well known[36] that derivatives of α-propynylamine inhibit monoamine-oxidases irreversibly by alkylation of the enzyme. However such a hypothesis encounters serious objections. It was established previously[7] that on increasing the thioalkyl residue from SCH_3 to SC_7H_{15} in compounds $(C_2H_5O)CH_3P(O)SR$ the anti-CE activity was significantly increased but the size of k_{OH} was practically unchanged. This was explained by the fact that the size of the bimolecular rate constant for the reaction of OPIs with CE is determined mainly by the rate of formation of the enzyme–inhibitor complex which is the first stage of the reaction and not by the rate of phosphorylation which is the second stage. According to this analogy it is also obvious that the observed non-correspondence between the increase of k_{II} and k_{OH} on replacing an ethylenic by an acetylenic group in the S-alkyl residue may be explained by the significant acceleration of the adsorption of an acetylenic OPI onto the CE active surface. This increase of the adsorption rate may not be the same for the various CEs which differ in the structure of their active centres.

b) Change of anticholinesterase activity of acetylenic OPIs under various conditions

Specially conducted investigations[36] have shown that acetylenic OPIs possess some properties characteristic of typical OPIs. One of such properties is the loss of the ability of an OPI to inhibit a CE irreversibly on replacement of the phosphoryl oxygen by a sulphur atom, which was mentioned in the introduction. It has been established[11] that in contrast to compound (XVII) its dithio analogue $(C_2H_5O)_2P(S)SC\equiv CC_4H_9$ does not inhibit CE. Another acetylenic dithio derivative $(CH_3O)_2P(S)SC\equiv CC_4H_9$ does not possess anti-CE activity.

Considerable similarity has been observed between acetylenic and the usual OPIs in the character of the change in k_{II} vlaue on changing the pH and in the action of tetraalkylammonium ions.

The effect of tetraalkylammonium ions on the bimolecular rate constant for the reaction of ACE with an OPI was investigated at 25 °C and pH 7.5 and was assessed by the value of the inhibition constant K_i[37] which was found from the equation

$$k_{II,\,i} = k_{II}\frac{1}{(1+[I]/K_i)},$$

where [I] is the concentration of the irreversible inhibitor. Experimental points plotted on a graph having coordinates $1/k_{II}$ and [I] lay on a straight line cutting the abscissa axis at a distance equal to $-K_i$.

The effect of pH on the rate of interaction of cholinesterase with OPI was investigated at various values from 3 to 11.

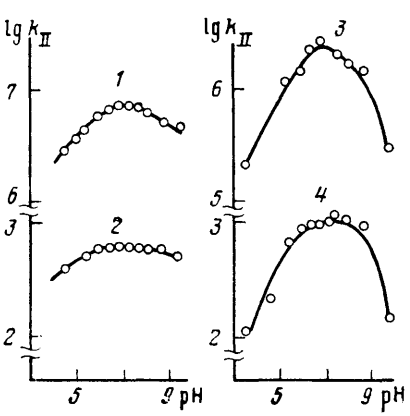


Figure 1. Dependence of the reaction rate of OPIs with ACE on pH; *1*, $(C_2H_5O)_2P(O)SC\equiv CC_2H_4SC_2H_5$; *2*, $(C_2H_5O)_2P(O)SCH_2.CH_2C_2H_4SC_2H_5$; *3*, $(C_2H_5O)_2P(O)SC\equiv CC_6H_{11}$-cyclo; *4*, $(C_2H_5O)_2.P(O)SCH_2CH_2C_6H_{11}$-cyclo.

The dependence of the size of k_{II} on pH when inhibiting ACE with an acetylenic compound and its saturated analogue is expressed by similar curves but the values of the pH optima of these curves were close and were in the pH range 7–8 (Fig. 1). It was established in experiments with ACE[38] that tetraalkylammonium ions reduced to a varying degree the interaction of this enzyme with the acetylenic OPIs (XXXIX) and (XLIV) and with their saturated

analogues (XXXIXa) and (XLIVa). The values of K_i proved to be practically identical for the tetraalkylammonium ions investigated (Table 15). It is evident that the changes in conformation and the degree of ionisation of the functional groups on the active surface of the enzyme occurring on changing pH or by the action of tetraalkylammonium ions proved to be the same when reacting cholinesterases with acetylenic OPI and with their saturated analogues. This indicates that the introduction of an acetylenic bond into the OPI molecule does not change the main features of the mechanism of inhibition of CE.

Table 15. Reversible inhibition constants (K_i, M) for ACE of human blood erythrocytes by tetraalkylammonium ions on reacting the enzyme with acetylenic OPI or their saturated analogues.[38]

OPI		K_i, M		
Compound No.	Formula	$(CH_3)_3N^+$	$(C_2H_5)_4N^+$	$(C_4H_9)_4N^+$
(XXXIX)	$(C_2H_5O)_2P(O)SC{\equiv}CC_2H_4SC_2H_5$	$1.2\cdot10^{-3}$	$1.6\cdot10^{-3}$	$5.1\cdot10^{-5}$
(XXXIXa)	$(C_2H_5O)_2P(O)S(CH_2)_4SC_2H_5$	$1.5\cdot10^{-3}$	$1.8\cdot10^{-3}$	$5.6\cdot10^{-5}$
(XLIV)	$(C_2H_5O)_2P(O)SC{\equiv}C-C_6H_5$	$4.0\cdot10^{-3}$	$3.3\cdot10^{-3}$	$7.2\cdot10^{-5}$
(XLIVa)	$(C_2H_5O)_2P(O)SC_2H_4-C_6H_5$	$6.1\cdot10^{-3}$	$5.0\cdot10^{-3}$	$6.0\cdot10^{-5}$

c) Reactivation

The bimolecular rate constant for reactivation ($k_{II,re}$ M^{-1} min^{-1}) was determined at 25 °C and pH 7.5 and calculated from the formula:

$$k_{II,re} = 2.303/\tau[R]\ \lg(v_0 - v_i)/(v_0 - v_\tau),$$

where v_0 is the initial rate of the enzymic hydrolysis of substrate, v_i the residual rate of hydrolysis after reaction of the enzyme with the OPI, v_τ the rate of hydrolysis of substrate after τ min reaction of the inhibited enzyme with reactivator of concentration [R]. In this formula $(v_0 - v_i)$ is directly proportional to the initial quantity of phosphorylated enzyme and $(v_0 - v_\tau)$ to the quantity of phosphorylated enzyme remaining after partial reactivation at time τ. 1,1-Trimethylene bis(4-pyridinaldoxime) dibromide (TMB-4)[38] was used as reactivator.

The most convincing proof of the phosphorylation of CEs on reaction with acetylenic OPI are the results of experiments on the reactivation of ACE inhibited by various OPIs. It follows from the data of Table 16 that ACE, inhibited by derivatives of diethyl phosphoric acid such as the acetylenic inhibitors (XXXIX) and (XLVI) and their saturated analogue (XXXIXa) and by the well known OPI paroxon, are reactivated by TMB-4 at identical rates. The observed similarity of the reactivation rate constants indicates that a phosphorylated enzyme of the same structure $E-O-P(O)(OC_2H_5)_2$ is formed by reaction of ACE with these compounds which differ markedly in structure. Similar results were also obtained in experiments with the acetylenic derivatives of dimethyl phosphoric acid (XLIII) and (XLIV) and with methylparoxon. In this case the reactivation rate constants were a little greater than in the experiments with the derivatives of diethyl phosphoric acid.

Table 16. Bimolecular rate constants ($k_{II,r}$) for the reactivation of inhibited acetylcholinesterase [reactivator was TMB-4, 1,1-trimethylene-bis(4-pyridinaldoxime) dibromide].[38]

Inhibitor $(C_2H_5O)P(O)R$		$k_{II,re}$, M^{-1} min^{-1}	Inhibitor $(CH_3O)_2P(O)R$		$k_{II,re}$, M^{-1} min^{-1}
Compound No.	R		Compound No.	R	
(XLVI)	$SC{\equiv}C-C_6H_5$	$0.82\cdot10^4$	(XLIII)	$SC{\equiv}C-C_6H_5$	$1.1\cdot10^4$
(XXXIX)	$SC{\equiv}CC_2H_4SC_2H_5$	$1.0\cdot10^4$			
(XXXIXa)	$SCH_2-CH_2C_2H_4SC_2H_5$	$0.97\cdot10^4$	(XLIV)	$SC{\equiv}C-C_6H_5$	$1.4\cdot10^4$
Paraoxon	$O-C_6H_4-NO_2$	$0.92\cdot10^4$	Methyl-paraoxon	$O-C_6H_4-NO_2$	$1.2\cdot10^4$

d) Anticholinesterase activity of hexynyltrimethylammonium ions

The results obtained form a basis for considering that the inactivation of cholinesterase by acetylenic OPIs is brought about by esterification of a serine hydroxyl by the appropriate phosphoric acid. Experiments seemed to confirm the initial conclusion that the origin of the acetylene effect should be sought in the effect of the acetylenic bond on the first stage of the inhibition, viz. on the rate of formation of the enzyme–inhibitor complex. Consequently the possibility of an interaction of the C≡C triple bond with structures located either in the region of the anionic site of the enzyme or near the phosphorylated serine hydroxyl has been investigated.[12]

It is known that tetraalkylammonium ions are reversible inhibitors of CE. It is highly probable that their action is effected by adsorption with the formation of simple ion pairs with the carboxylate anion at the anionic point of the enzyme. It has to be clarified whether the triple bond shows a strengthening action on the adsorption of such compounds. Quaternary ammonium ions containing alkynyl groups have been investigated.[14] However the experiments carried out on the inhibition of ACE and BuCE by such quaternary ammonium ions (Table 17) show that the introduction of an acetylenic bond into any position of the hexyl group [compound (LIII)] had practically no effect on the ability of hexynyltrimethylammonium ions [compounds (L)–(LII)] to inhibit reversibly the catalytic activity of the enzymes. The same values of I_{50} were obtained in experiments with trimethylpropynylammonium salts (LIV) and (LV). In reality there is no binding of the acetylenic group in the region of the anionic site of a CE.

The serine hydroxyl may be a binding region. Many authors have proposed its presence in the esterase site of cholinesterase.[1] This hypothesis will be considered below.

e) Cholinesterase hydrolysis of acetylenic substrates

It was mentioned above that acetylenic OPIs, like typical OPIs, phosphorylate the active site of CEs. Further, experiments with ammonium salts show that the acetylenic group does not show any effect on processes occurring in the region of the anionic site of the

enzyme. Nevertheless the acetylene effect (q) is present. Two alternative hypotheses may be proposed. Either the acetylenic group accelerates the formation of the enzyme–inhibitor complex by being adsorbed onto the active surface of the enzyme elsewhere than in the region of the anionic site and this adsorption improves the steric conditions for the attack by the phosphorus atom on the serine hydroxyl of the enzyme very effectively, or the triple bond participates directly in the phosphorylation of the enzyme, i.e. by reducing appreciably the energy of activation in this part of the reaction but not changing the final result. In both cases it remains unclear what occurs to the *S*-alkynyl residue after fission of the thioester bond. Does it remain bound to the enzyme or is it transferred into the reaction medium? The fact that the reactivation rate constants for ACE inhibited by acetylenic OPIs are practically equal to the reactivation rate constants for ACE inhibited by their saturated analogues does not rule out the possibility of forming a product of interaction of the acetylenic bond with any portion of the active surface of the enzyme. If the rate of freeing ACE from the remainder of the *S*-alkynyl group by the action of the reactivator is significantly greater than the rate of dephosphorylation then the presence of a product from the reaction of this group with the enzyme is by no means reflected in the size of the reactivation rate constant.

Table 17. Anticholinesterase activity (I_{50}, M) of trimethylhexynylammonium ions, with the acetylenic bond at different positions in the hexynyl chain, and of their saturated analogue.[14]

Inhibitor		I_{50}, M	
Compound No.	formula	ACE	BuCE
(L)	$(CH_3)_3\overset{+}{N}C{\equiv}CC_4H_9Br^-$	$1.0\cdot10^{-3}$	$2.7\cdot10^{-3}$
(LI)	$(CH_3)_3\overset{+}{N}CH_2C{\equiv}CC_3H_7\cdot Br^-$	$3.0\cdot10^{-4}$	$2.0\cdot10^{-4}$
(LII)	$(CH_3)_3\overset{+}{N}C_2H_4C{\equiv}CC_2H_5\cdot Br^-$	$1.1\cdot10^{-3}$	$7.4\cdot10^{-2}$
(LIII)	$(CH_3)_3\overset{+}{N}C_6H_{13}Br^-$	$2.1\cdot10^{-3}$	$6.5\cdot10^{-3}$
(LIV)	$(CH_3)_3\overset{+}{N}CH_2C{\equiv}CH\cdot Br^-$	$3.5\cdot10^{-3}$	$7.5\cdot10^{-3}$
(LV)	$(CH_3)_3\overset{+}{N}CH_2C{\equiv}CH\cdot I^-$	$1.3\cdot10^{-3}$	$1.5\cdot10^{-2}$

The experiments carried out on the reactivation of the enzyme showed convincingly that the acetylenic OPIs, like the usual OPIs, phosphorylate cholinesterases but they do not give an answer to the problem of the fate of the *S*-alkynyl group.

There are considerable methodological difficulties in the detection in the reaction medium of an acetylenic mercaptan or a product of its conversion during experiments on the inhibition of CE by acetylenic OPIs. In these experiments the concentration of CE active centres in the reaction medium usually does not exceed 1×10^{-9} M and consequently the possible concentration of the *S*-alkynyl residue or its conversion product may not be more than the value indicated. This is a thousand times less than the minimum concentration of SH groups which can be determined by contemporary chemical methods.

The interaction of cholinesterase with *S*-alkynyl esters of thioacetic acid, viz. $CH_3C(O)SCH_2C{\equiv}CH$ [compound (LVII)] and $CH_3C(O)SC{\equiv}CC_4H_9$ [compound (LVIII)] has been investigated in order to clarify this problem.[38]

If the acetylenic group forms a stable complex with the enzyme then these compounds should be irreversible inhibitors. Experiments showed that both compounds were hydrolysed, although slowly, by both ACE and BuCE. Ellman's reagent, present during the enzymic hydrolysis, pointed to the formation of a compound possessing an SH group in the reaction medium. It is possible that this compound is either an acetylenic mercaptan, which reacts with the Ellman reagent at the moment of fission from the substrate molecule, or a product of its conversion. Control experiments, in which the Ellman reagent is added after the end of enzymic hydrolyis, also showed the presence of a product with an SH group. When such a reaction mixture was protected from access to oxygen of the air the concentration of SH groups remained practically unchanged for an extended period. Consequently a stable product with an SH group is formed from the unstable *S*-alkynyl group split off from the substrate molecule or from the acetylenic OPI molecule. It is possible that the conversion of the *S*-alkynyl group occurs by the following scheme:

$$HS{-}C{\equiv}C{-}R \rightarrow S{=}C{=}CHR \xrightarrow{H_2O}$$
$$\rightarrow S{=}C(OH){-}CH_2R \rightarrow HS{-}C(O){-}CH_2R,$$

$$HSCH_2C{\equiv}CH \rightarrow HSC{\equiv}C{-}CH_3 \rightarrow S{=}C{=}CH{-}CH_3 \xrightarrow{H_2O}$$
$$\rightarrow HSC(O){-}CH_2CH_3.$$

Evidently such conversion products of the *S*-alkynyl group are also obtained on alkaline hydrolysis of both acetylenic OPIs and of the acetylenic substrates.

As was established in experiments on the alkaline hydrolysis of acetylenic OPI and substrates,[38] the number of micromoles of alkali spent in the neutralisation of the products formed was almost twice the number of micromoles taken in the experiments on the compounds, i.e. the alkali is bound not only by the appropriate phosphoric or acetic acid but also by the conversion product of the acetylenic mercaptan. According to the data obtained the acid properties of this product exceed those of the usual mercaptans, which is confirmation of the scheme shown.

It was established further[38] that the catalytic activity of the cholinesterases was unchanged during enzymic hyrolysis of the acetylenic substrate. As follows from Fig. 2, the quantity of compound (LVIII) taken is hydrolysed completely by BuCE. A new portion of this compound added to the reaction mixture at the same concentration is hydrolysed at the same rate. The slopes of the curves in coordinates of 'concentration of thiol product formed' against 'time' in the initial period of enzymic hydrolysis for the two portions of substrate proved to be equal. Analogous results were obtained in experiments with compound (LVII). Consequently the products of enzymic hydrolysis do not cause irreversible inhibition of the catalytic activity of the enzyme.

The *S*-alkynyl esters of thioacetic acid therefore act only as substrates in relation to the cholinesterases. The low rate for enzymic hydrolysis is most likely caused by slow desorption of the resulting mercaptan. Evidently among the numerous examples of cholinesterase hydrolysis of various carboxylic acid esters the

hydrolysis of acetylenic substrates is a rare case in which the rate of enzymic hydrolysis is limited by the desorption of the reaction product.[39]

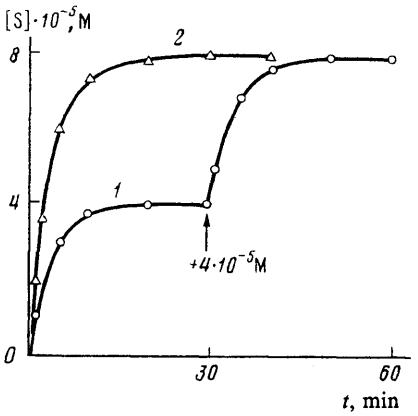


Figure 2. Cholinesterase hydrolysis of substrate $CH_3C(O).SC{\equiv}CC_4H_9$ (S) at different initial concentrations: *1*, 8 × 10^{-5} M, *2*, 4 × 10^{-5} M with subsequent addition of a new portion of substrate (indicated by the arrow).[38]

IV. Toxicity of acetylenic organophosphorus inhibitors

The method of determining the toxicity of OPIs for white mice on subcutaneous administration and the method of determining the contact toxicity for the beet aphid *Aphis fabae Scop.*, the rice weevil *Calandra oryzae L.*, the imago and larvae of the fourth instar of the Colorado beetle *Leptinotarsa decemlineata Say.*, larvae of the second instar of the Podisus bug *Podisus maculiventris Say.* and the spider mite *Tetranychus urticae Koch* have been described previously.[15] The mouse toxicity was characterised by the LD_{50}, the dose of the substance in mg kg^{-1} causing death of 50% specimens, and the toxicity for arthropods by the size of the LC_{50}, the concentration of compound in mg $litre^{-1}$ causing death of 50% specimens also 24 h after applying the OPI.

Only a small proportion of the compounds shown in Tables 12 and 13 were used in the toxicological investigation. Mostly these were compounds with high anti-CE activity (Table 18). The test objects for the toxic action of these compounds were white mice, beet aphids, rice weevils and spider mites. It follows from the data of Table 18 that the *S*-ethynyl esters of dialkyl thiophosphoric acids possess high insecticidal activity, exceeding that of the standard (chlorofos for beetles, carbofos for aphids) 10–100 times in certain cases. At the same time their saturated analogues proved to have low toxicity for arthropods. The introduction into the OPI molecule of an acetylenic bond in the α-position relative to the phosphoryl-mercapto group leads to a significant enhancement of the anti-CE activity and of the insecticidal properties. The efficiency of such enhancement depends on the OPI structure and is manifested in a different way for each compound for the arthropods investigated.

It is generally acknowledged that CE inhibition is the main reason for the toxic action of the organophosphorus insecto-acaricides.[40] However a direct link between the toxicity of the organophosphorus compounds and their inhibitory activity towards the CE of the given representatives of the arthropods or mammals exists in those fairly rare cases when compounds close in structure are investigated. The absence of such a link is explained chiefly by differences in losses of compound during the time taken to be transferred from the site of administration in the organism to the synaptic CE and in non-uniform conversions during metabolism.[40,41]

Table 18. Toxicity of *S*-ethynyl esters of dialkyl thio- and dithiophosphoric acids $(RO)_2P(Y)SC{\equiv}CX$ and their saturated analogues $(RO)_2P(Y)SCH_2CH_2X$ (compounds numbered 'a').[15]

Compound No.	OPI		LD_{50}, mg kg^{-1} mice		LC_{50}, mg $litre^{-1}$					
					beet aphid		beetle		spider mite	
	R	X	Y=O	Y=S	Y=O	Y=S	Y=O	Y=S	Y=O	Y=S
(LVI)	CH_3	C_4H_9	2.7	470 (175)	4	60 (15)	30	20 (0.7)	100	1000 (10)
(XXIX)	CH_3	$CH_2SC_2H_5$	9.2	390 (42)	57	53 (1)	500	400 (0.8)	300	400 (1.3)
(XVII)	C_2H_5	C_4H_9	0.45	235 (470)	45	30 (0.7)	200	90 (0.5)	10	300 (30)
(XXXVI)	C_2H_5	$CH_2SC_2H_5$	3.5	210 60	45	39 (0.8)	100	200 (2)	10	400 (40)
(XXXVII)	C_2H_5	$CH_2SC_4H_9$	2.4	460 (192)	48	150 (3)	150	300 (2)	200	300 (1.5)
(XXVII)	C_2H_5	$CH_2OC(O)CH_3$	0.5	270 (540)	12	150 (12)	700	7000 (10)	700	3000 (4)
(XLVI)	C_2H_5	C_6H_{11}-cyclo	1.2	500 (416)	0.1	0.1 (1)	3	1 (0.3)	7	50 (7)
(XLIV)	C_2H_5	C_6H_5	8.2	465 (57)	50	120 (2.4)	300	1000 (3.3)	100	100 (1)
(XVIIa)	C_2H_5	C_4H_9	160	400 (2.5)	*	*	*	*	*	*
(XXXVIa)	C_2H_5	$CH_2SC_2H_5$	24	300 (12.5)	*	*	*	*	*	*
(XXVIIa)	C_2H_5	$CH_2OC(O)CH_3$	210	400 (1.9)						
Standards		chlorophos	–		–		300		–	
		carbophos			30		–		–	
		metaphos			–		–		20	

*Compounds of low toxicity for arthropods. Death of test objects at concentration of 500 mg $litre^{-1}$ for mites and 100 mg $litre^{-1}$ for aphids were only 5–10%.

Footnote. Values of the thione effect *T* are given in parentheses [for mammals $T = LD_{50}$ (Y = S)/LD_{50} (Y = O) and for arthropods $T = LC_{50}$(Y = S)/LC_{50} (Y = O)].

It follows from Tables 12 and 13 that of the *S*-ethynyl esters of diethyl phosphoric acid the strongest inhibitors of CE are compounds (XXVII) and (XLVI), while compound (XLVI) (Table 18) is surpassed by compound (XVII) in its toxic action on mice. Compounds (XVII), (XXXVI) and (XXXVII) surpass compound (XXVII) in their toxic action on mites, although these compounds are weaker than compound (XXVII) in anti-CE activity by a ratio of 30–80. Only for aphids was a satisfactory link

observed between the anti-CE activity and toxicity of these compounds.

Since the toxicities of the investigated thiophosphoric acid esters for mice are relatively large these compounds do not satisfy contemporary requirements for highly selective insecto-acaricides. It is known that replacement of a phosphoryl (P=O) group by a thiophosphoryl (P=S) group in an OPI leads to a reduction in toxicity since thione derivatives are devoid of anti-CE activity and their toxic action *in vivo* is brought about only after enzymic oxidative desulphurisation which occurs at different rates in different forms of animal.[40,41] This reaction is provided in the system by microsomal oxygenases with cytochrome P-450 as the central unit. This process is usually accomplished significantly more rapidly in arthropods than in mammals, which possess a relatively low activity of these enzymes.[41] As a result the replacement of a phosphoryl group in OPIs by a thiophosphoryl group markedly reduces their toxicity for mammals and in the same way increases the selectivity of their action on arthropods. The selective toxicity of compounds in this case is assessed most graphically (Table 18) by the size of the 'thione effect' (T) which is the ratio of the toxicity of the thione compound ($LD_{50,S}$ and $LC_{50,S}$) to the toxicity of its oxygen analogue ($LD_{50,O}$ and $LC_{50,O}$).

Acetylenic (8) and saturated (3) derivatives of dithiophosphoric acids, which are analogues of the monothio compounds, have been synthesised and investigated.[15] In the text they will be referred to by the number of the oxygen compound with the index S. Their toxicities and the size of the thione effect are given in the same Table 18. The thione derivatives investigated differ from one another in toxicity to a larger degree than do the oxygen analogues. For example, for beetles the toxicity of compound (XLVI,S) has a $LC_{50,S}$ value of 1 mg litre^{-1}, but the toxicity of compound (XXVII,S) has a value of 7000 mg litre^{-1}.

It was extremely important and unexpected that on replacing a phosphoryl by a thiophosphoryl group in the acetylenic compounds the toxicity was changed very little for arthropods but was strongly reduced for mammals. Some acetylenic derivatives of dithiophosphoric acid proved to be 100 times less toxic for mice than the corresponding derivatives of monothiophosphoric acid. The size of the thione effect for compounds (XVII), (XXVII) and (XLVI) was more than 400. This sharp fall in toxicity for mammals on replacing the phosphoryl oxygen by sulphur in OPIs is observed for the first time. In contrast to the acetylenic compounds the saturated analogues are characterised by significantly smaller values of the thione effect. Values of T were from 2 to 12 which is natural for the usual organophosphorus insecto-acaricides.

The size of the thione effect for arthropods was in the range 0.5 to 1 in all cases. A thione effect equal to 1 might be regarded as the result of complete conversion of the dithio into the monothio compound by oxidative desulphurisation by certain isoenzymes of cytochrome P-450. Obviously such a assumption is naive as values of the thione effect of less than 1 contradict this conclusion. Such low values for the thione effect may be explained by the presence in addition of further oxidative desulphurisation and deocmposition processes which are catalysed both by oxidases and by other enzymes.[41] Low values for the thione effect were detected for compounds (LVI) and (LVI,S) in experiments with other representatives of the arthropods, viz. Colorado beetle and Podisus bug. It follows from Table 19 that in all cases the size of the thione effect was less than 1, particularly in experiments with Podisus (T = 0.09).

In order to clarify the mechanism of the thione effect for the acetylenic organophosphorus compounds the interaction has been studied[38] of compounds of general formula $(C_2H_5O)_2P(Y)R$, where R = $C{\equiv}CC_4H_9$, $SC{\equiv}CC_4H_9$, and Y = O or S, and also of their saturated analogues with cytochrome P-450 from Wistar rat liver microsomes and from the abdomen of houseflies. The effect of the OPIs on cytochrome P-450 was studied by a known procedure.[17]

Table 19. Toxicity (LC_{50}, mg litre^{-1}) of compounds $(CH_3O)_2P(Y).SC{\equiv}CC_4H_9$ for Colorado beetles and for Podisus bugs.[41]

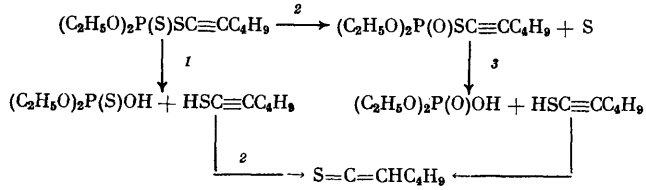
Y	LC_{50}, mg litre^{-1}		
	Colorado beetle		Podisus bug
	imago	larvae IV instar	larvae II instar
O	1900	1500	75
S	790	1050	6.5
	(0.42)	(0.7)	(0.09)

Table 20. Reaction of compounds $(C_2H_5O)_2P(Y)R$ with cytochrome P-450.[17]

OPI			Decrease in cytochrome P-450 content, %	
compound No.	R	Y	rat liver microsomes	fly abdomen microsomes
(XXXVII, S)	$SC{\equiv}CC_4H_9$	S	22.2±2.5	60±6.5
(XXXVII)	$SC{\equiv}C_4H_9$	O	22.2±1.7	27.5±1.5
(XXXVIIa, S)	$SCH_2CH_2C_4H_9$	S	0	10.5±3.7
(XXXVIIa)	$SCH_2CH_2C_4H_9$	O	0	0
(LVII)	$C{\equiv}CC_4H_9$	O	0	0
(LVIIa)	$CH_2CH_2C_4H_9$	O	0	0

It is seen from Table 20 that after incubation of cytochrome P-450 from rat liver microsomal fractions in the presence of NADPH, destruction of enzyme occurs only by the action of the acetylenic thioesters of monothio- and dithiophosphoric acids (XXXVII) and (XXXVII,S) but in the case of cytochrome P-450 from fly abdomen destruction also occurs in the presence of the saturated compound, the *S*-hexyl dithiophosphate (XXXVIIa,S). The analogous *S*-hexyl monothiophosphate (XXXVIIa), having no thiol group like the esters of the phosphonic acids (LVII) and (LVIIa), does not react with the microsomal cytochrome P-450. It is obvious that the destructive action is not possessed by the compounds (XXXVII), (XXXVII,S) and (XXXVIIa,S) themselves but by products of their conversion. One of the most probable conversion routes for esters of phosphorus thioacids may be cleavage of the thioester bond by certain cytochrome P-450 isoenzymes. A normal mercaptan is formed from thioesters with a saturated R group. The mercaptans formed in the case of the acetylenic

thioesters are unstable and are readily converted into thioketenes as shown in the scheme.



The ability of thioketenes to react with any compound containing a labile hydrogen atom is well known.[17] It may therefore be taken that butylthioketene, formed by the metabolism of the acetylenic compounds (XXXVII) and (XXXVII,S), reacts with the appropriate groups in the haem region of cytochrome P-450 causing its destruction. It is known from the literature[42] that destruction of cytochrome P-450 is observed when organic compounds with unsaturated bonds add to the protoporphyrin ring of haem. The thioketene formed causes destruction of the monooxygenase and in this way reduces the rate of detoxification of acetylenic OPIs thereby aiding the retention of their toxicity. The saturated mercaptans formed on deactivation of the saturated analogues (XXXVIIa) and (XXXVIIa,S) are incapable of destroying the enzyme.

Another metabolic route for the thione esters of phosphorus acids is their activation by the process of oxidative desulphurisation. It is also effected in a microsomal monooxygenase system but seemingly by other cytochrome P-450 isoenzymes. A sulphur atom is formed which it is claimed is able to bind covalently with the cytochrome active centre causing its degradation.[43] In actual fact diethyl *S*-hexyldithiophosphate (XXXVIIa,S) displays a destructive action on fly abdomen cytochrome P-450. Only the sulphur atom formed in the oxidative desulphurisation of this compound may possess this action in this case since the other metabolite, hexylmercaptan, cannot exert a degradative action on a cytochrome as follows from the experiments with compound (XXXVIa). In addition it is evident from Table 20 that compound (XXXVIIa,S) does not possess a destructive action on the family of isoenzymes of rat liver cytochrome P-450, which evidently indicates the insignificant content of the isoenzyme effecting the oxidative desulphurisation in rat liver microsomes compared with fly abdomen microsomes.

Insect cytochrome P-450 is therefore able to activate the dithio derivatives used but rat cytochrome P-450 is less well suited for this.

The reasons stated explain logically why compound (XXXVII) reduces the content of cytochrome P-450 to the same extent in rat liver microsomes and in fly abdomen microsomes but compound (XXXVII,S) acts more strongly on the cytochrome P-450 from fly abdomen microsomes.

The introduction of a thioethynyl group into an OPI molecule, which contains a phosphoryl group, leads to high toxicity not only as a result of an increase in anticholinesterase activity but also by reducing its detoxification rate by destroying specific cytochrome P-450 isoenzymes. These processes proceed at approximately the same rate in mammals and arthropods.

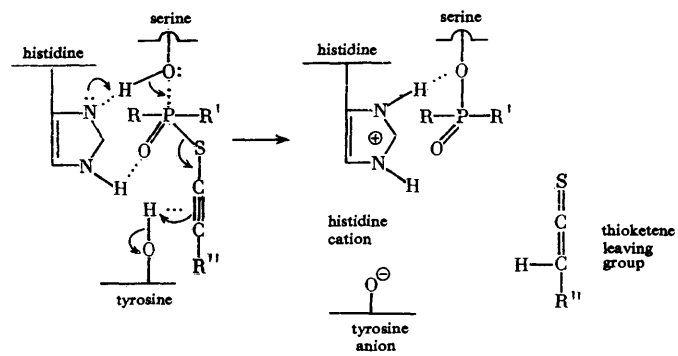
The activation of *S*-ethynyl esters of dialkyl dithiophosphoric acid by specific cytochrome P-450 isoenzymes in mammals and arthropods proceeds at different rates. These processes occur at a higher rate in arthropods than in mammals. Evidently these are the chief factors in the display of the thione effect observed by us.

V. Conclusion

The results of the investigations carried out show that thioesters of monothioacids of phosphorus containing an acetylenic bond in the thioester group are a new class of organophosphorus inhibitors possessing very high anticholinesterase activity.

Analysis of the mechanism of action of these OPIs on CE leads to the conclusion that the role of the acetylenic group consists of the formation of an enzyme–inhibitor complex which is then converted into a phosphorylated enzyme or of the significant acceleration of the phosphorylation step leading to the same phosphorylated enzyme. In connection with the first hypothesis it must be said that to date there are no clear data on the location of the binding portion. It may only be assumed that it is not in the region of the anionic site but is a small distance from the esterase centre. It is probably impossible to consider the binding zone as strictly fixed, its location may vary within known limits when reacting the enzyme with inhibitors of various structure. This follows from Koshland's theory[44] on the induced fit of an enzyme active centre to the structure of susbtrates and inhibitors when reacting with them. The correctness of this conclusion is indicated by the fact that OPIs with an acetylenic bond in the β-position are characterised by high values for the acetylenic effect. For example compound (XV), $CH_3(C_2H_5O)P(O)SCH_2C\equiv CCH_2SC_2H_5$, on reaction with arthropod CE gives inhibition rate constants k_{II} of 2.5×10^7 to 1.1×10^9 M^{-1} min^{-1} and values of the acetylene effect q of 590 to 38 000. Consequently the part of the enzyme binding the actylenic group to the active surface is accessible not only to compounds with the acetylenic group in the α-position but also to compounds with a β-acetylenic group. In the latter case it is evident that there are definite restrictions since the disposition of the functional portions of the binding onto the active surface of the enzyme corresponding to a compound with an α-positioned acetylenic bond will not correspond to a compound with a β-acetylenic bond.

It is possible to represent the second hypothesis by an extended scheme of phosphorylation of the esterase site of the enzyme, comprising a serine hydroxyl group, a histidine imidazole ring and a tyrosine phenolic hyroxyl with the inhibitor acetylenic group forming a π-complex bond with the tyrosine proton.



Lengthening of the conjugation chain in which transfer of a proton from tyrosine to the acetylenic bond and from serine to histidine occurs and there is remote transfer of an electron pair from the histidine nitrogen to the tyrosine oxygen must sharply reduce the activation energy of the phosphorylation. It is possible that at such an orientation of the OPI at the moment of attack adsorption onto the anionic point of the CE loses its value. It is understood that the

normally phosphorylated enzyme must be formed as a result of such a process but the rate of its formation must be appreciably higher.

It is not ruled out that these two hypotheses do not contradict one another. All depends on the time (moment) of forming the π-complex of the tyrosine phenolic hydroxyl with the acetylenic π-bond.

The effect of the acetylenic bond depends markedly on the structure of the compound. Compound (XX), $(C_2H_5O)_2$.P(O)SC≡CH, the simplest of the acetylenic OPIs investigated, possesses very high anti-CE activity. Replacement of the acetylenic hydrogen in this compound by various hydrocarbon residues does not increase but reduces anti-CE activity in relation to many CE in the majority of cases. A substituent with a sulphonium grouping proved to be weakly effective. Consequently the acetylenic OPIs with the substituents indicated above are not oriented on the catalytic centre of the enzyme in the best way. As is known[44] the complementarity of the inhibitor molecule with the enzyme active surface, which causes 'productive' adsorption in the final account, depends generally on the compatibility of the various forms of their interaction such as ion–ion, ion–dipole, dipole–dipole, hydrophobic and, in our case, on the orientation of the acetylenic group as well. When these interactions are compatible the adsorbed OPI molecule is oriented on the active centre so that the phosphorus atom and the serine hydroxyl of the enzyme are spatially drawn together and phosphorylation occurs. When the interactions are 'incompatible' the inhibitor molecule is disposed so that the phosphorus atom and the serine hydroxyl are spatially separate, the acetylenic bond is unable to participate and phosphorylation is hindered.

High physiological activity and selectivity of action are characteristics of acetylenic OPIs. Selectivity in relation to arthropods is sharply increased on replacing the phosphoryl group in them by a thiophosphoryl. The toxicity for mice is thereby reduced, occasionally by a hundredfold, while for OPIs without an acetylenic group it is reduced by no more than 20 times.[40] The toxicity of the same acetylenic OPI for arthropods is changed very little by this and in several cases the opposite effect is observed. The toxicity of esters of dithiophosphoric acid exceeds the toxicity of esters of monothiophosphoric acid.

The properties of the acetylenic organophosphorus compounds which are so unusual require further study of the metabolic features of these compounds in mammals and arthropods.

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Translated from *Uspekhi Khimii* **60** 1777–1816 (1991) U.D.C. 577.15+591.818+547.963+612.118

Lectins in the investigation of receptors

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ABSTRACT. Problems of the purification and characterisation are considered for approximately 270 receptors (including cell surface and organelle enzymes), which are glycoconjugates (mainly glycoproteins) from animals, plants and microorganisms, using various lectins (mainly lectin sorbents). An analysis has been carried out of the stages of lectin affinity chromatography of receptors (choice of detergent, use of organic solvents, elution with carbohydrates, etc.). Examples are given of procedures for the purification of receptors, including the use of paired columns and combination chromatography on lectins. The possibility of separating sub-populations of receptors using lectins has been demonstrated. Examples are given of the use of lectins in the analysis of the oligosaccharide structure of receptors. Cases are recorded of the interaction of receptors with endogenous lectins and of receptor lectins with endogenous glycoconjugates. It has been shown that lectins, in combination with glycosidases and antibodies, may be useful in the investigation of receptors.

The bibliography contains 406 references.

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I. Introduction

In recent years the study of receptors has been at the centre of investigators' attention due to their participation in biorecognition at various levels of the organisation of living systems.[1–9] It has been established that key (important in the metabolic sense) interactions between receptors and external agents (endogenous and exogenous, soluble and bound to cell surfaces or cell organelles) proceed in many cases by specific bonding between lectins (carbohydrate-binding proteins) and glycoconjugates.[10–22] The problems of purifying and characterising receptors with a selection of lectin sorbents or labelled lectins are therefore of interest to biologists and chemists. A large number of publications has appeared since the publication of the review by Lotan and Nicolson[23] on the purification of membrane glycoproteins by lectin affinity chromatography. These have extended our ideas on the possible use of lectins in the study of receptors and enzymes bound to cellular structures (see reviews[21,22,24–27] for example).

The aim of the present review is to examine the purification and characterisation of receptors of various types using lectins, chiefly lectin sorbents.

II. Interaction of immobilised lectins with receptors

Results are summarised in Tables 1 and 2 of the use of lectin affinity chromatography for the purification of receptor glycoproteins, including enzymes bound to cellular structures (see also reviews[22–24,26]). It is evident from Tables 1 and 2 that receptors possess an affinity for a wide range of lectins. Wheat-germ lectin (WL) is the most frequently used which is explained by the widespread distribution on its receptor glycoproteins of polyantenna sialylated glycans, branched residues of *N*-acetyl-D-glucosamine, *O*-glycoside-bound *N*-acetyl-D-glucosamine residues, hybrid oligosaccharides and glycans of the polylactosamine type (see below for investigations of receptor structure with lectins).

1. Results of the use of lectin affinity chromatography for the purification of receptors

It is evident from the data shown in Tables 1 and 2 that the use of wheat lectin enables 50–100-fold purification of Ca-channels, opioid receptors and glycoproteins of olfactory neurones.[47,61,74,90,117,193] Concanavalin A (Con A) is highly effective in the purification of phospholipase A_1 (165 times, based on enzyme activation[269,270]) and pea (*Pisum sativum*) lectin in the purification of fibroblast glycoproteins (58 times, by affinity HPLC [187]). Some lectins, which are relatively rarely used in lectin affinity chromatography, may also prove to be extremely useful, e.g. castor-oil plant (*Ricinus communis*) lectin (CL) in the purification of the glycoproteins induced by Epstein–Barr virus and of the cholecystokinin receptor [144 and 440 times respectively,[98,223] gorse (*Ulex europaeus*) lectin-I (GL-I) in the purification of the cholecystokinin receptor (300 times)[99]] and the lectin from seeds of *Vicia bungei* which is specific for α-mannose in the purification of opioid receptors (200 times[60]). Lectin affinity chromatography is the most efficient step in receptor purification in these and in other cases (see Tables 1 and 2).

Stabilisation of receptor preparations is achieved by lectin affinity chromatography. This is important for their preservation (for example, in the case of dopamine receptors[76]). This is evidently linked with the removal of contaminating hydrolases and oxidases.[92] Occasionally investigators have found activation of receptors in eluates from the lectin sorbent, as in the case of receptors of insulin,[91] phospholipase A_1 [269] or Ca^{2+}-dependent peptidase.[295] Activation of the glycoconjugates indicated above may occur both by the removal (separation in eluates) of inhibitors (glycoconjugates and proteins) and by the stabilisation of receptors in comparison with an unstable control (before purification). An appreciable

increase in the yield of receptors, up to 150% of the initial activity, is achieved in specially selected cases.[269]

Simple immobilisation of glycoconjugates (low yield at a high percentage of binding) with their simultaneous purification from contaminants is possible during affinity chromatography on lectins. This occurs in the case of α_1-adrenergic and lactogenic receptors, epitectin (Ca-antigen), receptors of thyrotropin and interleukin 4 and sulphotransferase.[65,108,112,163,214,256] As in other cases of oligomeric receptors, subunits with a predominant affinity for the given lectin (glycosylated subunits) are bound primarily with the lectin sorbent and provide subsequent directed assembly of the receptor (the addition, for example, of non-glycosylated subunits) as in the case of receptors of α-latrotoxin, fibronectin, insulin-like growth hormone, cGMP-channel, Na^+,K^+-ATPase and antigens of trypanosomes[43,123,134,201,235,302,303] and also receptor complexes.[51,126,202]

Table 1. Purification of receptors (R) on immobilised lectins (IL).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
Receptors of cations, low molecular compounds, receptor complexes from animal tissues and cells		
Animal gut Na^+/glucose transporter, 75 kD	Con A (b)	[28]
Hexose transporter from hamster ovocytes deficient at Lec-1, 40 kD form 55 kD form	WL (10–20% b), Con A (80–90% b) WL (25–40 b) Con A (60–75 b)	[29]
GABA transporter from bovine brain, 80 kD	WL (b)	[30]
Serotonin transporter from chromaffin granules of bovine adrenal, 80 kD DEAE → HA → PC → WL	WL (b)	[31]
L-Glu transporter from rat brain	WL (50%; 12 times)	[32]
GABA transporter/L-Glu transporter from rat brain WL → HA → DEAE	WL (20%; 6 times)*	[33]
R for L–Glu from *Nephrops* muscle, sensitive to quisqualate, 74+65 kD Con A→Ultragel	Con A (57%; 178 times)*	[33a]
GP from Na^+-channel from locust brain neurones/saxitoxin R, 240–260 kD	WL (34%; 2.7 times) Con A (33%)	[34]
Na^+-channel from the eel *Electrophorus electricus*, 285 kD	Slug L better than WL (out of 11 lectins)	[35]
Na^+-channel from presynaptic rat brain membranes	WL (80% b)	[36, 37]
GP of K^+-channel from rat brain/dendrotoxin-binding R, DEAE → AC → WL	WL (44%; 6 times)	[38]
Na^+-Ca^{2+}-exchange GP from dog heart sarcolemma, 160 kD, DEAE → WL	WL (50%; 1.7 times)	[39]
Na^+-Ca^{2+}-exchange GP from the outer segment of bovine eye rods, 215 kD, DEAE → WL	WL (20%; 1.7 times) CL-2 (b)	[40, 41]
Ca^{2+}-binding GP from bovine heart sarcolemma	WL (> 60%)**	[42]
GP of the cGMP entry channel from bovine eye rod photoreceptors, 63+240 kD	Con A (63 kD b)** out of 5 L	[43]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
Na^+/K^+-antiporter from rat renal brush border membranes	Binding with 5 biotinyl-L***	[44]
Complex of 1,4-dihydropyridine R and Ca^{2+}-channel from chick heart DEAE → Hexylamine → WL	WL (70%; 3 times)	[45]
Dihydropyridine R/Ca^{2+}-channel blockers from rabbit skeletal muscle, 142+56+30 kD, WL(1) → DEAE(HPLC) → WL(2)	WL(1) (70%, 24 times)* WL(2) (66%; 1.7 times)	[46]
Chick heart Ca^{2+}-channel sensitive to dihydropyridine, 140 kD, DEAE → Con A → WL	Con A → WL (42%; 132 times), including WL (88%; 97 times)*	[47]
Dihydropyridine R from rabbit skeletal muscle 53+160 kD, WL→DEAE→Dihydropyridine	WL (85%; 14 times)*	[48, 49]
Complex of dihydropyridine R and Ca^{2+}-channel from rabbit skeletal muscle, 340 kD, WL → DEAE	WL (38%; 39 times)*	[50]
Complex of dihydropyridine R and rabbit skeletal muscle dystrophin, 360 kD (36+43+52+61+94 kD) WL → DEAE	WL (100% b), affinity for α_2-SU of dihydropyridine R in the case of Con A and WL	[51, 51a]
Ca^{2+}-channel blocker R from rabbit skeletal muscle, 56+150 kD	WL (b)	[52]
Complex of dihydropyridine R and *L* type Ca^{2+}-channel from bovine adrenal, 185–190 kD	WL (b)	[53]
α_2-like component of Ca^{2+}-channel from chick heart muscle, 139 kD	WL (removal of component 197 kD)	[54]
Inositol triphosphate R from boovine aorta smooth muscle microsomes, 224 kD Heparin→WL	WL (46%, 2.4 times)	[55]
Inositol triphosphate R from rat cerebellum, 260 kD, DEAE → Heparin → Con A → GF; Heparin → Con A → Mono Q (HPLC)	Con A (60%; 5 times)	[56–58]
Opioid R from chick, rat, bovine and human brain	WL (40–60%; 30 times) best of 7 lectins	[59]
Opioid R from rat brain, 45 kD	*Vicia bungei Ohwi* L (200 times) better than WL	[60]
Complex of opioid R and rat brain guanine-binding protein sensitive to whooping cough toxin, 41+39 kD, WL → Phe	WL (20–50%; 100–40 times)	[61]
Opioid R from neuroblastoma–glioma hybrid NG cells 108–15, 58 kD	WL (b)	[62]
Opioid R from human placenta	WL (of 5 lectins)	[63, 64]
α_1-adrenergic R from mouse BC3HI and hamster DDT1 smooth muscle cells	WL (affinity for the hamster cell R was 6 times weaker than for the mouse cell R)	[65]
α_1-adrenergic R from rat brain and liver, Heparin → AC → WL	WL (45%; 8 times, brain) (48%; 2.6 times, liver) binding–100%	[66]
α_1-adrenergic R in a complex with guanidine-binding protein	WL (68%; 5 times)*, removal of unglycosylated guanidine-binding proteins	[66a]
α_1-adrenergic R from DDT1 and MF2 muscle cells, 80 kD, Antagonist → WL → GF (HPLC)	WL (70–90%; 10 times, binding > 90%)	[67]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
α_2-adrenergic R from human thrombocytes, 64 kD, AC → Heparin → WL → AC → Heparin	WL (74%; 5 times)	[68]
β-adrenergic R from mouse S49 lymphoma cells	WL, Con A (effect of swainsonine) binding > 75%, yield 50%	[69]
β_1-adrenergic R from turkey erythrocytes	6 L (differences from mammalian R)**	[70]
β_2-adrenergic R from hamster erythrocytes and lungs, 62 kD	WL, Con A (tissue specificity)**	[71]
Dopamine D1 R from bovine brain and parathyroid, 64 kD	WL, Con A (but not SL, AL)**	[72]
Dopamine D2 R from bovine brain caudate nuclei	WL (but not Con A)	[73]
Dopamine R from bovine brain caudate nuclei, 95 kD, AC → WL	WL (52%; 49 times)	[74]
Dopamine D2 R from bovine caudate nuclei and olfactory tubercle	WL (b 68%; yield 100%, separation of forms of R**	[75]
Dopamine D2 R from bovine striatum, WL → AC; AC → GF → WL	WL (80%; 10 times), stabilisation of R	[76, 77]
Cocaine R (dopamine transporter) from bovine striatum synaptosomes	Con A (b)	[78]
Dopamine transporter from rat brain caudate nuclei and striatum, SU 58 kD	WL (b)** Con A (no b)	[79]
Dopamine transporter from dog brain striatum	WL (95%; 10 times)	[80]
Histamine H1 R from mouse smooth muscle differentiated BC3H1 cells, 68 kD	Con A (30%; 25 times)**	[81]
Octopamine R/neurohormone R/adenyl cyclase activator R from luminescing organs of the glow-worm *Photinus Pyralis*, SU 75 + 79 kD	Affinity for Con A**(blotting)***	[82]
Muscarinic acetylcholine R from porcine atrium cordis	WL (55%; 20 times)	[83]
Acetylcholine R from bovine brain cortex, 73 kD	WL (b 90%; yield up to 65%)** Con A**	[84]
Acetylcholine R from rat muscle fibres	WL (b)	[85]
Acetylcholine R from rat brain cortex	WL better than Con A**	[86, 87]
Acetylcholine R from the electric organ of the eel, α + β + γ + δ (SU)	Labelled*** L-FGA (b δ- and γ-SU) WL (b δ-SU) Con A (b all SU)	[88]
Ryanodine R from rabbit brain and muscle	WL (no b) Con A (no b) LL (no b)	[51a, 88a]

Receptors of peptide and protein hormones and growth factors from animal tissues and cells

Insulin R from human placenta WL → LL → CL-1	WL (98%; 22 times) PL (45%; 14 times) LL (30%; 15 times) Con A (20%; 5 times) CL-1 (15%; 7 times)	[89]
Insulin R from human placenta WL → Insulin; Con A → Insulin	WL (54%; 7.5 times) WL (40%; 5 times)	[90, 90a]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
Insulin R from human IM9 lymphocytes WL → CL-1 → PL	WL (70%; 21 times) CL-1 (50%; 50 times) CL-2 (30%; 50 times) PL (25%; 26 times) LL (20%; 15 times) Con A (10%; 5 times)	[89]
Insulin R from rat skeletal muscle	WL (80%; 70 times)	[90a]
WL → Insulin	WL (94 – 120%; 7 times)	[91]
Insulin R from rat brain and liver, SU 135 + 95 kD DEAE → Con A → Insulin → WL	Con A (93%; 36 times) WL (94%; 2.3 times; removal of insulinase)	[92]
Formyl-peptide R from rabbit peritoneal neutrophils, 50 – 70 kD (fMet-Leu-Phe) → WL	AC → WL (74%; 203 times)	[93]
Vasopressin V1 R from rat liver, 58 – 68 kD, GF → WL → HA → DEAE	WL (84%; 6 times)	[94]
Peptide transporter from rabbit small intestinal brush border membranes, 127 kD, WL → DEAE	WL (b)	[95]
Vasoactive intestinal peptide R (neurotransmitting hormone R) from rat liver, 80 + 56 kD	WL (b 50%;)**, but not Con A	[96]
Vasoactive intestinal hormonal peptide R from rat lung, 58 kD	WL (b)	[97]
Cholecystokinin R from rat pancreas, 80 – 90 kD, CL-2 → Affigel	CL-2 (about 100%; 440 times)	[98]
Cholecystokinin R from rat pancreas, 95 kD S-Sepharose → GL-1 → GF	GL-1 (47%; 300 times) better than WL	[99]
Cholecystokinin R from rat pancreas, 85 – 95 kD	WL (b)**	[100]
R from liver bile duct cells, 110 kD	WL (b)	[101]
R of luteinising hormone and choriogonadotropin from rat ovary, 73 kD or 90 – 93 kD, WL → Choriogonadotropin	WL (70%; 18 times)**	[102 – 104]
R of luteinising hormone and choriogonadotropin from porcine ovary Sepharose 6B → Con A	Con A (30 – 40%; 4 – 10 times)	[105]
Lutropin R from porcine ovary, 22 + 40 + 66 kD Hormone → Con A	Con A (50 – 75% b)	[106]
Folliotropin R from bovine testes, 240 kD (SU 60 kD) DEAE → WL	WL (92%; 3.7 times) two types of GP	[107]
Thyrotropin R from bovine thyroid, 316 + 115 + 54 kD Thyrotropin → GrL	Thyrotropin → GrL (3%; 808 times) GrL (84% b) WL (70% b) CL-1 (69% b) Con A (60% b)	[108]
Thyrotropin R from thyroids of patients with Graves' disease, 70 + 50 + 35 kD WL → Thyrotropin	WL (26%; 4.7 times; b more than 90%)	[109]
Somatostatin R from rat pancreas, 400 kD (100 + 56 + 21 kD, SU)	WL (75%; 7 times)	[110]
Somatostatin R from rat brain	WL (50% b; yield 67% of bound form)	[111]
Lactogenic R from mouse liver, SU 62 + 100 kD (in complex with human growth hormone 20 kD)	Con A (95% b; yield 30%) CL-1 (81% b; yield 69%) LL (52% b; yield 38%) WL (27% b)	[112]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
Lactogenic R from rat ovary Con A → Choriogonadotropin	Con A (yield 60%)	[113, 114]
Corticotropin releasing factor R from rat anterior pituitary and brain, SU 75 and 58 kD respectively	WL 20% (b)** Con A (b)	[115]
Growth β-transforming factor R from chick and human tissue, mouse 3T3 cells	WL (b)	[116]
Platelet growth factor R from porcine uterus WL → Mono Q → (Ab to phosphotyrosine)	WL (99%; 90 times)*	[117]
Fibroblast growth factor R from bovine brain, 125–165 kD DEAE → Mono Q → WL → (Growth factor)	WL (100% b), to remove heparin	[118]
Insulin-like growth factor I R from phaeochromocytoma PC12 cells and bovine adrenals	WL (Purification 36–72 times)	[119]
Insulin-like growth factor I R from human placenta	WL (b)	[120]
R for platelet-derived growth factor from cat brain, 145 kD	WL (b)**	[121]
Growth hormone R from cultured human lymphocytes	WL better than Con A, LL, CL-1, CL-2	[122]
Insulin-like growth factor II R from human lipid cells, 260 kD (SU 87+60 kD)	WL (b)	[123]
Heparin-binding growth factor R from human hepatoma Hep G2 cells, 130 kD	WL (b)**	[124]
Macrophage and granulocyte colony-stimulating factor R from human placenta, neutrophils and leukemic cells lines, 84 kD	WL (b)	[124a]
α-Interferon R from human lymphoblastoid *Namalva* cells	WL (47%; 13 times)*	[125]
Human β-interferon R, 110 kD WL → Ab	WL (90% b; yield 68%)	[126]
γ-Interferon R from human foreskin fibroblasts Interferon → CL-1	CL-1 (100%; 2.6 times)	[127]
γ-Interferon R from human placenta, 90 kD WL → Interferon	WL (b)**	[128]
Other receptors and animal antigens		
Complement CR1 R from human peripheral nerve myelin, 190 kD	LL (b)	[129]
Immunoglobulin Fc-fragment R from lymphocytes of patients with chronic leukemia LL → GF	LL (b)	[130]
α_2-Macroglobulin R from human placenta, 420 kD GF → Macroglobulin → Mono Q → WL	WL (b)	[131]
Mouse lactotransferrin R, 130 kD	Con A, L-FGA (b)**	[132]
Fibronectin R from rat hepatocytes and fibroblasts, 155+115 kD WL → (Fibronectin hexapeptide)	WL (b)	[133]
β-SU R of mouse sarcoma fibronectin, 135 kD LL → WL → AC → HA	WL (no b, purified by filtration)	[134]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
R of fibronectin/integrin from rat liver parenchymal cells, SU 110 kD WL → Fibronectin	WL (b)**	[135]
Antigen associated with integrins from plasma membranes of human placenta cells, SU 50 kD WL → γ-Interferon → B6H12 (Ab)	WL (b)	[136]
β_1-SU of integrin (R of fibronectin from larvae of amphibian *Pleurodeles waltl* GF → Con A	Con A (b)	[137]
Transferrin R from mouse NS-1 plasmacytoma cells, SU 90–95 kD	4 L (b GP)**	[138]
Transferrin R from chicken oviduct, 180 kD (SU 91 kD)	4 L (b GP)	[139]
Vitronectin R from human M21 melanoma cells	Con A, LL (b)	[140]
Vitronectin R/integrin $\alpha_v\beta_3$/fibronectin R from human placenta LM 609 (Ab) → WL	WL (b)	[141]
Integrin $\alpha_1\beta_5$ (adhesion R of vitronectin) from human placenta LM 6–9→MN142→WL	WL (b)	[142]
Fibrinogen R (GP-IIb/IIIa-like R) from human endothelial cell lines, 150+(110–125)+95 kD AC → WL → (Ab to GP-IIIa)	WL (9b 100%)	[143]
Laminin R (200/120 kD-integrin) of B50 neuroblastoma cells (integrin $\alpha\beta_1$) WL → Laminin	WL (b)	[144]
Adhesin R of endothelial cells of bovine embryo aorta and human umbilical vein (not a member of the cadherin family), 130 kD WL→Ab	WL (b)	[145]
Adhesin R of neural cells from C2 muscle cells	AL (b)	[146]
Adhesin R of substrate from mouse OTT6050 teratocarcinoma cells, 125 kD	CL-1 (b)	[147]
GP-Ib of human platelets/Willebrand factor R, 165 kD (SU 143+22)	WL (removal of actin and GP-IX)	[148]
GP-Ib of human platelets/adhesion R to vessel subendothelium WL → DEAE	WL (b)	[149]
GP-IIb/IIIa of human platelets Con A → Heparin → GF → WL	Con A (b GP-IIb/IIIa+thrombospondin+fibrinogen), WL (removal of fibrinogen)	[150]
GP-IV of human platelets LL → WL	LL (removal of GP-IIb/IIIa by binding), WL (b GP-IV, Ib)	[151]
GP-IV of human platelets (CD 36-like), 88 kD WL → WL → GF; DEAE → WL → GF	WL (b)	[152]
GP-V of human platelets Superose 12 → Mono Q → WL	WL (66%; 7 times)*	[153]
GP-IX of human platelets, 17 kD WL → (Ab to GP-Ib) → GF (HPLC)	WL (b)	[154]
Thromboxane A-2 R/prostaglandin H-2 R from human platelets GF → WL → Red agarose → GF (HPLC)	GF → WL (22%; 1620 times)*	[155]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
Glycocalicin of human platelets WL → Mono Q	WL, Con A, CL–1**, E-FGA	[156, 157]
Bean lectin R from porcine spleen lymphocytes	FGA (b)	[158]
Peanut lectin R from mouse immature thymocytes, 170–180 kD	AL (b)	[159]
GP Thy-1 (antigen) of mouse thymocytes Con A → (Ab to Con A) → GF	Con A (83%; 19 times)	[160]
Antigen Thy-1 of mouse thymocytes, less than 27 kD + 28 kD	Thorn apple lectin (<27 kD not b 50%; retarded 25%; 28 kD b and desorbed 25%)**	[161]
Mammalian interleukin 3 R, 140 kD	WL (b)	[162]
Interleukin 4 R from gibbon MLA 144 line T-lymphocytes, 130 kD CM → WL → Interleukin 4	WL (35%; 4.5 times) CM (filtration) → WL (10–15 times)	[163]
CDw44 antigen from T-lymphocytes of patients with chronic leukemia, 85 kD F10-44-2 (MAb) → DEAE → WL → CM → GF	WL (b)	[164]
Leukosialin (sialoformin, CD 43) from human leucocytes (MOLT-4 cells), 95 kD	WL and CL-1 (b 100%), Con A and LL (partial b); desorption with detergent (except for WL)**	[165]
Leukosialin from human line HL-60 promyelocytes WL → Ab	WL (b)	[166]
Leukosialin from human K562 erythroleukemic leukocytes, 105 kD	WL better than other lectins	[167]
Lymphocytic antigen from membrane, 28 kD	LL (b)**	[168]
GP (H-antigen) containing fucose from human erythrocytes DEAE → (aleuria lectin)	Aleuria lectin (b)**	[169, 170]
GP containing A-antigen from human blood group A (+) erythrocytes, 500 kD (SU 42–55 kD)	Snail lectin (b)	[171]
GP containing Cad-antigen from human blood Cad-group erythrocytes	Dolichos L better than snail L, WL, E-FGA, Maclura L	[172]
Glycophorin M from human blood St^a-group erythrocytes	LL (removal of glycophorin N)	[173]
Glycoprotein precursors of blood group N antigen with Thomson–Friedenreich (T) antigen activity from patients with malignant carcinoma of the ovary (*Vicia unijuga* L)→AL	*Vicia unijuga* L (b), AL (b)	[174]
Glycophorins A, B, N from human blood Dantu-group erythrocytes	LL (no glycophorin N b)	[175]
Glycophorins A, B, C, E from human erythrocytes WL (HPLC) → Cu^{2+}-chelate	WL (separation of A+B+C and E–no b	[176]
Glycophorin A from human MM- and NN-erythrocytes	WL (b 100% for MM and 70% for NN), CL-1 (b of asialoglycophorin)	[177–179]
Gonococcus R from human erythrocytes (band-3), 186 kD (SU 93 kD)	Con A (b)	[180]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
GP of adipocyte ghosts from porcine great omentum, 47+79 kD PL → DEAE → GF	PL (b)	[181]
Lipoprotein R from insect fat body, 120 kD DEAE → HA → Con A → AC	Con A (b)*	[182]
R of cytolytic (antitumour) activity of mouse peritoneal macrophages, 153+140+90 kD	WL (b)	[183]
R for the activation of cytotoxic activity from mouse macrophages, 460 kD (110+170)	*Eristalis* L (b)	[184]
R for *Mycoplasma pneumoniae* microbe from human lung MRC-5 fibroblasts	WL (b)	[185]
GP of type II alveolar cells of rabbit and rat lung, 230 and 200 kD respectively	Maclura L (b)**	[186]
GP from human diploid fibroblasts PL (HPLC), Con A (HPLC)	PL (purification 58 times) Con A (purification 6 times)	[187]
GP induced by aldosterone from toad bladder epithelial cells, 65+70 kD	WL (purification 20 times)** Con A (b)	[188]
Epidermal factor R from A-431 cells, 170 kD	Con A and LL (b OS)**	[189]
Unique kidney antigen in human renal disease, 98+105 kD	Thorn appleperoxidase L (b) out of 5 L***	[190]
GP-II from chromaffin granules of bovine adrenals, SU 80–100 kD	WL (b)	[191]
GP-1 associated with ovocyte lysosomal membranes from the chinese hamster, SU 135+115 kD	Bovine heart Ln (b), Tomato Ln (b)	[192]
Transmembrane GP from frog olfactory neurones, 95 kD	WL (50 times)	[193]
Antigen 2B8 from rat olfactory neurones, 215 kD	WL, CL-1 (b asialoGP)	[194]
GP of oligodendroglial cultured cells, 99+77 kD IEC → WL	WL better than Con A, LL (no b with CL-1 LL SL, dolichos L)	[195]
GP from bovine brain oligodendroglia, 99+77 kD IEC → WL	WL (yield 70%)	[196]
GP from human brain myelin and oligodendrocytes, 120 kD AL → AL	AL (b)	[197]
Antigen of mouse cerebellum Purkinje cells, 400 kD GF → Con A → GF	Con A (b)	[198]
GC binding hyaluronic acid from 8-week mouse brain (GC is more than 50% proteoglycans) PL → GF → DEAE	WL (89–100%; 22 times)	[199]
R for α-latrotoxin (neurotoxin) from bovine brain cortex, 280–320 kD (200+160+79+43) DEAE → WL → Ab	WL (70%; 4 times), b α-SU of toxin (200+160)	[200, 201]
Complex of scorpion α-toxin with rat brain Na-channel	WL (b β-SU of Na-channel)	[202]
GP of cows milk lipid droplets GP-1, 2, 3, 4, 5, 6, 7	Con A, WL GP-1, 2, 6 b GP-3, 4 retarded GP-7 not b	[203]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
R for endogenous factor–cobalamin from porcine and human ileum, 75+65+43 kD	WL, LL and Con A (b 45–79%); WL (b 75 kD); LL and Con A (b 75+65+43 kD)	[204]
Histocompatibility antigens H-2^b from mouse RBL-5 tumour cells GF → WL → Ab	WL (80%; 8 times)	[205]
Other class II histocompatibility antigens	5 lectins***	[206–208]
GP of mouse small intestine and teratocarcinoma cells Dolichos L → dolichos L	Dolichos L	[209]
GP binding collagen from mouse MDAY-D2 lymphoreticular tumour cells (collagen type II R), 110+130 kD WL → L-FGA → GF	WL (b)	[210, 211]
GP from human embryonic PA-1 carcinoma cells, 80–120 kD	Thorn apple L (b)	[212]
R for type I fimbriae (lectin) of *E. coli* from guinea pig erythrocytes, 65 kD	Fimbriae type I, Con A (b)**	[213]
SialoGP of Morris hepatoma 7777 cells	WL (b)	[178]
Epitectin (Ca-antigen) of human pharyngeal carcinoma cells, 1–1.5 MD (390+350 kD) Ab → WL	WL (irreversible binding)	[214]
Preneoplastic antigen in liver carcinogenesis from malignant nodes of rat liver, 145 kD (2 SU) GF → Con A	Con A (73%; 6 times)	[215]
GP of human malignant melanoma SK-Mel-37 cells, 110 kD Con A → WL	Con A → WL (b)	[216]
GP of rat hepatoma cells, 130 kD Con A → GF → (Ab to alkaline phosphatase)	Con A (b)	[217]
GP of rat liver and Morris hepatoma 7777 cells, 60+80+100 kD Con A (HPLC), Con A	Con A (HPLC) (b)	[218]
Antigen from Walker 256 rat carcinoma cells, 57 kD CM → WL → Phe; Con A	WL (removal of 98% contaminating protein)	[219]
GP of human embryonic PA-1 carcinoma cells, 80–120 kD	Thorn apple L (b)	[166]
GP of HM-1 pluripotent embryonal carcinoma cells, more than 90 kD	*Phytolacca* L (b 48%) Thorn apple L and lotus L (17% b), PTL (no b)	[220]
Dystrophin complex from rabbit dystrophic skeletal muscle, 156+50+43+35 kD	WL (removal of myosin and ATPase)	[51, 221]
Tumour antigen associated with *Herpes simplex* virus from human liver carcinoma, 70 kD GF → DEAE → GF → Con A	Con A (b)	[222]
GP of BNK-21 cells infected with *Herpes simplex* virus	Con A (b)	[203]
Major GP induced by Epstein–Barr virus, 320 kD DEAE → CL-2	CL-2 (100%; 144 times)	[223]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, %; purity, times in parentheses, notes)	Refs.
Histocompatibility antigens HLA-DR and MB from human lymphoblastoid cells transformed by Epstein–Barr virus	CL-2 (b)	[224]
R for measles *virus* from *Vero* cells	LL (b) PL (b)	[225]
R for the minor group of rhinoviruses from human *HeLa* cells, 450 kD LL → GF → IEC	LL (yield 100%) CL-2 (yield 100%) Con A (yield 20%)	[226]
Transcript GP of nuclear pore membranes of monkey COS-1 cells, 62 kD	succWL (b)**	[227]
Glycoconjugates of inducers of human and animal diseases		
Recombinant GP-160 of HIV-1 from Vero cells infected with two vaccinia viruses LL → (Ab to GP-41) → mono Q → LL	LL (b)	[228]
Prion GP from brains of hamsters with virus-like infection, scrapie type of illness, 26+28 kD	LL, CL-1 (b asialoGP)** out of 6 lectins	[229]
Antigen of the pneumonia initiator, *Pneumocystis carinii* bacteria, from infected ferret lungs, 66–110 kD Superose-12 → Con A	Con A better than WL (SL and asparagus lectin no b)	[230]
Bacterial antigens (vaccines) of the *Bordetella* family	L (b)	[231]
GP from the coating of spores of *Bacillus sphaericus* 1593 (toxin for gnatworm) *Culex pipiens*	Con A (b)	[232]
GP of plasma membranes of *Spiroplasma citri*, 84 kD	Con A (b)	[233]
Antigens of promastigotes of 14 strains of *Leishmania*, 14–86 kD	Potential lectin sorbents (14 L)***	[234]
Surface antigens of protozoa *Trypanosoma brucei brucei* variant AnTat 1.1, 60+94 kD Con A → HPLC (RP)	Con A (separation of 94 and 60 kD)	[235]
Antigens of epimastigotes of protozoa *Trypanosoma cruzi* (72 kD) and specimens of the metacyclic phase (90+85+55 kD) CB → DEAE → WL → Con A → GF (72 kD) CB → DEAE → WL → HA → Con A (55 kD)	WL (different affinity for each antigen)	[236]
GP-85 of infectious tripomastigote form of *Trypanosoma cruzi*, including sialic acid and residues of fucose and α-1,3-galactose	WL → WL**	[237]
Protective Ag of ringed tick (vaccine), 86 kD WL → Con A → EP → WL → GF (HPLC)	WL and Con A (b)	[238]
Filarial surface antigens of adult nematode–parasites *Brugia malayi*, 29+(17–200) kD	Con A, WL, SL, lotus L	[239]
Tegumental glycoconjugate antigens of adult specimens of *Schistosoma mansoni*, 23–300 kD, 24 kD	Con A and LL** (out of 7 lectins)	[240–242]
GP of *Schistosoma mansoni* from infected mice, 170 kD	AL (b)	[243]
Virulence antigens of the 3rd stage of the nematode–parasite *Trichinella spiralis*	LL (b)	[244]

Table 1 (contd.).

Receptors, sources, schemes of purification (sorbents)	Result of using IL (yield, % purity, times in parentheses, notes)	Refs.
Glycoconjugates of microscopic fungi		
Adhesin R of cells of the slime fungus *Dictyostelium discoideum* at a late stage of development, 95+(40–50) kD	WL (b)	[245]
GP-34 specific for the 'stalk' stage of the slime fungus *Dictyostelium discoideum* NC4 (absent from spores)	WL (b)	[246]
Antigens of the mycelial fungi *Aspergillus fumigatus, Mucor pusillus, Petriellidium boydii, Trichophyton rubrum*	Con A (b)	[247]

*Lectin affinity chromatography was the most effective purification stage;
**Investigation of receptors in combination with their treatment with endo- and exoglycosidases;
***Affinity for labelled lectin.

Abbreviations used

Ab—antibody;
MAb—monoclonal antibody
AL—arachis lectin
Asn—asparagine
ATP—adenosine triphosphate
AC—affinity chromatography
b—binding
BSA—bovine serum albumin
CB—Cibacron Blue
cGMP—cyclic guanosine monophosphate
CL—castor oil plant lectin
CM—carboxymethyl
Con A—concanavalin A
DEAE—diethylaminoethyl
EP—electrophoresis
GF—gel filtration
GL—gorse lectin
GP—glycoprotein(s)
Gp—glycopeptides
GrL—griffonia lectin
HA—hydroxyapatite
HIV-1—human immunodeficiency virus type 1
HPLC (RF)—high performance liquid chromatography (reversed phase)
IEC—ion-exchange chromatography
L—lectin(s)
L-FGA, E-FGA—bean lectin (leuco and erythro forms)
LL—lentil lectin
OS—oligosaccharides
PL—pea lectin
PS—phosphocellulose
PTL—potato tuber lectin
SDS—sodium dodecyl sulphate
SL—soyabean lectin
SU—subunits
succWL—succinylated wheat-germ lectin
Receptor nomenclature from *Trends in Pharmacological Sciences*, 1991, Supplement, 35 pp

Purification of receptors or separation of their subpopulations is also possible by retardation of the glycoprotein during elution from the lectin sorbent without the use of desorbing carbohydrates (i.e. due to weak affinity interactions with the lectin).[161,203,284] Separation by retardation on elution has also been described for mixtures of glycopeptides when using immobilised bean or castor-oil plant (*Ricinus communis*) lectin which confirms the effect of glycans on elution behaviour.

The simplest procedures for purifying receptors comprise filtration through one lectin sorbent (absence of binding) and binding with another lectin sorbent (concentration of receptors) for example by the scheme: wheat-germ lectin (WL^-)→Con A^+ or Con A^-→WL^+, as in the case of trypanosome antigens or rat kidney ATPase.[236,301] Other purification schemes are also used, for example lentil (*Lens culinaris*) lectin (LL^+)→WL^+ (fibronectin receptor[134]), LL^+→Con A^+ (prothrombin precursor[317]), WL^+→LL^+→castor-oil plant lectin-1 ($CL\text{-}1^+$) (insulin receptor[89]), WL^+→bean leucoagglutinin ($L\text{-}FGA^+$).[210,211] The combination of Con A^+→WL^+ is used in the case of melanoma antigens, dipeptidase IV and Mg^{2+}-ATPase,[216,290,291,305] and WL^+→Con A^+ in the case of the protective antigens of arthropods.[238] The examples of combination chromatography on lectins indicated above enable the separation of multiple forms (subpopulations) of receptors and an increase in the overall yield of any receptor heterogeneous in the carbohydrate portion. An example of appreciably increasing yield is the purification of dipeptidyl-dipeptidase IV by affinity HPLC on paired columns of immobilised Con A and WL.[291] In several cases rechromatography of antigens and receptors on immobilised LL,[228] WL,[46,69] dolichos (*Dolichos biflorus*) lectin[209] or peanut (*Arachis*) lectin[197] is used.

As is evident from Tables 1 and 2 the maximum degree of purification of receptors when using a particular type of lectin is achieved in the majority of cases by varying the first stages of purification immediately after solubilisation of the receptors with detergent. However it must be remembered that chromatography of crude preparations may lead to irreversible contamination of the lectin sorbent and a reduction in its affinity capacity.[125,150,291] In addition preferential binding of some receptors at the expense of others to WL at the first stage of purification may be expected, for glycoproteins from thrombocytes for example.

Lectin affinity chromatography of receptors is frequently used in combination with other affinity sorbents. Paired columns of immobilised thyrotropin and griffonia (*Bandeiraea simplificifolia*) lectin-I (GrL-I) enable thyrotropin receptors to be purified 808-fold.[108] Immobilised heparin and WL are convenient, following

(Con A)-sorbent, for the removal of thrombospondin and fibrinogen from a preparation of thrombocyte glycoproteins IIb–IIIa.[150] Immobilised WL is convenient, following immobilised fibroblast growth factor (elution of heparin receptors), for the removal of heparin from the receptor preparation.[118] After chromatography of thymocyte Thy-1 antigen on (Con A)-sorbent immobilised antibody to Con A was used to remove lectin molecules partially washed out from the sorbent with desoxycholate.[160] When purifying carcinoma cell galactosyl transferase the filtrate from the (CL-1)-sorbent was applied to immobilised *N*-acetyl-D-glucosamine.[254]

Table 2. Purification of enzymes (receptors) bound to cell surfaces and organelles with immobilised lectins.

Enzymes, sources, purification schemes	Result of using IL (yield, %, purification, times, notes)	Refs.
Oxido-reductases		
L-Trp oxidase of field cabbage (peroxidase-like)	Con A (83%, 4 times)	[248]
Ribonucleotide reductase of rat liver, SU 89 kD	Con A (b)	[249]
Peroxidase from human placenta	Con A (90%, 20 times); removal of eosinophilic peroxidase, myeloperoxidase, catalase and cytochrome P-450	[250]
Dopamine-β-hydroxylase associated with the β-adrenergic R from bovine adrenal medulla Con A→DEAE→GF (HPLC)	Con A (66%; 120 times)*	[251]
Dopamine β-hydroxylase from rat adrenal, 300 kD (SU 75 kD) Con A → GF (HPLC) → IEC (HPLC)	Con A (removal of chromogranins)	[252]
Tyrosinase from hamster melanoma DEAE → GF → Con A	Con A (80%; 7 times)*	[253]
Transferases		
N-Acetylglucosaminide-β-1,4-galactosyl transferase of mouse F9 carcinoma cells IEC → XL–1 → Acetylglucosamine → α-Lactalbumin	CL-1 (no b)	[254]
Galactosyl transferase of the Golgi apparatus of the budding yeast *Schizosaccharomyces pombe*, 61 kD DEAE (HPLC) → UDP-hexanolamine → Con A → Mono Q	Con A (73%; times) GL-1 (b)	[255]
Tyr-protein sulphotransferase of the Golgi apparatus of bovine adrenal cells, 50–54 kD	WL (b 37%)**	[256]
N-Heparan-sulphate sulphotransferase of rat liver, 97 kD DEAE → Heparin → ADP → WL	WL (44%; 3 times)	[257]
Oligosaccharyl transferase, stabilised with phosphatidylcholine, of calf thyroid microsomes	Con A (b)	[258]
Tyr kinase of cat brain (R of colony stimulating factor type 1 or obtained from growth factor of thrombocytes), 145 kD	WL (b)**	[121, 259]
Tyr kinase of insulin R of rat brain and liver	WL (b)	[260, 261]
Protein kinase/interleukin-1 R from rat liver mesangial cells in culture (SU 48 kD)	WL (b)	[262]
Phospholamban kinase of mammalian heart sarcoplasmic reticulum cells, SU 56+53 kD	affinity for Con A	[263]
Arginine-specific ADP-ribosyl transferase of animal skeletal muscle microsomes, SU 39 kD DEAE→Con A→GF (HPLC)	Con A (88%; 50 times)* WL (no b)	[264]
Poly A polymerase of the nucelar membrane of rat liver cells, 64 kD	Con A (5 times)**	[265]
Esterases		
p-Nitrophenyl acetate esterase type A from rat liver microsomes, 61 kD Con A → GF → DEAE → HA	Con A (80%; 3 times)	[266]
Carboxy esterase E1 from rat liver microsomes, 175 kD (SU 59 kD)	Con A (b)**	[267]
Peptidase associated with acetylcholinesterase of the electric eel and ewe brain basal ganglia AC → GF → Con A	Con A (b)	[259]
Alkaline phosphatase of fly integument, 180 kD Con A → GF → GF	Con A (b)	[268]
Phospholipase A-1 of rat liver lysosomes Con A → Chromatofoc. → GF; (Orange + Red agarose) → Con A → Phe	Con A (156%; 165 times)*	[269, 270]
Acid phosphatase of promastigotes of Mexican and Brazilian Leishmanii (inhibited with citrate) GF → DEAE → Con A	Con A (72%; 14 times)*	[271]
3′-Nucleotidase/nuclease of promastigotes of *Leishmania donovani*, 43 kD	Contains Asn-OC, available for L**	[272]
5′-Nucleotidase of rat heart, 74 kD CM → Con A → DEAE → ADP	Con A (123%; 13 times)	[273]
5′-Nucleotidase of rat kidney, 69 kD Con A → ADP	Con A (94%; 17 times)	[274]
5′-Nucleotidase of bovine thyroid, 150 kD (2 SU) LL → AMP	LL (81%; 10 times)*	[275]
Cell wall ribonuclease of the fungus *Aspergillus oryzae*, similar to ribonuclease T-2-L in carbohydrate composition	Possible affinity for Con A	[276, 277]
Sphyngomyelinase of human placental lysosomes, 123 kD (SU 62 kD) Con A → Sphyngosylphosphorylcholine → Hexyl → IEC (HPLC)	Con A (100%; 21 times)	[278]
Nucleotide pyrophosphatase of human placenta CB → AMP → WL → ADP → GF → DEAE	WL (96%; 2 times)	[279]
Nucleoside diphosphatase type B from rat brain, 75 kD (thiamine pyrophosphatase associated with 1D4) DEAE → Con A → GF → CB → Cu^{2+} chelate → GF	Con A (48%; 6 times)*	[280]
Glycosidases		
α-Glucosidase of human placental lysosomes, 110 kD Con A → GF	Con A (99%; 12 times)	[281]
Glucosidase II-processing GP from cow mammary gland, 290 kD Con A → HA → DEAE	Con A (79%; 8 times)	[282]
Glucosidase II-processing GP from bean shoots and soya cell culture, 220 kD (2 SU) DEAE → HA → Con A → GF	Con A (73%; 10 times)	[283]

Table 2 (contd.).

Enzymes, sources, purification schemes	Result of using IL (yield, %, purification, times, notes)	Refs.
α-1,2-Mannosidase-processing GP from rabbit liver microsomes, 52 kD DEAE → Con A → GF → CB → GF	Con A (77%; 27 times)*	[284]
β-Fructofuranosidase from radish cell walls (similar to cytoplasmic)	4 L	[285]
Trehalase of the American cockroach, 110 kD Con A → GF	Con A (48%; 32 times)	[286]
Trehalase of the brush border of rabbit renal cortex Phe; Con A	Con A (b 20%)	[287]
Saccharase–isomaltase complex from a biopsy sample of human small intestine, 210+212+245 (SU 145+130 kD)	LL (all forms b), snail L (b 212 and 245 kD)	[288]
N-Acetylglucosaminidase from spermatozoids of the surface membrane of *Phallusia mammilata*, 158 kD (2 SU) DEAE → Phenyl → Con A → EP	Con A (69%; 2.5 times)	[289]
Proteases		
Dipeptidyl peptidase IV of rat liver Con A → WL → Arg; Con A (HPLC) → WL (HPLC)	Con A → WL (74%; 46 times), Con A (84%; 32 times)	[290, 291]
Carboxypeptidase N from human placenta, 280 kD HA → LL → Histargin	LL (27%; 2.5 times)	[292]
Carboxypeptidase M from human placenta, 62 kD	Con A (b)	[293]
Aminopeptidase N from rabbit intestine	WL (b)	[95]
Aminopeptidase N from porcine intestinal mucosa, 130 kD SU (Stilbenedisulphonate) → Con A	Con A (37% yield, removal of SU 90 kD)**; affinity for CL-1, WL, tomato L	[294]
Peptidase dependent on Ca^{2+} participating in the action of the pairing pheromone of yeast *Rhodosporidium toruloides* (type 'a' cells) DEAE → Con A	Con A (107%; 3.3 times)	[295]
Proteinase of the surface of promastigotes of various *Leishmanii* species, 63 kD SU	Con A and LL (b)	[296]
Trypsin-like proteinase/esterase specific for Arg from rat liver insulin R	Con A (b)	[297]
Cysteine proteinase/neutral gelatinase from human malignant LOX melanoma cells SU 170 kD Sephacryl → WL	WL (purification; 10 times; removal of metalloproteinase with SU 50 kD	[298]
Other hydrolases		
Lipoamidase of pig brain, 140 kD CM → DEAE → GF → WL	WL (purification 10 times)	[299]
Ampicillin acylase of bacteria *Pseudomonas melanogenum*, 146 kD (2 SU)	Contains 13% hexose with probable affinity for L	[300]
NAD-glycohydrolase of bovine thyroid (probable thyrotropin R) GF → LL	LL (b)	[301]
Na^+, K^+-ATPase of rat kidney cortex microsomes, 95+54 kD Con A → WL	Con A (no b), WL (b β-SU, 54 kD)	[302, 303]

Table 2 (contd.).

Enzymes, sources, purification schemes	Result of using IL (yield, %, purification, times, notes)	Refs.
β-SU, Na^+, K^+-ATPase of rat brain (adhesion molecule on brain glial cells) and porcine intestine, 60–80 kD	WL and CL-1**, better than Con A	[303–305]
Mg^+-ATPase of rabbit skeletal muscle, 107 kD Con A → WL → IEC (HPLC)	Con A, WL, LL (b)	[51, 306]
ATPase of dog kidney and human K562 cells (P-glycoprotein), 170 kD	WL, Con A and CL-1 (b), AL (no B)	[307–309]
ATPase 'P' type (forming phospho intermediate) from cholinergic synapses of cells of the electric organ of *Torpedo californica*, 110+104+98+60 kD HA → WL → GF (HPLC)	WL (71%; 2 times)	[309a]
GTPase of rat olfactory neurones, 55 kD	Con A-FITC (b)***	[310]
Lyases		
Carbonic anhydrase of ovine salivary gland, 540 kD (SU 45 kD) Sulphonamide → WL → GF	WL and Con A (b)**	[311]
Catalytic component of bovine brain adenylate cyclase sensitive to hormone, 120 kD	WL (30%; 2 times)	[312]
Catalytic component of the adenylate cyclase system of bovine brain cortex sensitive to calmodulin, 155 kD Calmodulin → WL	WL (52%; 12 times)	[313]
Atrial natriuretic factor R with and without cyclase activity (guanylate cyclase) from bovine adrenal glomerula cells GTP → WL	WL (55%; 1.3 times)	[314]
Particle-bound highly active guanylate cyclase of rat lung Con A → GTP	Con A (25%; 3–6 times)	[315]
Phosphorylated form of guanylate cyclase of sea urchin sperm, 160 kD GTP → DEAE → Con A	Con A (5 times)	[316]
Carboxylase from rat liver microsomes dependent on vitamin K	Con A (b 80%) LL (b 70%)	[317]

*Lectin affinity chromatography was the most efficient step in the enzyme purification

**investigation of the enzyme in conjunction with its treatment with endo- and exoglycosidases

***affinity for non-immobilised lectin

Abbreviations used (see also Table 1)

ADP—adenosine diphosphate
AMP—adenosine monophosphate
ATP—adenosine triphosphate
FITC—fluorescein isothiocyanate
GrL-I—griffonia lectin-I
GTP—guanosine triphosphate corr
RNA—ribonucleic acid
UDP—uridine diphosphate

Enzymes are named in accordance with the International Classification (Enzyme Nomenclature, Recommendations of the Nomenclature Committee of the International Union of Biochemistry, Orlando, Acad. Press, 1984, 646 pp).

Tandem chromatography has also been used in other combinations of a lectin sorbent with non-lectin sorbents. Paired columns with immobilised Con A and phenylalanine are effective in the purification of phospholipase A_1,[270] with Affigel S-145 and with immobilised WL in the case of the thromboxane A_2 receptor.[155] A technologically simple procedure is the filtration of partially purified receptors through carboxymethyl sorbents before and after immobilised WL for receptors of interleukin 4 and glycoprotein CDw 44.[163,164] The possibilities of tandem chromatography using a lectin sorbent are well illustrated for the thromboxane receptor which was purified 1620-fold on paired columns directly from the crude solubilised protein extract.[155] In addition paired combinations of lectin and non-lectin sorbents give an increase in the yield of receptors.[155]

The use of immobilised Con A, PL, WL and CL-1 in variants of affinity HPLC is promising for the purification of membrane-bound glycoproteins.[176,187,218,291]

2. Solubilisation of receptors and features of the lectin affinity chromatography of receptors

Many factors are important when carrying out lectin affinity chromatography. These are the solubilisation method to increase receptor solubility, buffer composition (detergent type, organic solvents, buffer types, pH, ionic strength, presence of metal cations or EDTA, the need to reduce disulphide bonds in proteins, protease inhibitors, phospholipids, etc.), method of application, washing and elution, times and temperatures. For each receptor purification it is necessary to select the optimum procedure for lectin affinity chromatography depending on the lectin sorbent chosen (lectin type, matrix, means of lectin immobilisation, capacity of sorbent for conjugated lectin or binding of model glycoconjugates, conditions for regeneration and storage for repeated use). The actual procedure for chromatography on a lectin sorbent under the conditions selected is a simple operation. The complexity of working with a lectin sorbent is seemingly determined by the presence in these proteins not only of carbohydrate-binding regions but also of regions of hydrophobic binding, binding of cations of divalent metals and by the presence of other domains.

Perhaps the most complex factor is the selection of the means of solubilising receptors (type of detergent or solubilisation by treatment with hydrolases).

Most frequently 0.5–1.0% Triton X-100 (TX-100) is used for the solubilisation and lectin affinity chromatography of receptors. TX-114 has also been used, for example in the case of glycoproteins of thrombocytes and kidney.[149,152,190] Carbohydrates are also used occasionally for solubilisation instead of TX.[202] Since high concentrations of TX-100 cause desorption (washing off) of lectin from the sorbent,[218] lectin affinity chromatography of receptors is carried out at concentrations of detergent lower than in the initial solubilisation in the crude extracts when using immobilised Con A,[218,255,259,286] WL [97,119,125,202,279] or dolichos lectin.[209] Extremely low TX-100 concentrations (0.01–0.02%) were effective in the purification of olfactory receptors.[107,309] The absence of TX-100 did not permit elution of receptors even at high carbohydrate concentrations (0.5–1.0 M) in the case of (Con A)-sorbent.[182,215,259] As a rule, it is important to control the ionic strength of the buffer when selecting the detergent concentration. The buffer ionic strength is usually increased during lectin affinity chromatography from 0.1–0.2 M to 0.4–0.5 and even to 1 M NaCl or KCl in the case of receptors of neurotoxin or bovine dopamine.[75,200] Chromatography of receptors on WL-sorbent is carried out as a rule in the presence of 5–10 mM Mg^{2+} ions[77,97,107,119,125,279] and/or 1–2 mM Ca^{2+} ions.[45,46,50,52,131,133,142–145,200] Ca^{2+} cations are also used in the chromatography of receptors on FGA- and (CL-2)-sorbents but in the case of Con A-, LL- and (pea lectin)-sorbents 0.5–1.0 mM manganese, potassium and magnesium chlorides are used together.

Various combinations of TX-100 and Na desoxycholate are also used,[34,210,211,239,289] although in some cases the preferential use of nonionic detergents (TX-100 and CHAPS) rather than cholate has been recorded, such as on solubilisation of the serotonin transporter, Na-channel, etc.[23,31,36] Cholate (0.5–1.5%) is used in the solubilisation of erythrocyte Cad-antigen, liver esterase, the antigens of nematode parasites and AIDS virus, 5′-nucleotidase and macrophage receptors.[172,184,239,266,275] During lectin affinity chromatography the cholate concentration may vary depending on the type of receptors being investigated. For Dopamine receptors 0.2–0.3% is used,[73–75] for tumour glycoproteins[210,211,216] and proteins of T-lymphocytes[160,164] and thrombocytes 0.4–0.5%,[154] for thyroid gland glycoproteins[275,289] 0.6% and for the L-Glu receptor 0.05%.[33a]

A 0.5–2% solution of 3-[3-(cholamidopropyl)dimethylammonium]-1-propanesulphonate (CHAPS) is widely used for the solubilisation of receptors.[57,77,94,111,112,248,265] It is seemingly promising to use fractionation of receptors with detergents. In the case of vasopressin receptors, contaminants are removed by a preliminary treatment with 0.5% CHAPS and the actual receptors are solubilised in high yield on subsequent treatment of the extract with 2% CHAPS.[94] When solubilising Ca-binding sarcolemma glycoproteins and receptors of corticotropin releasing factor 6–8 mM CHAPS is used.[42,115] The concentration of CHAPS varies in the following way during chromatography on WL-, Con A- or (CL-2)-sorbent: 20 mM for the glutamate receptor,[33] 0.1–0.8% for other transporter glycoproteins[28,41,52] and 1% for receptors of inositol triphosphate, the bacterial antigen of infected ferret lung cells and carboxypeptidase M.[55,230,293]

One more nonionic detergent, Nonidet P-40 (NP-40), is widely used for the solubilisation of receptors at concentrations of 0.5–2%.[72,129,143,159,161,212,224,283,295,303] Lower concentrations of NP-40 are used during chromatography on lectins, e.g. 0.1–0.2% for WL- and (Con A)-sorbents,[72,318] 0.4–0.5% for immobilised Con A,[258] LL,[168] WL,[100,145] AL [159] and thorn apple lectin.[212] The concentration of NP-40 was reduced from 0.4 to 0.07% at the stage of eluting receptors with carbohydrate.[258] The need to use 0.4% NP-40 for oligosaccharide transferase is explained by the fact that the glycans of this glycoprotein bound to asparagine are inverted inside the membrane vesicles and do not react with the lectin without previous treatment with a relatively high concentration of detergent.[258]

Digitonin (1–2%) is also used for the solubilisation of receptors.[45–47,50,51,53,54,59,61,64–66,68,76,79,80,93,98] Occasionally it is expedient to change the type of detergent. Thus, after solubilisation of receptor complexes with 1% digitonin (for example Ca channels) the components of the complexes may be separated successfully using 1% TX-100.[54,84] Digitonin (0.1%) is used in the chromatography of opioid receptors,[59,61,64] receptors of dopamine and cholecystokinin,[76,79,80,98] α_1-adrenergic receptors,[65,66] and receptors of dihydropyridine and Ca channels.[45–47,49–51,53] Chromatography is usually carried out in this way on WL-sorbent although there are also data for immobilised CL-2,[98] LL and Con A.[59,64,98,305]

n-Octyl-β-D-glucopyranoside (0.05–0.2 M) is also used for the solubilisation of receptors.[128,131,135,137,141,144,226] The octylglucoside (40–50 mM) is included at the stage of purification by gel filtration as in the case of β_1-integrin and sphingomyelin.[137,278] The octylglucoside (2 mM) is used during chromatography of glycoproteins of animal lung alveoli on immobilised *Maclura* lectin.[186] Yeast peptidase solubilised in NP-40 was chromatographed on (Con A)-sorbent in the presence of 0.3 mM octylglucoside.[295]

Sodium dodecyl sulphate (SDS: 2%) is also used for the solubilisation of receptors of slime mould antigen,[246] the cationic detergent DTAB for H^+,K^+-ATPase[303] and 8 M urea for the bacterial antigen of infected ferret cells.[230] Tween-20 or Tween-40, Renex-30 or Brij are used for lymphocyte receptors[130,160,164] Lubrol PX for adenylate cyclase and guanylate cyclase[312,313,315,316] and lysolecithin in combination with other detergents for Mg^{2+}-ATPase.[305] Replacement of Brij (0.5%) by cholate (0.5%) or Zwittergent (1%) is used in the purification of antigens on WL-sorbent.[164,238] Emulgen-109P (1%) is also used for the chromatography of fucosylated erythrocyte proteins on immobilised aleuria (*Aleuria aurantia*) lectin,[169] Zwittergent (0.5%) in place of TX-100 (0.5% for the chromatography of Purkinje cell antigen on (Con A)-sorbent,[198] Tween-60 (0.1%) in the purification of adenylate cyclase[312,313] and Lubrol (0.1–1%) in the purification of guanylate cyclase[315,316] on immobilised WL and Con A respectively.

Occasionally $C_{12}E_8$ [n-dodecylocta(ethyleneglycol) monoester] is used, 1% for solubilisation[307,309a] and 0.1% for lectin affinity chromatography.[294]

Traditionally SDS is used during lectin affinity chromatography, 0.01% at the stage of eluting with *N*-acetyl-D-glucosamine for WL-sorbent,[40,302] 0.1–0.5% for (Con A)-sorbent[203,235,318] or WL-sorbent,[246] 1% for the non-specific elution of receptors, particularly for immobilised SL, CL-1, Con A and LL.[165,195,318] The use of such a set of non-specific elutions will possibly be useful for regenerating lectin sorbents. However, it is necessary to keep in mind that SDS may be precipitated as a solid in the presence of metal cations,[203] and may wash out lectin from the sorbent and reduce the lectin capacity, as in the case of immobilised Con A.[235] In addition some proteins are able to form complexes (such as dimers) even in the presence of SDS as in the case of the opioid receptors.[62]

The multistage process of receptor chromatography on a lectin sorbent (application, different variants of washing the sorbent, elution of receptors) is characterised by a reduction in detergent concentration or by variation of combinations of different detergents and by the possible absence of detergent at the very last stage, viz. elution of receptors with carbohydrate. This is seen when purifying thrombocyte glycoprotein-Ib,[148] lymphocyte antigen CD 43,[165] dopamine receptors,[77] sarcolemma receptors,[42] yeast galactosyl transferase,[255] insulin receptors[92] and adrenal glycoproteins[191] using immobilised WL. The detergent itself (SDS) was ineffective even at high concentrations in comparison with *N*-acetyl-D-glucosamine in eluting the purified receptors from the WL-sorbent.[165] Desorption of receptors with carbohydate without a detergent (TX-100) did not occur for the (Con A)-sorbent (see above).

Treatment of extracts or purified membrane glycoproteins with a chloroform–methanol mixture was also carried out to solubilise phospholipid-containing glycoproteins (such as ligatin) or to remove lipid contaminants.[171,237,319] Treatment with organic solvent is seemingly also important when regenerating the lectin sorbents used in the first stages of purifying receptors because of the contamination of the sorbents with glycolipids.[291]

Apart from the means of solubilisation enumerated above there is undoubted interest in the data on the solubilisation of receptors with hydrolases since the soluble receptors obtained frequently do not even require the presence of detergents in the elutant during lectin affinity chromatography. Phospholipase C is used for the solubilisation of hepatoma glycoproteins,[217] trypsin for lysosomal enzymes,[280] trypsin in combination with TX-114 for CD 36 antigen,[152] Ca^{2+}- and thiol-dependent proteinase for thrombocyte glycoprotein-Ib,[148] papain for lymphocyte Fc-receptors solubilised with Tween and Renex and purified on a WL-sorbent[130] and lysozyme for the treatment of the high molecular form of fly integument alkaline phosphatase associated with chitin and purified on a (Con A)-sorbent.[268] Trypsin was also useful for the separation of the subunits of the saccharase–isomaltase complex from human intestinal membranes.[287]

Organic solvents are used together with detergents during receptor chromatography on immobilised lectins and improves the stabilisation of receptors while reducing hydrophobic interactions between receptor and lectin. Ethyleneglycol is used in chromatography on (Con A)-sorbent, 1 M for the purification of Thy-1 antigen,[160] 20% for phospholipase A_1 [269] and 10% (together with 25% glycerol) for guanylate cyclase.[316] The increase in concentration of ethyleneglycol used may be compensated by a reduction in the concentration of carbohydrate eluting the receptors,[160] which indicates the possibility of also using carbohydrate for reducing the hydrophobic binding of receptors with the lectin. Chromatography on immobilised GL-1 was carried out in the presence of glycerol (5%) but the concentration of glycerol was varied when using WL-sorbent from 10% [38,50,52,111,117,163] [for (Con A)-sorbent[310]], to 20% [155,246,257] [for (Con A)-sorbent[258]] or 30%.[107]

β-Mercaptoethanol (1 mM)[235,303] was used in the purification of the rat inositol triphosphate receptor and of trypanosome antigens on a (Con A)-sorbent and 10 mM β-mercaptoethanol in combination with 2% detergent in the isolation of the glycosylated subunits of ATPase on WL-sorbent.[56] Evidently other agents capable of reducing disulphide bonds in protein complexes may also be used.

Problems of eluting receptors, bound to lectin sorbents, with carbohydrates are important. Excess concentrations of carbohydrates are usually used (up to 0.5 M, more rarely 1 M monosaccharide) as in the following, α-methyl-D-mannopyranoside and α-methyl-D-glucopyranoside for Con A, LL- and PL-sorbents, *N*-acetyl-D-glucosamine for immobilised WL and thorn apple lectin, lactose or D-galactose for immobilised CL-1, CL-2, AL and SL, *N*-acetyl-D-galactosamine for SL and L-fucose for immobilised GL-1 and aleuria lectin. Occasionally stepwise elution with increasing concentrations of carbohydrate or a linear carbohydrate gradient is used, such as in the purification of membrane-bound oxidase[248] and histamine receptors[81] on (Con A)-sorbent or membrane-bound lipoamidase,[296] receptors of dihydropyridine and dopamine transporter[49,80] on WL-sorbent. Firstly this enables removal of contaminating glycoproteins with a lower affinity for the lectin, secondly, it permits separation of subpopulations of receptors close in physicochemical properties, thirdly, it enables removal from the sorbent of firmly bound glycoproteins with the aim of regenerating the immobilised lectin, fourthly, it affords a quantitative assessment of the strength of the binding of the purified receptors to the lectin in order that excessive concentrations of carbohydrate are not used for subsequent desorption. It was shown that lipoamidase was eluted at 60 mM *N*-acetyl-D-glucosamine,[296] dopamine transporter at 125 mM *N*-acetyl-D-glucosamine,[80] histamine

receptors at 80 mM α-methylmannoside,[81] but Trp oxidase was separated into forms eluted at 10, 20 and 50 mM α-methylglucoside respectively.[248] Before elution of receptors with a carbohydrate specific for the lectin it was useful to wash the lectin sorbent either with lower concentrations of the same carbohydrate (a variant of the stepwise elution with carbohydrate) as for LL- and (Con A)-sorbents[134,293,294] or with a carbohydrate non-specific for the lectin at a relatively high concentration (0.5 M) as for WL- and (griffonia lectin-I)-sorbents.[108,183,227] When working with immobilised bean lectin, the elution of lymphocyte receptors was carried out without using carbohydrate (monosaccharides were unsuitable for this lectin which is specific for oligosaccharides) by acidifying the elutant to pH 3 [158] as was used for the elution of eukaryote nuclear glycoproteins during chromatography on WL-sorbent.[227]

When working with immobilised WL, significantly more effective eluting agents are used in place of *N*-acetyl-D-glucosamine. These include chitotetraose,[192] 3–10 mM chitotriose[100,110–112,163] or 15 mM chitobiose (containing 10 wt.% chitotriose as contaminant) as for immobilised thorn apple lectin.[161] It is not excluded that contaminating chitotriose and chitobiose in commercial preparations of *N*-acetyl-D-glucosamine make an appreciable contribution to the specific desorption of the receptors indicated above.

Provision of a relatively long contact time for the immobilised lectin and the glucoconjugate solution (when applying it) and with the desorbing carbohydrate (when eluting glycoconjugates and regenerating the sorbent) is a feature of lectin affinity chromatography. The contact time depends on the temperature. For complete binding of receptors with a WL-sorbent incubation of the mixture was carried out for 16–70 h at 4 °C [93,107,154,155,239] or 1.5–3 h [53,110,111] under conditions of suspending the sorbent[53,107,110,154,239] or recycling application of the receptors onto the sorbent as a variant of the column chromatography.[79,91,92,111,155] Elution of receptors from WL-sorbent with carbohydrate was carried out overnight[93] or for 1.5–3 h at 4 °C,[53,75] 15–20 min at room temperature[194,342] or with a double treatment with carbohydrate for 30 min and longer.[92,107,163] Extended contact of receptors and sorbent was also used for immobilised thorn apple, lentil, soyabean and lotus lectins.[134,212,239] When working with (Con A)-sorbent, the application of receptors was carried out for 12–21 h at 4 °C [239,316] or for 4 h at room temperature.[265] Desorption was carried out with portions of carbohydrate after incubation for a period of several hours[47,92,269] and increasing the temperature to 37 °C with the aim of reducing the hydrophobic binding of receptors to the lectin.[25,280]

An important factor of lectin affinity chromatography is the affinity or sorption capacity of the lectin sorbent determined either by binding model standard glycoproteins or by the quantity of lectin immobilised in 1 ml gel (the companies manufacturing lectin sorbents usually indicate the capacity from the amount of lectin in 1 ml gel). Since the data shown in Tables 1 and 2 comprise lectins immobilised on agarose in an overwhelming majority, data on the capacity of agarose sorbents will be considered below. The commercial preparations of WL-agarose (Sepharose, Affigel) most frequently used have the following lectin capacities: 5 or 1–2 mg ml^{-1} gel (Pharmacia, Sweden[65,214]), 6–10 mg ml^{-1} (E.Y. Lab., USA[36]), sorbent manufactured by Miles–Yeda (Israel[320]), 1 mg ml^{-1} (Bio-Rad, USA[124]) etc. In some cases investigators have synthesised the sorbents themselves, for example WL-Sepharose 4B (6–20 mg ml^{-1} [35,48,117]), WL-Affigel-10 (5–10 mg ml^{-1} [83,196]) and WL-Reactigel-6X (5 mg ml^{-1} [109]). Comparison of the synthesised WL-Sepharose sorbents with various lectin capacities in the range 0.08–10 mg ml^{-1} showed that one glycoprotein (glycophorin A for example) was well bound on the low capacity sorbent (0.08 mg ml^{-1}), but for other glycoproteins (such as fetuin, ovomucoid and α_1-glycoprotein or orosomucoid) capacities of more than 3 mg lectin per ml gel were necessary.[176] Erythrocyte glycophorin receptors and receptors from hepatoma cell were successfully obtained from crude extracts in good yield and a high degree of purity by purification in one step on WL-Sepharose (0.08 mg ml^{-1}).[176] When purifying insulin receptors, it was shown that the maximum yield of receptors was achieved using Miles-Yeda WL-sorbent in comparison with similar sorbents from other companies.[320] WL-agarose with a capacity of 4 mg ml^{-1} or above is most frequently used for purifying receptors. Exceptions are hepatoma cell sialoglycoproteins[124,176] and α_1-adrenergic receptors.[320] It was noted that when applying an excess quantity of receptors to a WL-sorbent its sorption properties were increased and there was a corresponding increase in the yield of material bound.[83] The same effect may also be observed on increasing the contact time of receptor and lectin (see above).

In the majority of the cases shown in Tables 1 and 2 the WL-sorbents are used as sialo-specific reactants for binding sialoglycoproteins which may readily be checked by treating the receptors with sialidase.[256] Immobilised succinylated WL is used as a sorbent specific for *N*-acetyl-D-glycosamine, as in the purification of the nuclear pore protein of mammalian cells,[227] or unmodified WL-sorbent for the purification of oligodendroglial glycoproteins.[196] It is better to use immobilised slug (*Limax flavus*) lectin in place of WL-sorbent for the purification of glycoproteins (such as eel Na-channels) which contain polysialic acids [(NeuAc-α-2,8-)$_n$].[35] Among the other widely used lectinagarose sorbents those with relatively high capacities may be mentioned such as 10–16 mg ml^{-1} gel for Con A (Pharmacia, Sweden), 12 and 4 mg ml^{-1} gel for CL-1 and bean erythroagglutinin.[156] The capacity of LL-Sepharose is 2 mg ml^{-1} gel (Pharmacia, Sweden). (Con A)-Sepharose of low capacity (0.5 mg ml^{-1}) is used for the purification of yeast peptidase.[295]

The means of immobilising the lectin onto the agarose may influence the binding of receptors. A comparison of the various means of activating Sepharose for the subsequent immobilisation of Con A showed that the maximum capacity of the sorbent for lectin at minimum selectivity towards glycoproteins was achieved for activation with cyanogen bromide, a significant reduction in capacity at maximum selectivity was found for activation with divinyl sulphone and intermediate results were obtained with glutaraldehyde.[321] Lectin–agarose sorbents immobilised with a carbodiimide have also been used for the purification of receptors.[156] It was noted that irrespective of the means of activating agarose the selectivity of the lectin sorbent was increased when applying an excess amount of the glycoprotein being purified.[321] It is possible that the reason for the irreversible binding of part of the applied glycoprotein when using a lectin sorbent obtained from cyanogen bromide-activated Sepharose (such as LL-Sepharose) is the presence of unblocked residues of carbonate and imidocarbonate groups, which are eliminated by previous treatment of the activated agarose with 0.1 N HCl.[322] An additional treatment of the immobilised lectin with glutaraldehyde in the presence of the appropriate lectin carbohydrate is recommended for the stabilisation of lectin sorbents with the aim of preventing washing out of lectin and reducing the sorbent capacity particularly in the presence of detergent.[58,318]

III. Investigation of receptor glycans with lectin sorbents

A selection of lectins with a known oligosaccharide specificity may serve as an effective instrument for the structural analysis of receptor glycans (see reviews on the specificity of lectins towards glycans[323,324] or glycoconjugates[21]). Such an analysis frequently leads, with the aid of combined chromatography, to lectins of the desired glycoproteins or their glycopeptides and oligosaccharides (see examples in reviews[21,25,26]) sometimes combined with treatments of the glycoconjugates with glycosidases, with glycosoxidases, with chemical modification of the carbohydrate portion or with chemical deglycosylation. The choice of lectin may prove to be useful for the separation of the receptors obtained into sub-populations depending on their microheterogeneity in carbohydrate. For example, glycophorin A type N, in contrast to glycophorin A type M, does not have glycans bound to asparagine (Asn) which enables both types to be separated readily on immobilised LL [173,175] but not on a WL-sorbent.[177] Glycophorins A, B and C are readily removed from glycophorin E by their specific binding to immobilised WL.[176] The Thy-1 antigen does not have glycans bound to serine/threonine (Ser/Thr) and its separation into three sub-populations occurs due to the Asn-glycans 1) not reacting with the lectin fraction, 2) being retained (emerging in a large volume of eluent) and 3) bound (as a result of glycans of the polylactosamine type).[161] The neural cell adhesion molecules (N-CAM) of brain contain tissue-specific Ser/Thr-bound glycans with an affinity for immobilised AL,[146] and also polysialic acids possibly reacting with slug lectin.[35,325] The hexose transporter in defective cells has unmasked Asn-glycans of the oligomannose type but in normal cells these glycans are masked by Asn-glycans of complex type which reduces the affinity for Con A and increases binding with WL.[29] Tri- and tetra-antenna (poly-antenna) Asn-glycans of a complex type are detected in lactotransferrin and transferrin receptors and are particularly numerous in the transferrin receptor according to results from the interaction with L-FGA.[132,138,139] The varying ratio of Asn-bound glycans of various types is readily determined for various histocompatibility antigens and their α- and β-chains using combinations of lectin affinity chromatography of the oligosaccharides by the analysis of the three fractions from (Con A)-sorbent, the three fractions from (CL-1)-sorbent and the two fractions from LL-sorbent.[207,208]

The oligosaccharide structures of the erythrocyte β_1-adrenergic receptor and of β-fructofuranosidase[70,284] have been established with the aid of lectins, as has the common localisation in subunits of glycans of the oligomannoside and of complex types in dopamine receptors,[72] the distribution of poly-antenna sialylated oligomannoside glycans and of glycans with a branched residue of *N*-acetyl-D-glucosamine in the four non-identical sub-units of the acetylcholine receptor.[88] The presence has been revealed of glycans of the lactosamine type in the β-sub-unit of the thrombocyte Ib receptor and in the α_2-like component of the Ca-channel sensitive to dihydropyridine or in both sub-units of the intestinal peptide receptor,[54,96,149] and also in two sub-populations of the dopamine receptor, in the receptors of corticotropin releasing factor and in α_1-adrenergic receptors.[65,75,115] Differences between six of the seven glycoproteins of milk lipid droplet membranes were successfully detected with the aid of two immobilised lectins (Con A and WL) as a result of the retention of these glycoconjugates on elution.[203]

Chromatography on lectin is important not only for the assessment of glycan structure and correcting the carbohydrate microheterogeneity of receptors but also for obtaining functionally active sub-populations of receptors, such as in relation to the enzymic activity of receptors.[57,110,314] When purifying on lectins glycoprotein receptors with an established glycan structure it is possible to take the features of the interaction of a lectin with standard reagents into account for subsequent standardisation of the lectin specificity.

When studying receptors it is possible to use a set of lectins in combination with glycosidases and in combination with antibodies. In essence, the combined use of lectins and antibodies is foreseen in all antigen purification procedures since initially antigens are precipitated from extracts by immunoprecipitation (in Tables 1 and 2 several cases are shown of immunoaffinity chromatography jointly with a lectin sorbent). Since immunoprecipitates comprise a collection of polypeptides (such as sub-units) the localisation of glycans in antigen components by lectins enables one to speak of the intra-antigenic specificity of lectins. Often the carbohydrate structures in the glycoconjugates themselves emerge in the role of antigens important for biorecognition.[10,11,170,326] In addition carbohydrates may play an appreciable role in receptor function, as in the case of complement receptors, the transporter activity of Na^+/H^+-antiporter and of the glucose transporter.[44,129,327] In other cases glycans of a particular type are not important for receptor function, for example the receptor of lutropin or *E*-cadherin.[104,328] It is possible that glycans are important for the directed assembly of receptor components (see above) and also serve to anchor the lectins and lectin-like effectors. There is scope for the purification of antigens using lectins as is evidenced by the data on the antigenic specificity of lectins in relation to cells.[329–331]

IV. Interconnection between receptors, endogenous lectins and enzymes

The antigens of human leucocytes and their interaction with adhesion receptors and receptors of homing lymphocytes have attracted considerable interest from investigators.[4–9] As a rule the antigens of leucocytes are glycoproteins,[165] such as CD 36, CD 43, CD 44, CDw 44,[152,164,199,332,333] which react with immobilised lectins. In addition some antigens themselves display the properties of lectins (for example CD 14 binds lectin lipopolysaccharide[334]) or adhesins (such as antigens CD 8, CD 11, CD 19, etc.[335,336]). In addition antigens are frequently associated with enzymes. Leukemia antigen CD 13 is aminopeptidase N,[337] CD 45 is a protein-tyrosine-phosphatase,[338] C 73 is an exo-5′-nucleotidase[339] etc. Antigen 1D 4 from mammalian brain is not only associated with a type B nucleoside-diphosphatase but also reacts with lectins forming a triple complex.[340] Enzymes forming part of the so-called adhesin molecules on cell surfaces participate actively in the functioning of membrane channels (such as Na^+,K^+-ATPase of rat brain[304]) and serve as receptors of polydomain proteins of the extracellular matrix (for example, chicken muscle 5′-nucleotidase is a fibronectin receptor[341]). In addition a serine esterase is necessary for the development of monocyte adhesion due to IgG receptors (antigen CD 32) and carboxypeptidase N (kininase I) possibly functions with peptide hormone receptors (kinins).[292,342] An important role in cell metabolism is played by the membrane-bound enzymes of tyrosine metabolism, such as tyrosyl-protein sulphotransferase (which reacts with a sialo-specific lectin[256]), tyrosinase (which reacts with an

α-mannose-specific lectin[253]), tyrosine kinases in the composition of insulin receptors[260,343–345]), receptors of insulin-like growth factor type I,[120] receptors of type I colony stimulating factor or growth factor obtained from thrombocytes,[121,260] interleukin-3 receptors,[162] receptors of the Ca^{2+} antagonist or Ca-channel blockers,[52] and receptors of lysosomal enzymes.[346] Receptors with tyrosine kinase and other protein kinases react specifically with WL (see Tables 1 and 2) and the receptors of the lysosomal enzymes themselves display the properties of lectins specific for mannose-6-phosphate. It was also shown that the phosphorylation of proteins by kinases may be inhibited by initiation factor 2 reacting with a lectin specific for the *N*-acetylglucosamine residue,[347] although the activation of receptors containing kinases by binding with a sialospecific lectin is also possible.[91] The data presented indicate the close interaction of cellular antigens, enzymes and lectins forming a single complex functioning system. Other examples of modulation (inhibition or activation) of membrane enzymes by lectins have been shown previously.[25] The highly effective procedures listed in Tables 1 and 2 for the purification of receptors and membrane-bound enzymes of various classes of the International Classification (achieving a degree of purification of 50–440 times on a lectin sorbent) are additional proof of the possibly important role of the participation of endogenous lectins in the regulation of such receptor systems.

An important role in biorecognition is discharged by a receptor lectin[10,12,20,326,348] which has been well studied in the case of mammals and is a complicatedly organised oligomeric high molecular glycoprotein with a set of functionally different domains (collagen type, carbohydrate-binding portions, carbohydrate-containing portions as targets for other lectins, growth factors regulators of the complement system, etc.). Examples are the receptors of mammalian liver asialoglycoproteins,[16] receptors binding IgE or IgG (antigens CD 16, CD 32, CD 64),[336,342,349] homing receptors[350–356] and other adhesion proteins with lectin properties.[357,358] Each of the receptor proteins indicated may under definite conditions function according to one of the domains expressed, consequently it is occasionally difficult to determine whether the receptor is behaving as a lectin or as a donor of carbohydrates in a reaction with another glycoprotein. In such cases help is obtained from an analysis of the primary amino acid sequence or analysis of the nucleotide sequence with subsequent recognition of portions of homology with known lectins. Thus the similarity has been demonstrated for lectin domains of the Fc receptor for IgE and lectin-35, which contains RNA, and other soluble lectins,[349,359,360] IgE and IgG receptors,[349] a laminin-binding receptor of the non-integrin type and lectin-35,[361] ELAM-1 adhesion molecules and lectins,[358] insulin-like growth factor II and the mannose-6-phosphate receptor[362–364] and for elastin receptors and galactose-binding lectins.[365,366] A biochemical and immunological similarity has been shown for the type III complement receptor (antigens CD 11b and CD 18) with lectins and with conglutinin,[336,367] the β-glucan-specific receptor of monocytes (lectin) and the phagocytosis receptor of complement alternative route activators,[368] the receptor of circulating mannosyl glycoproteins from liver sinusoidal cells (lectin) and cerebellum lectin R1,[369] and also the erythrocyte lectin receptors, glucose transporters and band 3, 4 and 5 proteins,[370,371] carbohydrate transporter and nucleotide-binding protein.[372] Other receptors and antigens also participate in lectin–glycoconjugate interactions, such as the interaction of endogenous ceruloplasmin (ferroxidase) and human erythrocytes,[373,374] complex-formation between antigen CD 4 and the 160 kD coat glycoprotein of human immunodeficiency virus type 1,[375] antigens CD 4, CD 8, CD 2 and CD 3 and mitogenic exogenous (foreign) lectins of plants or microbial virulency factors.

Other examples of receptors similar to one another may be found in Table 1. In addition, a structural and functional similarity between the elastin and laminin receptors[380] and between the α_2-macroglobulin receptor and the low density lipoprotein receptor[381] has been shown.

Examples of receptor lectins and adhesins of various organisms (including microorganisms) may also be found in books.[26,376] Besides the lectins mentioned above with the usual (frequently met) specificity towards carbohydrates (mannose-, galactose- and fucose-specific) the specificity of new lectins as potential instruments for the analysis of glycoconjugates must be mentioned. Receptor ligatin is specific for mannose-6-phosphate in glycoprotein composition,[26,319] lectins of T-suppressors from fish roe are α-rhamnose-binding,[12,26] receptors of lymphocyte homing display sialospecificity and an affinity towards sulphated fucan,[353,354] the colonisation factors of bacteria possess an increased affinity towards sulphated glycolipid,[18] adhesive lectins of Protozoa (parasites, such as the stimulators of amoebic dysentry) are directed to a galactoso/*N*-acetylgalactosamine-specific protein,[377] receptor lectins of insect larvae (such as mosquitos) are *N*-acetylglucosamine-specific,[378] the sorption domains on polysaccharides of several microorganism glycosidases and receptors of macrophage phagocytosis are β-glucan-specific,[27,368] the core protein of cartilage proteoglycan behaves as if xylose-specific, type I fimbria of bacteria and lectins of several plant bulbs recognise glycans of the oligomannoside type[21] and the lectin receptors of hepatocytes are specific for the L-glycero-D-mannoheptose residue in lipopolysaccharides.[20,379] After solubilisation of such receptor lectins (with enzymes, low ionic strength, etc. see above) the preparations obtained may be used in a set with the other commercial lectins as described above.

V. Conclusion

Potential targets for lectins may be not only the glycoproteins listed above (see also Tables 1 and 2) but also proteoglycans bound to the cell surface (such as the hyaluronate-binding receptor or the high molecular form of insect alkaline phosphatase associated with chitin,[199,268] polysaccharides with various degrees of branching and bond type,[21,382] lipopolysaccharides,[20,21,379] lipophosphoglycans[298] and glycolipids[18,21]). Apart from the external and cell surface-bound glycoconjugates many intracellular glycoconjugates bound to organelles have been described, which react with a wide selection of lectins,[11] including poly A polymerase, ribonucleotide reductase and glycoprotein 62 of the nuclear membrane[227,249,265] galactosyl transferase of the Golgi apparatus,[255] phospholipase A_1, tyrosine kinase and lysosomal α-glucosidase,[269,280,346] eukaryotic ribosomal initiation factor-2,[347] glycosidases for processing glycoproteins of the endoplasmic reticulum[281–283] and others (see Tables 1 and 2). Procedures have been described for the purification and separation of proteoglycans, polysaccharides and unidentified glycoconjugates on lectin sorbents.[21,26,382,383] After solubilisation in 95% tetrahydrofuran in water glycolipids may be separated successfully on immobilised lectins, such as on (snail lectin)-sorbent.[384] Bacterial lipopolysaccharides may also in principle be separated by selective precipitation with lectins, particularly in the case of various Ra type lipopolysaccharides.

Different variants of qualitative and quantitative microanalysis using a set of lectins are used for the detection and identification of receptor glycoconjugates.[21,27] Lectin–peroxidase conjugates are widely applied in histochemistry particularly in cases of human cancer and other diseases.[385] Lectins labelled with peroxidase or biotin are most widely used in blotting variants of analysis, such as in the case of blood cell membrane glycoproteins,[387] histocompatibility antigens,[20] sarcolemma glycoproteins[42] and acetylcholine receptors.[88] Lectin conjugates of this same type are used with multiwell plates for immunoenzyme analysis in the study of receptors of native cells of proto- and eukaryotes,[388–390] plasma membrane receptors[391] or purified receptors, such as erythrocyte receptors for type I fimbriae of bacteria and the phosphomannosyl receptor.[213,392] In this way lectin analysis supplements the use of antibodies to a significant extent.[18,386,393]

Investigators have shown increased interest in receptors of microorganisms both in the composition of the cell surface of eukaryotes and the surface of protokaryotes (see Tables 1 and 2). This is linked with the recognition of types of lectin, i.e. glycoconjugates, in infection and immune processes,[13–15,376] with possible use of lectins in medical diagnostics,[394,395] and also when working with bacteria, yeasts and fungi (examples[393,395–401]).

Data on the interaction of lectins with glycans of soluble glycoproteins[24,26] may be used in the lectin analysis of forms of these glycoconjugates bound to cellular structures, since a significant affinity has been established for the carbohydrate portion of them as in the case of RNAase T_2-L of *Aspergillus oryzae*,[276] β-fructofuranosidase[284] and mammalian liver α-1,2-mannosidase,[283] and also of recombinant glycoprotein-160 of the AIDS virus.[228] Such affinity is explained by the general rules for the biosynthesis of glycoprotein glycans in the endoplasmic reticulum and Golgi apparatus of cells. In addition, in the process of glycoprotein secretion into the extracellular space, glycoproteins remain bound in several cases to the cell surface or are solubilised by endogenous hydrolases (see above on the solubilisation of receptors).

It must be noted that the possibilities of lectins (there is even a set of what would have seemed to be fairly well studied commercial lectins) are still far from being exhausted since our ideas on the specificity of lectins towards oligosaccharides, glycopeptides, neo-glycoproteins (more broadly neo-glycoconjugates) and natural glycoproteins with a known distribution of glycans on the protein surface are constantly being extended, particularly in recent times. The specificity of commercial lectins towards bacterial glycoprotein,[22] steroid glycoside[402] and carbohydrate-containing antibiotics, animal glycolipid and bacterial lipopolysaccharide[21] has not been investigated in practice. New types of carbohydrate–peptide bonds are being discovered, viz. Rha-Rha-Rha-Asn for bacilli, Gal-β-1,3-Ga1*N*Ac-Ser/Thr for fungi, Fuc-Ser/Thr,[403,404] Glc-α-1,6-Glc-β-1,6-Glc-α-1-Asn [405] and Glc*N*Ac-Ser/Thr [11] for mammals. The latter two structures react with immobilised Con A and WL respectively.[11,405]

The procedures for obtaining lectin preparations are therefore relatively simple,[382,385,406] and the list of highly purified lectins from microorganisms, invertebrates, plants and animals is growing rapidly.[26,376] The use of lectin sets in combination with glycosidases and antibodies as fine instruments for the analysis of glycoconjugates is extremely promising.

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Translated from *Uspekhi Khimii* 60 1817–1836 (1991) U.D.C. 577.122.5

Special features of the synthesis of peptides containing secondary amino acids

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ABSTRACT. Features of the condensation reactions of secondary amino acid residues using various methods for the activation of the carboxyl component are discussed. Problems connected with racemisation and side reactions in the synthesis of peptides containing secondary amino acids are considered.

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I. Introduction

In the present review the term secondary amino acid is taken to mean Pro and *N*-substituted amino acids in which the substituent is an alkyl radical (methyl in the majority of cases).†

Until recently the use of secondary amino acids in peptide chemistry has fluctuated and has been limited primarily to Pro, the amino group of which is the least hindered. However because of the spread of attention to this area of chemistry, other secondary amino acids have become involved in condensations and the experimental data presently available enable certain general conclusions to be drawn on the main features and peculiarities of the use of secondary amino acids in peptide synthesis.

When considering the features of condensation at a secondary amino acid residue it is necessary to consider separately the acylation of the secondary amino group of these amino acids and their derivatives since condensations in which secondary amino acids participate as the carboxy component are no different in practice from those of the usual amino acids. Only the most general features of the latter variant will therefore be given.

The presence of bulky side chains in amino acid carboxy components leads to a decrease in the rate of condensation.[2] An alkyl substituent on the nitrogen atom of a secondary amino acid generates additional steric hindrance to the formation of the peptide bond but this effect is less significant than the influence of the side chain. In the most common cases of activation the presence of a substituent on the nitrogen atom in *N*-methylamino acids and in Pro has practically no effect on the yield of product.[3]

The presence of any protecting group on the *N*-alkylamino group of a carboxyl component begins to show an appreciable influence on the reactivity of the carboxyl group only in cases of the sterically most hindered condensations and the best yields are achieved when using Z and Fmoc rather than a Boc protected amino group.[4]

II. Methods of acylating secondary amino acids and their derivatives

In spite of the increased nucleophilicity of a secondary amino group (the pK of which is 1–1.5 units higher than for an amino group[5]) which must aid acylation, the duration of condensations in these cases is sharply increased and yields of peptides are reduced. This is explained by the shielding of the nucleophilic centre which is displayed to the smallest extent by Pro and increases with the increase in size of the *N*-alkyl substituent. For example in the synthesis of tripeptide fragments of an enkephalin analogue yields are reduced from 70 to 40% on increasing the size of the radical R.[6,7]

$$\text{Boc—D-Ala—Gly} + \text{(N-R)Phe(4-F)—NH}_2 \xrightarrow{\text{DCC/OBT}} \rightarrow \text{Boc—D-Ala—Gly—(N—R)Phe(4-F)—NH}_2$$

R = Me, Et, cyclo-Pr.

The ability of secondary amino acids to be acylated is also reduced with an increase in the bulk of the side chain and by the presence of branching at the α- and β-carbon atoms.[5] Thus steric factors play the chief role in the acylation of secondary amino acid residues and this must be considered when choosing variants of the condensation reaction.

Until recently special methods had not been developed for acylating secondary amino acid residues and traditional acylating reagents were used for this, such as active esters and symmetrical or mixed anhydrides of amino acids. The carbodiimide method was also used for the activation of the carboxyl component.

† Abbreviations used are those recommended by the IUPAC–IUB Commission[1] and also the following: Abu—α-aminobutyric acid, Aib—α-aminoisobutyric acid, BOP—[(benzo-triazol-1-yl)oxy]-tris(dimethylamino)phosphonium hexafluorophosphate, BOP–Cl—bis(2-oxo-3-oxazolidinyl)phosphinic chloride, t-Bu—t-butyl, Lac—lactic acid, (*N*–Me)Bmt—(4*R*)-4[(*E*)-2-butenyl-4,*N*-dimethyl-*L*-threonine, HOBT—*N*-hydroxybenzotriazole, HOSu—*N*-hydroxy-succinimide, Piv–Cl—pivaloyl chloride, SPip—thiopipecolic acid, DKP—diketopiperazine, DCC—dicyclohexylcarbodiimide, THF—tetrahydrofuran.

1. Active ester method

To effect nucleophilic attack on the carbonyl carbon atom of a carboxyl component by a secondary amino acid the carboxyl group must be well activated.

$$R^2{-}NH{-}CHR^1{-}COOX + R^3{-}NH{-}CHR^4{-}COOY \rightarrow$$
$$\rightarrow R^2{-}NH{-}CHR^1{-}CON(R^3){-}CHR^4{-}COOY,$$

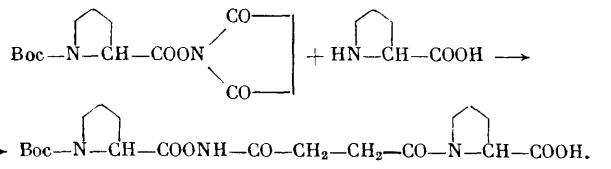
where R^1 is the side chain of the carboxy component, Y and R^2 are protecting groups, R^3 is alkyl, R^4 is the side chain of the amino component and X is an electron-accepting group.

Pentafluorophenyl esters are used fairly successfully for the acylation of secondary amino acids, particularly Pro.[8,9] If the condensation is conducted with the least sterically hindered residues Pro or (*N*-Me)Ala then from 1 h to 1 d is required for complete reaction, although the reaction time is 5–30 min when condensing at a primary amino group by this method which is comparable with the time for acylation with anhydrides.

The electron-accepting properties of pentachloro- and pentafluorophenol are clearly linked with their pK values (5.2 and 5.5 respectively) and determine the reactivity of the corresponding activated esters. However, although pentachlorophenol is a stronger acid as a result of its weaker + *M* effect,[5] the ratio of the aminolysis rates for a primary amino group by pentachloro- and pentafluorophenyl esters is 1:40. This is linked with the steric hindrance of the electrophilic centre by the chlorine atoms in the *ortho* position, since fluorine atoms having a small atomic radius do not cause such hindrance.[5] Thus the application of pentachlorophenyl esters for the acylation of amino acids is of doubtful expedience.

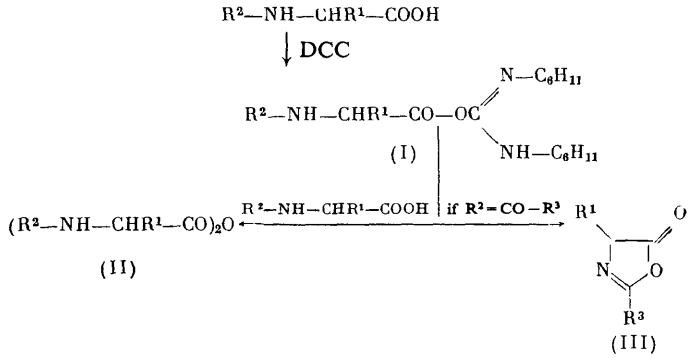
2,4,5-Trichlorophenyl esters of amino acids acylate (*N*-Me)Ala and Pro residues satisfactorily on catalysis by HOBT.[9,10] It is not excluded that HOBT esters are the real acylating reagents in this case.

When using HOSu esters, which are insufficiently reactive, a side reaction of succinoylating secondary amino acid residues is observed.[11–13]



2. Carbodiimide method

DCC was introduced into peptide synthesis in the mid-fifties.[14] When reacting equimolar quantities of DCC and a urethane-protected amino acid a mixture is formed of an *O*-acylurea (I) and a symmetrical anhydride (II).



The anhydrides (II) acylate secondary amino acid residues fairly readily but the efficiency of an *O*-acylurea (I) as an acylating reagent for secondary amino acids has not been assessed. When urethane protection is present on the amino group of the carboxy component, racemisation is reduced to a minimum and the use of the DCC method usually leads to a good yield on extended (days or longer) reaction at temperatures from 0 to 20 °C.[3,15–18] Other conditions being equal, the activation of the carboxy component with DCC leads to a higher yield than on using 1-ethyl-3-(dimethylamino)-propylcarbodiimide.[19] When activating fragments not containing *C*-terminal Pro or *N*-acylaminoacids having no urethane protection by the DOC method, an oxazolone (III) may act as acylating agent and its efficiency in relation to secondary amino acids is also unclear.[11]

Recently activation of the carboxy component with DCC has frequently been carried out in the presence of HOBT or HOSu due to numerous side reactions and racemisation. This procedure suppresses the formation of *N*-acylureas and leads to minimum racemisation of the amino acid residue. The duration of acylation is unchanged by this.[20] Many examples of the use of the DCC/HOBT method have been described in the literature for the acylation of secondary amino acids in satisfactory and good yield.[6,7,9,13,21] However for the reaction of Piv–Pro with (*N*-Me)Phe–OMe and Boc-*D*-Ala–(*N*-Me)Leu–(*N*-Me)Leu with (*N*-Me)Val–OBzl the DCC/HOBT method does not lead to the formation of the required product and in the latter case the reaction does not go even in boiling THF.[2,22]

The DCC/HOSu method is not used as frequently as the DCC/HOBT method for the acylation of secondary amino acid residues but there are examples of its fairly successful use. Thus the yield was 96% in the reaction of Boc–Ala with (*N*-Me)Leu–OBzl when using DCC/HOSu and was 82% in the reaction of Z–Pro with Sar–(*N*-Me)Val–OBu^t.[3,23] On the other hand the yield was 10% on condensing Z–Val with (*N*-Me)Leu–OBu^t and 2% overall on using preformed Z–Val–OSu. Under analogous conditions the DCC/HOBT method gave 50% yield.[13] There are numerous data on the acylation of the sterically less hindered Pro residue by this method when yields were 60 to 80% at 20 °C with a reaction time of 20–48 h.[24–26] The use of the DCC/HOSu method turned out to be unsuccessful for the reaction of Z–Arg(Z_2)–Arg($Adoc_2$) with Pro–Pro–Lys(Boc)–Gly.[27] It has also been shown that the DCC/HOBT method gives fewer side products than the DCC/HOSu method.[21]

3. Symmetrical anhydride method

This method is a variant of the DCC method, a double excess of carboxy component being involved in reaction with DCC. The *O*-acylurea (I) formed first reacts with the excess of carboxy component and is converted into a symmetrical anhydride (II). At the present time the symmetrical anhydride method is used mostly in solid phase synthesis and frequently gives good results when making peptides containing secondary amino acids. Thus an analogue of substance P containing (*N*-Me)Phe and Sar was obtained in 60% yield.[28] However in this case a single acylation of the secondary amino acid residue requires no less than 16 h reaction time in place of the more usual 30 min to 1 h.[5,28] An increase in the reaction temperature gives an increase in the reaction rate and in the yield of the desired product. On heating Boc–Pro anhydride with *D*-(*N*-Me)Leu–OMe to 130 °C for 5 min the dipeptide was obtained in 97% yield. The product was contaminated by the epimer according to NMR spectroscopy.[19]

A serious limitation to the carbodiimide method is the impossibility of obtaining anhydrides from peptide fragments and from amino acids without urethane protection although they are formed from other *N*-acyl substituted derivatives of Pro and possibly of other secondary amino acids.[11] The symmetrical anhydride method also gives a whole range of side products linked with the use of DOC in peptide chemistry.

4. Mixed anhydrides with alkylcarbonic acids

The method of mixed anhydrides with alkylcarbonic acids is the most frequently used of the traditional methods of forming peptide bonds for acylating secondary amino acids.[20]

$$Z-NH-CHR^1-CO-O-COOR^2 + R^3-NH-CHR^4-COY \rightarrow$$
(IV) (V)

$$\rightarrow Z-NH-CHR^1-CON(R^3)-CHR^4-COY + R^2-OCON(R^3)-CHR^4-COY$$
(VI) (VII)

In spite of the high reactivity of the anhydrides (IV) the yield of peptide (VI) is frequently less than when the carbodiimide method is used. The main reason for this is the presence in the carboxy component (IV) of two reaction centres and the ambiguous nature of the reaction as a result. The preferred direction of attack depends on the nature of the substituents R^1, R^2 and R^3. The presence of groups R^1 and R^3 hinder the formation of peptide (VI) more strongly the greater their molar volume and degree of branching.[29,30] In some cases the mixed anhydride method is not generally suitable. For example in the reactions of Boc–*D*-Ala–(*N*-Me)Leu–(*N*-Me)Leu with (*N*-Me)Val–OBzl (–20 °C, 26 h),[22] Boc–Phe with a fragment containing *N*-terminal (*N*-Me)Ala [9] and Boc–Ile with Pro–Leu–Ser(Bzl)–Arg(NO_2)–Leu–Phe–OMe [31] it did not lead to the formation of the desired products.

A branched group R^2 increases the electron density on the carbonyl carbon atom of the alkylcarbonic acid residue and hinders it to some extent which reduces the possibility of attack on the latter by the secondary amino group. The acylation of secondary amino acids using mixed anhydrides of isobutylcarbonic acid (IV, R^2 = iso-Bu) is preferred to the use of anhydrides of ethylcarbonic acid (IV, R^2 = Et).[20] Thus when acylating a tripeptide containing an *N*-terminal Pro residue with a mixed anhydride of ethylcarbonic acid the urethane EtOC(O)–Pro–Lys(For)–Asp was obtained in 61% yield.[32] The use of anhydrides of isobutylcarbonic acid is also accompanied by the formation of the urethanes (VII),[33–35] and their yield depends on the choice of solvent in which the condensation is carried out and on the types of base used. For the reaction of Z–Gly–Phe with Pro–OMe the yield of urethane increases from 13 to 33% along the series THF, chloroform, DMF.[36] A minimal quantity of urethane is formed when using *N*-methylmorpholine or *N*-Methylpiperidine on obtaining the anhydrides (IV).[37]

The molecular weight of both the secondary amino and the carboxy component have a significant influence on the yield of product.[20] For example the yields on fragment condensation of Boc–*D*-Ala–Gly and Boc–Tyr–*D*-Ala–Gly with (*N*-Me)Phe–Met-ol were 70 and 50 % respectively.[38]

In spite of the relative stability of pure mixed anhydrides (IV) at temperatures up to 25 °C, they disproportionate with the formation of symmetrical anhydrides in the presence of even traces of base, and the amino component itself may cause this.[22,39] To suppress this process the condensation is carried out at –20 to –15 °C, but to increase the yield it is desirable to carry out the reaction at a higher temperature.

Of all the above reactants the symmetrical anhydrides are the most acceptable for the acylation of secondary amino acids but for the most sterically hindered condensations of the type of Boc–(*N*-Me)Val with (*N*-Me)Val–OBu^t, even they are ineffective.[2]

5. Mixed anhydrides with pivalic acid and phosphorus acids

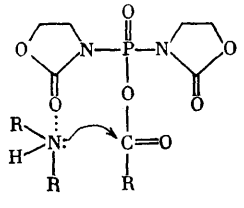
At the present time the mixed anhydrides obtained from Piv–Cl and BOP–Cl are the best known and most widely used reagents for acylating secondary amino acids. In particular they have been used successfully in the synthesis of the cyclic undecapeptide cyclosporin A and its analogues which contain seven secondary amino acids.[22,40–42]

Piv–Cl was first used in peptide chemistry in 1962.[43] However the mixed pivalic anhydride method has not been widespread in usual condensations seemingly due to the possibility of forming *N*-pivaloyl peptides.[20] For example in the reaction of the acetonide of (*N*-Me)Bmt with Abu–Sar–(*N*-Me)Leu–Val–(*N*-Me)Leu–Ala–OBzl a mixture was obtained of heptapeptide and *N*-pivaloyl hexapeptide in a 1 : 1 ratio.[42] It was later shown that the formation of *N*-pivaloyl peptides does not occur when acylating secondary amino acids with mixed pivalic anhydrides.[22] Other virtues of this method are the high acylating ability of the anhydride and its thermal stability up to 50 °C even in the presence of triethylamine and *N*-methylmorpholine which enables the most sterically hindered condensations to be effected.[2,22]

Some authors[2,44] regard the significant duration of the stage of forming the mixed pivalic anhydride in chloroform a disadvantage of this method. It is recorded that the yield of the desired peptide depends markedly on the duration of the activation. Thus for the reaction of Boc–*D*-Ala–(*N*-Me)Leu–(*N*-Me)Leu with (*N*-Me)Val–OBzl the yield of tetrapeptide is 60% when activating the carboxyl component with Piv–Cl for 2 h and 88% for 4 h.[22] However on carrying out the activation in THF the formation of the mixed pivalic anhydride is complete after 5–20 min at –20 °C.[13,45,46]

Activation of secondary amino acids with urethane protection with Piv–Cl is not accompanied by racemisation even at elevated temperature. Only in the case of the extremely sterically hindered condensation of Z–(*N*-Me)Val with (*N*-Me)Val–OBu^t for 24 h at 50 °C was 6% epimer detected in the dipeptide.[2] Fragment condensations using Piv–Cl are accompanied by racemisation, the extent of which depends on a large number of factors.[2,22,40]

In 1980 BOP–Cl was proposed as a reagent for the synthesis of esters and other derivatives of carboxylic acids.[47] Its high efficiency when forming peptide bonds at residues of secondary amino acids was shown for the first time in 1985.[4] A mechanism of electrophilic catalysis at the condensation stage has been proposed to explain this effect.[2]



It has been recorded that BOP–Cl is a more effective reagent than Piv–Cl for carrying out sterically very hindered condensations.[2,4] Thus in the reaction of the mixed anhydride of Z–(*N*-Me)Phe and pivalic acid with (*N*-Me)Val–OBu^t a positive result is achieved only at enhanced temperature while BOP–Cl

enabled preparation of the product in 92% yield after 48 h at 20 °C in this condensation.[2] The difference in yields of product when using BOP–Cl or Piv–Cl is reduced with a reduction in steric limitations. Thus in the reaction of Z–Pro–(*N*-Me)Phe with Ala–Bu^t both reagents lead to the formation of tripeptide in 85% yield but in this condensation racemisation was 38% with Piv–Cl and on using BOP–Cl it was 64%.[2] This ratio is less in other examples. Usually the use of BOP–Cl is accompanied by less racemisation than the use of Piv–Cl in fragment condensations.[2] This is possibly explained by the high reactivity of the mixed anhydride of the carboxyl component with the phosphoric diamide compared with its mixed pivalic anhydride, consequently the long condensation time in the second case leads to an increase in the extent of racemisation of the carboxy component.[48]

One further advantage of BOP–Cl is the possibility of using it as a condensing reagent in a one-pot synthesis without preactivating the carboxy component as a separate stage. The analogous method using Piv–Cl leads to the formation of up to 40% *N*-pivaloyl peptide,[22] which is explained by the lower reactivity of BOP–Cl towards an amino group compared with carboxylate anion.[49] However the best results of all were achieved by carrying out the preparation of the mixed anhydride of the carboxy component and the diamidophosphoric acid as a separate stage since otherwise some contamination by the BOP-amino component is formed.[2]

Carrying out sterically hindered condensations using BOP–Cl, as for Piv–Cl, may be accompanied by a little racemisation of the carboxy component even in the presence of urethane protection of its amino group. For example 4% epimer was obtained in the reaction of Z–(*N*-Me)Val with (*N*-Me)Val–OBu^t.[8] In this case it is possible to suppress the racemisation by the addition of HOBT but not HOSu.[2] However on adding HOBT the overall yield of dipeptide was sharply reduced (from 92 to 21%). This fact is readily explained by the formation of an HOBT ester of the carboxy component caused by steric factors. This ester is a weak acylating agent in such difficult condensations.

It is also interesting to record the BOP–Cl proved to be ineffective in condensations of *C*-α-methylamino acids. For example after carrying out the reaction of Boc–Aib with Aib–OBzl none of the desired product was detected.[4]

It is possible to regard the possibility of disproportionation of such mixed anhydrides as being a drawback of the use of BOP–Cl for the activation of both secondary and primary amino acids, particularly at long reaction times.[2,4] The relatively poor solubility of BOP–Cl in certain organic solvents, especially those used in peptide synthesis, should also be noted.[41]

It is also possible to use BOP–azide, which is a fairly stable compound, in place of BOP–Cl for the activation of the carboxy component. When carrying out preactivation with BOP–azide (10 min, 0 °C) in the condensations of Boc–Ala with (*N*-Me)Phe and Z–Phe with (*N*-Me)Ala–OMe the yield of dipeptide was 60% after 4 h.[50]

The use of diethyl phosphorocyanidate as an activating reagent has been described. In the condensation of Boc–Pro with *D*-(*N*-Me)Phe–*D*-Ala–Val–Ant–OMe (2 h, 0 °C, then 24 h, 20 °C) the pentapeptide was formed in 89% yield.[51]

Data have appeared recently on the use of diphenyl phosphinic chloride as a highly efficient activation reagent for the acylation of secondary amino acid residues.[13,52–55] The advantage of this reagent over BOP–Cl was shown in the activation of both primary and secondary amino acids in the synthesis of cyclosporin fragments.[54] The use of diphenyl phosphinic chloride for the activation of a carboxy component with a urethane protected amino group was not accompanied by racemisation of the latter but the process of forming the mixed anhydride was analogous to activation using Piv–Cl.[53,54] An advantage of diphenyl phosphinic chloride is the speed of formation and the stability towards disproportionation of mixed anhydrides made from it.[48,56]

Of the new condensing reagents mention must be made of benzotriazolyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with which a fragment condensation at an (*N*-Me)Bmt residue has been effected without racemisation of the carboxyl component.[40,57]

Other condensation methods have occasionally been used for secondary amino acid residues. Thus a new reagent was proposed recently, viz. 1,2-dihydro-4,6-dimethyl-2-thiooxo-3-pyridinecarbonitrile, and was used in the synthesis of a protected (8–11)cyclosporin fragment without racemisation and with yields at the condensation stages of 80–87%.[58] It is interesting that this reagent may be used for building up a chain both by traditional activation of a carboxyl group or by activation of the amino group of an amino component. To effect condensation in this case it is also necessary to have an equimolar quantity of triphenylphosphine present.[59]

Occasionally the azide method is used for fragment condensations at a Pro residue.[59] The *N*-carboxyanhydride method gives poor results for similar condensations.[60] Good results were recorded using Woodward's reagent K in solid phase synthesis for the acylation of secondary amino acids.[61]

III. Side reactions caused by the presence of secondary amino acids in peptides

In addition to the peculiarities described above, complications also arise when obtaining esters and amides of secondary amino acids and on removing protecting groups during peptide synthesis. All these processes proceed with significantly more difficulty or are accompanied by side reactions which are absent when working with unsubstituted amino acids.

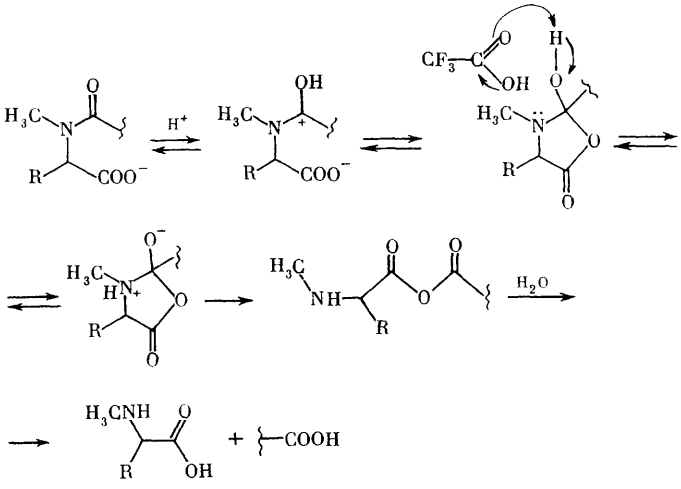
For example Sar–OMe is obtained in only low yield when using a solution of thionyl chloride in methanol while both Gly and many other amino acids give good yields of methyl esters under these conditions.[62] The t-butyl ester of Val is obtained in quantitative yield after 4 h at 20 °C when using isobutene in the presence of sulphuric acid. Under the same conditions the reaction of (*N*-Me)Val is incomplete even after 96 h.[41]

The saponification of alkyl esters of secondary amino acids proceeds with significantly more difficulty than in the case of the corresponding derivatives of unsubstituted amino acids. For example under identical conditions the rate of saponification of Sar–OMe is five times slower than for Gly–OMe,[62] and the hydrolysis of Lac–Pro-*D*-(*N*-Me)–Leu–OMe even with a three-fold excess of sodium hydroxide proceeds only to 90% after 2 h.[19] It has been reported that it is impossible to obtain the hydrazide of Bz–(*N*-Me)Val from its methyl ester by reaction with hydrazine hydrate.[21] Similarly the aminolysis of alkyl esters of secondary amino acids is difficult, consequently their amides are obtained by treating an activated ester or mixed anhydride of the protected secondary amino acid with an amine.[6,7,63] Occasionally the roundabout method of obtaining the amide of an amino acid with subsequent alkylation of its amino group is used.[6,7] A similar approach is applied to the synthesis of fragments consisting only of

secondary amino acids. For example on treating the tripeptide Boc–Leu–Leu–Val–OBzl with methyl iodide in the presence of silver oxide, methylation of the nitrogen atoms of all three amino acid residues occurs.[44] Milder conditions are used to prevent methylation of the urethane nitrogen atom (CH_3I, K_2CO_3, 18-crown-6, DMF, 20 °C).[64] Such a method of synthesis of tripeptide sequences of secondary amino acids enables prevention of the formation of cyclic dipeptides (DKP) in a 1 + 2 cocondensation.[44]

Data have recently appeared on the ready fission of the peptide bond on acid treatment of peptides containing sequences of two or more secondary amino acids.[65,66] Two mechanisms have been proposed by which such fission may occur. The first of these, in which the hydrolysis process does not depend on acid strength in the medium in which it occurs, has acquired the name exopeptolysis. The second, which depends on acid strength, is called endopeptolysis. Both mechanisms assume a ready transition of the peptide bond into the *cis* form and the spatial approach of the appropriate portions of the molecule.

Exopeptolysis may be illustrated by the example of the dipeptide Tfa–(*N*-Me)Phe–(*N*-Me)Ala which is split 29% at the peptide bond in a medium of formic acid after 120 h at 20 °C and 21% in trifluoroacetic acid under the same conditions.[65] At the same time the alkyl esters of this dipeptide are stable in trifluoroacetic acid.[65,66] The following mechanism has been proposed for exopeptolysis.[65]



Endopeptolysis is characteristic of tripeptides made up of secondary amino acids through the *N*-terminal position may be occupied by a Gly residue. The peptide bond between the second and third secondary amino acids is readily split in acid medium in such tripeptides, particularly in cases when the *N*-terminal secondary amino acid is Pro.[66] The rate of hydrolysis of such tripeptides depends sharply on the strength of the acid in which the reaction is effected, i.e. trifluoroacetic ≫ formic ≫ acetic acid. The sensitivity of tripeptides towards acidic fission is proportional to the steric strain about the amide bond between the second and third secondary amino acids, with the exception of the case when the first two positions of the triad are occupied by Pro residues.[66]

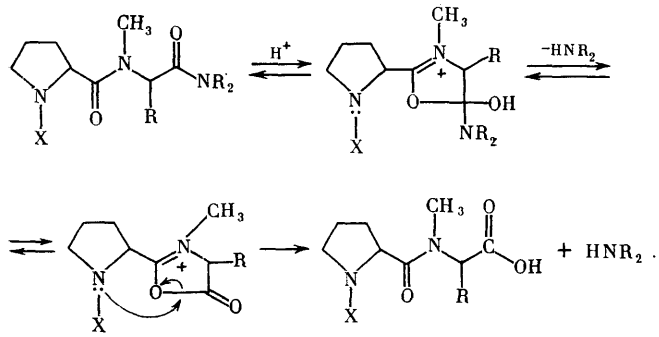
Z–Pro–(N-Me)Phe–SPip > Z–Pro–(N-Me)Phe–(N-Me)Ala,
Z–Pro–(N-Me)Phe–(N-Me)Ala–OMe > Z–Val–(N-Me)Phe–(N-Me)Ala–OMe, Z–Val–(N-Me)Phe–(N-Me)Ala,
Z–Pro–(N-Me)Phe–Ala–OMe ≫ Pro–(N-Me)Phe–NR_2 > > Pro–Pro–Pro, Pro–Pro–SPip, Pro–Phe–NR_2.

In certain cases the hydrolysis goes so easily that when deblocking the tripeptide Z–Abu–Pro–(*N*-Me)Phe–SPip–OBu^t fission of the *C*-terminal secondary amino acid is effected more rapidly than removal of the t-butyl protection. Endopeptolysis is difficult if the *N*-terminus in the triad is an unsubstituted secndary amino acid or the dipeptide Pro–Pro. If the sequence consists of alternating *L* and *D* isomers of secondary amino acids (*L*, *D*, *L*) then the rate of endopeptolysis is two orders of magnitude lower than for sequences containing only *L* isomers. Thus the tripeptide Z–Pro–*D*-(*N*-Me)Phe–(*N*–Me)Ala–OBu^t does not decompose in the presence of trifluoroacetic acid for several days but its *L*–(*N*-Me)Phe analogue is completely decomposed under the same conditions in 15 min.[2] The dipeptide Z–Pro–*D*-(*N*-Me)Phe–NMe_2 remains unchanged in trifluoroacetic acid for days while its *L* analogue loses the NMe_2 group completely under the same conditions after 14 h.[66] This may be explained by the fact that the energy barrier for the transition of a *trans* amide bond into the *cis* configuration for an *L*-, *D*-pair of amino acids in the triad is greater than for an *L*-, *L*-pair. It may therefore by considered quite definite that conformational factors plays a most important role in the stability of the peptide bond between secondary amino acids.

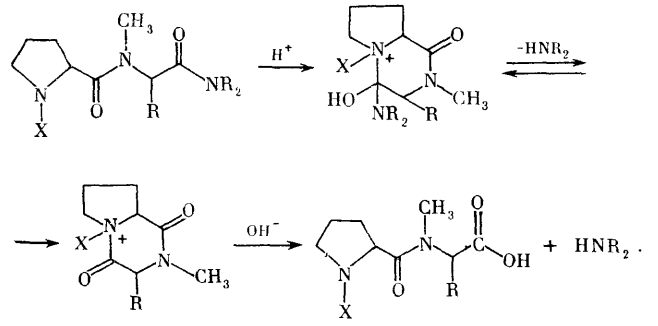
Two possible mechanisms have been proposed for the endopeptolysis reaction (the second is preferred) (see Scheme).[66]

Scheme

Oxazolonium



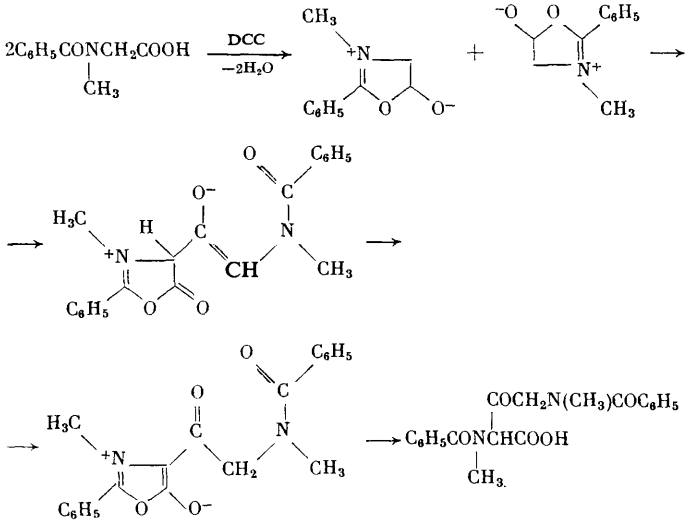
Diketopiperazine



Similar processes were observed in the synthesis of cyclosporin when for example the deblocking of the undecapeptide Boc–*D*-Ala–(*N*-Me)Leu–(*N*-Me)Leu–(*N*-Me)Val–(*N*-Me)Bmt–Abu–Sar–(*N*-Me)Leu–Val–(*N*-Me)Leu–Ala with a solution of trifluoroacetic acid in chloroform at 0 °C with subsequent neutralisation of the excess of acid led to a complex mixture of products among which were peptides of shortened sequence. The

avoidance of side reactions in this case was successful if the deblocking temperature was reduced to −20 °C.[40,42]

The side reaction of *C*-α-acylation of the Sar residue, observed on using the carbodiimide method, is also effected by an oxazolonium mechanism.[67]



The ease of forming DKPs from certain peptide derivatives is an extremely pressing problem when using secondary amino acids in peptide synthesis. This concerns primarily condensation reactions where a dipeptide ester containing a *C*-terminal secondary amino acid acts as the amino component. In this case the energies of the *cis* and *trans* configurations of the peptide bond are close and for the formation of DKPs it is necessary to overcome a significantly lower energy barrier for the *trans*−*cis* transition (since DKPs exist only as the *cis,cis* isomers) than in the case of a dipeptide containing no secondary amino acids.[3,5,20,68] The formation of DKPs in the case under consideration is most frequently catalysed by bases, especially by an excess of tertiary amine, frequently present in the reaction medium.[5,68,69] The rate of formation of a DKP depends on several factors except in the presence of a catalyst. The presence of side chains and radicals on the nitrogen atom of the secondary amino acids forming part of the dipeptide gives an energy advantage to the formation of the six-membered DKP ring due to the entropy factor. Steric hindrance has great importance in the nucleophilic attack on the carbonyl carbon atom by the amino group, and arises particularly in the presence of a side chain on the *N*-terminal amino acid.[68,69]

The rate of cyclisation of dipeptide esters consisting of two secondary amino acids is fairly high seemingly due to the enhanced nucleophilicity of the secondary amino group.[11] Thus the formation of DKP from the dipeptide (*N*-Me)Leu−(*N*-Me)Val−OBzl was the main obstacle in the synthesis of the (7−11) cyclosporin fragment when extending the peptide chain from the *C*-terminus.[22] The process of forming DKPs may not only compete with peptide synthesis but may completely exclude it when using a dipeptide ester as the amino component. This process is obviously particularly dangerous when using esters of dipeptides consisting of two secondary amino acids as the amino component since in this case the condensation time grows and there is a fairly high rate of DKP formation.

The presence of a side chain on the *C*-terminal secondary amino acid seemingly does not have an appreciable effect on the rate of DKP formation while the nature of the tertiary amine and the solvent in which the condensation is carried out influence it appreciably.[68,69]

The problem of DKP formation from dipeptide esters with a *C*-terminal secondary amino acid is a characteristic not only of synthesis in solution but also for the solid phase method of peptide synthesis based on chloromethylated resin. In the case of such a polymeric support DKPs are readily formed from the protected dipeptide benzyl esters at the stage of neutralising the dipeptidylpolymers with tertiary amine after deblocking.[70] In a similar situation, when using Sephadex LH-20 as the polymeric support, formation was also recorded.[71]

Furthermore it was observed that on using the DCC condensation method in solid phase synthesis on chloromethylated resin, DKPs were also formed at the stage of equilibrating the dipeptidylpolymer with a solution of the next amino acid.[72] In this case acid catalysis of DKP formation occurs and has been confirmed on numerous occasions in the classical synthesis of peptides. DKPs are formed most frequently when removing protecting groups from dipeptide esters with acids having pK_a 3−5. This effect is observed in the removal of a Z group by hydrogenation in solutions containing acetic acid or, for example, on removing 2-(4-biphenylyl)propyl-2-hydroxycarbonyl protection with formic acid.[18,73] The mechanism of such catalysis is obviously similar to the general acid catalysis mechanism.

It must also be noted that there is a danger of forming DKPs from dipeptide esters with a *C*-terminal secondary amino acid when removing Fmoc protection by the action of such strong organic bases as piperidine or diethylamine.[74,75] When using 4-(aminomethyl)piperidine in this situation 10−20% DKP is formed even from benzyl esters of dipeptides containing no secondary amino acid.[74]

If a phenacyl ester of a dipeptide is introduced into the condensation reaction instead of an alkyl or benzyl ester then the probability of DKP formation is increased.[5] Consequently to prevent this process it is recommended to use tertiary butyl esters of dipeptides.[3,22]

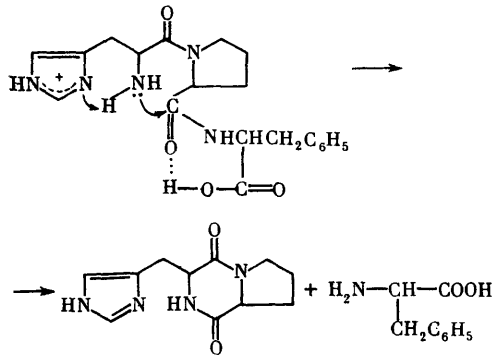
In certain cases cyclisation to a DKP may occur even with *N*-protected peptides. For example the 4-nitrophenyl ester of the dipeptide Z−Gly−Pro forms an (*N*−Z)-substituted DKP and in the course of condensing Z−(*N*-Me)Val with (*N*-Me)Val−OBu^t when using BOP−Cl, and particularly when using Piv−Cl at increased temperature, up to 10% of the corresponding DKP was obtained the mechanism of forming which is unclear.[2,75]

The DKP cyclo[(*N*-Me)Phe−(*N*-Me)Ala] is formed from the tripeptide cinnamyloxycarbonyl−Pro−(*N*-Me)Phe−(*N*-Me)Ala−OMe during column chromatography on silicagel and substituted Pro is split off.[76]

Although it is considered that trifluoroacetates and especially hydrochlorides of dipeptide esters consisting of any amino acids are completely stable,[72] the trifluoroacetate of the dipeptide (*N*-Me)Phe−(*N*-Me)Ala−OMe is converted into the DKP on storage in chloroform solution.[76]

It is also known that amides of dipeptides containing a *C*-terminal secondary amino acid are inclined to DKP formation.[77,78] For example, the dipeptide Phe(4-NO_2)−Pro−NH_2 forms the DKP during recrystallisation.[78] Individual cases of similar transamidations have been recorded when obtaining certain tripeptides. When treating the tripeptide His−Pro−Phe with 50% acetic acid fission of Phe occurs and the DKP (VIII) is formed after 24 h at 20 °C. Under the same conditions the tripeptide

Trp–Pro–Phe is stable and no traces of decomposition were detected after 24 h. The methyl ester of the first tripeptide is between these compounds in stability. In the opinion of the authors[79] the instability of the tripeptide His–Pro–Phe is explained by a combination of conformational factors favouring DKP formation and a so-called intramolecular catalysis.[79]



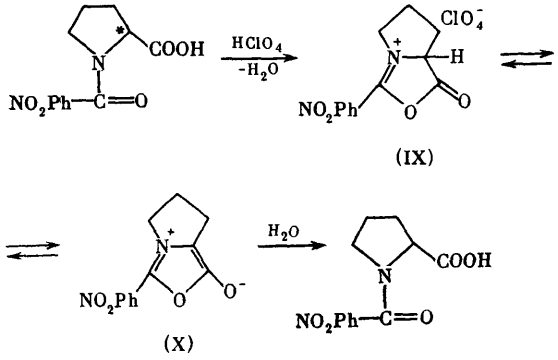
(VIII)

Intramolecular transamidation has also been described in the tripeptide *D*–Val–Pro–Sar which is 50% decomposed on storage for 3 weeks at 20 °C. It was reported that no sign of decomposition was detected for the hydrochloride of this peptide under the same conditions.[80]

The tripeptide Aib–Pro–Trp also shows an increased inclination towards intramolecular transamidation.[81]

IV. Racemisation of secondary amino acids in peptide synthesis

Proline is a unique secondary amino acid, widely distributed in nature, and has been used in peptide synthesis for a long time. Equally with Gly, Pro plays an important role as a *C*-terminal residue in fragment condensations which is linked with its high stability towards racemisation in activation processes and removal of protecting groups.[3,82] This was explained previously by the impossibility of effecting an oxazolonium mechanism of racemisation for its *N*-acyl derivatives because of the absence of a hydrogen atom on the tertiary nitrogen atom. However it was found in 1972 that *N*-acyl substituted Pro and other secondary amino acids may give the stable oxazolonium salts (IX) on treatment with perchloric acid.[67,83]

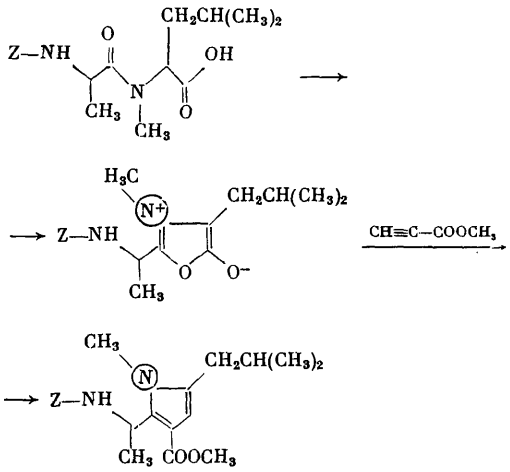


(IX)

(X)

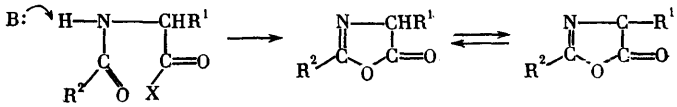
Complete racemisation of the Pro residue took place in 1 h at 20 °C on storing the salt (IX) in the presence of anhydrous perchloric acid. This process is connected with the equilibrium in the oxazolinium ion (IX)–mesoionic oxazolone (X) system, since it was shown that on precipitating salt (IX) from the reaction medium with dry ether no racemisation occurred on storing it in the dry state.[67] These facts serve to confirm the possibility of racemising *N*-acyl-Pro according to the oxazolonium mechanism but the formation from it of the mesoionic oxazolone (X) is difficult due to conformational restrictions and occurs only in the presence of strongly acidic reagents (perchloric acid). The extent of the structural limitations for other secondary amino acids is far lower than for Pro and the formation of the mesoionic oxazolone and consequent isomerisation is observed under the mild conditions of peptide synthesis. In addition their susceptibility towards racemisation according to the oxazolonium mechanism is extremely high.

The formation of the mesoionic oxazolone (X) is accompanied by the appearance of a rapidly disappearing bright yellow colouration of the reaction mixture (absorption λ_{max} = 400 nm). Subsequently its formation was successfully confirmed by reaction with the 1,3-dipolarophile acetylenecarboxylic acid.[3]



In 1981 NMR signals for the mesoionic oxazolone (X) were recorded on reacting Z–(*N*-Me)Val and Z–(*N*-Me)Ala with DCC and it was established that this ion is stable in deuterochloroform at −20 to −5 °C for 3 h.[21]

The formation of 5(4H)-oxazolones on activation of *N*-acylamino acids is explained by base catalysis but in the case of *N*-acyl secondary amino acids acid catalysis of the formation of the mesoionic oxazolone (X) takes place.[65,67,83] Consequently the presence of salts of strong acids and tertiary amines, normally accompanying almost any peptide condensation, is undesirable in the reaction mixture.[3,28] An excess of tertiary amine reduces the racemisation of secondary amino acid residues when using DCC and isobutyl chloroformate as condensing reagents.[3] A stronger base such as triethylamine is more effective than *N*-methylmorpholine.



On treating derivatives of *N*-acyl secondary amino acids with strong acids, such as when decarbobenzoxylating the dipeptide Z–Ala–(*N*-Me)Leu with a solution of 5.6 N hydrobromic acid in acetic acid, significant racemisation takes place and was linked with

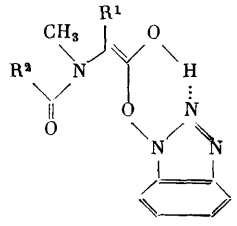
acid catalysed enolisation.[82] However the fact that the addition of water in this case sharply reduced the extent of racemisation indicates that in the above case a mesoionic oxazolone was formed in the anhydrous medium and no acid-catalysed enolisation took place.

Racemisation of secondary amino acid derivatives by enolisation may be catalysed both by alkali and by acid and its mechanism is evidently the same as for derivatives of the usual amino acids.[20,83]

It must be noted that the racemisation of derivatives of secondary amino acids rarely proceeds according to one mechanism. Frequently, depending on many factors, it is possible that either the oxazolonium or the enolisation mechanism may predominate.

The factors affecting the mechanism of racemisation include the method of activation, the nature of the substituents in the secondary amino acid residue, the polarity of the solvent used for the condensation, the pH of the medium, etc. Definite rules for this problem have now become apparent.

In particular the use of such well known antiracemisation additives as HOBT or HOSu in the activation of *N*-acyl secondary amino acids with DCC suppresses their racemisation by the oxazolonium mechanism.[3,21] HOSu proved to be more effective than HOBT which, while suppressing the formation of the oxazolonium ion, aids racemisation by the enolisation mechanism by being a stabiliser of the enolised form of *N*-alkylamino acid HOBT esters.[21]



In the condensation of Boc–Abu–Sar with (*N*-Me)Leu–Val–(*N*-Me)Leu–Val–(*N*-Me)Leu–Ala–OBzl by the mixed pivalic anhydride method no *C*-α-acylation side reaction, which proceeds through the formation of a mesoionic oxazolone [of the type of (X), see previous section], was observed.[40] The racemisation process in this case, as for DCC activation, is suppressed by an excess of triethylamine more efficiently than by *N*-methylmorpholine. This may serve as indirect confirmation of the fact that the racemisation of secondary amino acids when activated by Piv–Cl is explained by acid catalysed enolisation and not by the formation of an oxazolonium ion.[40]

It has been established that racemisation when using BOP, BOP–Cl and diphenylphosphinic chloride as activating reagents for *N*-acyl secondary amino acids is chiefly explained by the formation of an oxazolonium ion.[2,40]

The addition of HOBT or HOSu when using BOP–Cl has little effect.[84] According to other data HOBT has a weak influence on the suppression of racemisation but HOSu has no effect at all.[2,85] It has been recorded that on cyclising a hexapeptide by activation of an (*N*-Me)Phe residue with BOP–Cl the addition of HOBT increased the racemisation by even twofold.[86]

As in the case of the usual amino acids, urethane protection of an *N*-alkylamino group reliably prevents racemisation of a secondary amino acid.[3,21,22,40] For example, on carrying out the reaction of Boc–(*N*-Me)Leu with (*N*-Me)Val–OBzl using Piv–Cl the product contained no diastereomeric contamination even at 50 °C.[22] Only in cases of the most sterically hindered condensations when the reaction time was huge was a small degree of racemisation observed for a secondary amino acid with urethane protection. For example, the epimerisation of the (*N*-Me)Val residue activated by BOP–Cl in the reaction of Z–(*N*-Me)Val with (*N*-Me)–OBu^t was 4% after 2 d at 20 °C but less than 1% after 4 d at 0 °C.[2]

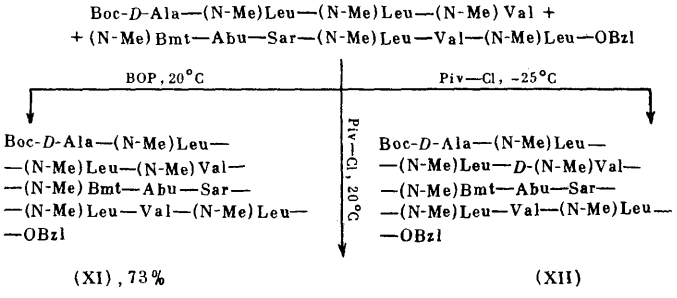
It was considered previously that the presence of urethane protection prevents racemisation of amino acids by the oxazolone mechanism.[20] It was established more recently that urethane protection may not be a reliable barrier to the formation of 5(4H)-oxazolones. Under certain conditions, for example with an excess of DCC in the reaction mixture, oxazolones are also formed from such amino acids, but they are extremely stable towards the tautomeric conversion which causes the racemisation.[11,87] However the presence of an excess of tertiary amine may in this case lead to marked racemisation.[11]

Racemisation proves to be extremely significant when activating *N*-acyl secondary amino acids by the DCC method if acetyl or benzoyl is used as the acyl group. If the same acyl groups are used on amino acids then racemisation is displayed to a lesser degree.[21]

Among the factors affecting the racemisation of amino acids the so-called asymmetric induction, which has been little considered until recently, may be mentioned.[88,89] This phenomenon explains the high extent of racemisation of *C*-terminal amino acid residues on activation or deblocking when a thermodynamically more favoured epimer is formed in the racemisation process.[22] This process may lead to the preferential formation of a product with reversed configuration, consequently the term 'racemisation' is unsuitable in this case and one should speak of a high degree of epimerisation.

On the other hand asymmetric induction may be caused by the different reactivites of *L* and *D* activated amino acids towards the asymmetric amino component. Thus an *L* isomer is activated, but the *D* isomer reacts more readily, then as a result of epimerisation occurring in parallel with the condensation it is possible to obtain a product containing residues chiefly of the *D* amino acid.[11,89] Occasionally this process leads to the complete inversion of the configuration of the amino acid being introduced.[40]

In certain cases the phenomenon of asymmetric induction may be a very valuable method of synthesis for individual epimers which are difficult to obtain by classical means. Thus when making a protected undecapeptide intermediate in the synthesis of cyclosporin by a 4 + 7 fragment condensation from identical amino and carboxy components, two different pure epimers are obtained depending on the reaction conditions.[40]



Mixture of (XI) and (XII) in a 4:1 ratio

When activating the tetrapeptide fragment with Piv–Cl racemisation of the (*N*-Me)Val residue occurs through the enol and because of the absence of steric constraints for this process the thermodynamically more favoured sequence of *L* and *D* amino acids

is formed. When activating the same tetrapeptide with BOP on oxazolonium ion is formed which due to steric constraints may react only in the *L* form.[40]

The increased tendency of derivatives of secondary amino acids apart from Pro to racemise on alkaline or acid treatment was explained previously by the ease of enolisation of these compounds under the conditions indicated.[82] Facilitated enolisation is linked with the absence of a hydrogen atom on the nitrogen atom or tertiary amides which *N*-acyl secondary amino acids are.

The hydrogen atom of *N*-acyl amino acids is significantly more mobile than a hydrogen atom of a carbon atom. By ionising first, the amide hydrogen atom prevents deprotonation of the hydrocarbon and provides the higher stability of an amino acid towards racemisation compared with secondary amino acids.

Experimental confirmation of the above is provided by the fact that treatment of (*N*-Me)Ile–OMe with alkali gives 1% epimer while Z–(*N*-Me)Ile–OMe having no hydrogen on the nitrogen atom gives 9% epimer under the same conditions. Analogously under alkaline conditions the ionisation of the carboxyl group prevents enol formation, and consequently racemisation, of Z–(*N*-Me)Ile.[82]

It is also reported that the electron-donating effect of the *N*-alkyl group is an additional factor facilitating the enolisation of secondary amino acids. However the enolisation mechanism presented may not explain the high stability towards racemisation of the Pro residue in the dipeptide Boc–Ala–Pro–OMe [less than 0.1% epimer in 1 N sodium hydroxide after 3 h).[82]

There are hints after the enhanced tendency towards racemisation of derivatives of secondary amino acids is impossible to explain fully by the absence of a hydrogen atom on a completely protected nitrogen atom preventing enolisation.[20] In order that this mechanism can be sufficiently justified it would be necessary for more than 90% of the amide groups in a peptide consisting of the usual amino acids to be converted under saponification conditions into the conjugate bases, which is improbable since the p*K* for monosubstituted amides lies in the 14–15 range. Furthermore these mechanisms do not explain the increased racemisation linked with the formation of a mesoionic oxazolone. Since disubstituted amides, which *N*-acyl secondary amino acids are, exist as *cis* and *trans* conformers which are close in energy, and monosubstituted amides have predominantly a *trans* conformation of the amide bond, it has been suggested that the *cis*-conformation existing more readily in *N*-acyl secondary amino acids facilitates the racemisation process.[20] Indirect confirmation of this hypothesis is the known ease of racemisation of residues of secondary amino acids in cyclic dipeptides on treatment with alkali. Both amide bonds in DKP has only the *cis* configuration.[90] It is evident that steric factors make a decisive contribution to the easing of racemisation of derivatives of secondary amino acids.

* *
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It may be concluded from the material considered above that no single traditional condensation method is able to guarantee success when acylating residues of secondary amino acids with the exception of the easiest cases. Such reagents as diphenyl phosphine chloride, BOP–Cl and Piv–Cl are capable of effecting the most sterically hindered condensations. Recently BOP–Cl has been used most widely for these purposes. In the synthesis of peptides containing secondary amino acids and especially for sequences of several secondary amino acids the risk of obtaining unstable compounds, which may decompose according to a different scheme, is sharply increased. The danger of decomposing such peptides is particularly high in the acidolysis process when removing protecting groups.

The side reaction of DKP formation is extremely acute and in certain cases requires a change in the synthesis strategy for peptides containing secondary amino acids.

The prevention or reduction of the extent of racemisation of secondary amino acid residues during peptide synthesis may be achieved mainly by known methods such as urethane protection or by adding agents to prevent racemisation. However the efficiency of these methods depends strongly on the carboxy and amino components reacting and on the condensing agent used. When using BOP and BOP–Cl the racemisation of secondary amino acid residues is caused mainly by the formation of the oxazolonium ion and when using Piv–Cl by acid catalysed enolisation.

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Translated from *Uspekhi Khimii*, **60** 1841–1874 (1991) U.D.C. 541.128.13

Problems of the chemical physics of heterogeneous catalysis

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ABSTRACT. A series of fundamental problems of the chemical physics of heterogeneous catalysis are considered: new methods for investigating the mechanism of heterogeneous catalysis making it possible to study the reaction *in situ* with a high degree of time resolution; the dynamics of the elementary step, including energy and electron exchange processes in catalysis; macrodynamics of heterogeneous catalysis, including the formation of dissipative structure; chain mechanisms; heterogeneous-homogeneous catalysis and the role of a multiphase structure in heterogeneous catalysis.

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I. Introduction

The advances in the theory of heterogeneous catalysis during the last decade are associated both with the rapid development of new physical research methods and the development of computational-theoretical methods, including quantum chemistry, the qualitative theory of differential equations, etc. The theory of the elementary step, the dynamics of the catalytic process, the organisation and self-organisation of complex catalytic processes, the structure of catalysts, and the structure of active centres can be included among the problems of the chemical physics of heterogeneous catalysis.

The present review deals with the dynamics of heterogeneous catalysis and the methods of study associated with it, i.e. the physical methods which make it possible to determine the rates of various processes directly under catalytic conditions. Problems concerning the structure of catalysts and the structure of active centres, which require special analysis, are not discussed.

The present development of the dynamics of catalysis is characterised by two tendencies.

The first (microscopic) tendency is associated with the transition of studies to the atomic-molecular and further the subatomic level, with the use of the advances in quantum chemistry and in surface science for the elucidation of the mechanism of the elementary step in adsorption and in catalysis, and with account being taken of the electron and energy transfer processes in the elementary step and of the role of individual energy levels in the molecule and in the catalyst in effecting the elementary catalytic step.

The second (macroscopic) tendency presupposes the establishment of the features of a complex catalytic process based on the knowledge of the rates of its constituent elementary reactions, the organisation and self-organisation of catalysis, and the construction of a complex catalyst based on the set of data concerning the optimum catalyst for accelerating a particular stage.

The study of the kinetics and mechansm of a catalytic reaction at a microlevel and a macrolevel makes it possible to solve the problem of choosing an active and selective catalyst for a specified reaction. For this purpose, it is necessary to elucidate the structure of the intermediate surface compound in catalysis and to demonstrate the dependence of the rates of reactions on the rates of formation and consumption of such compounds, to establish the relation between the rate of reaction and the structure and chemical composition of the catalyst and the electronic structure of its constituent atoms, and to investigate the changes in the structure of the catalyst under catalytic conditions and the electron and energy transfer processes. In order to meet these requirements, it is essential to apply on a broad front modern physical methods (X-ray diffraction analysis, electron diffraction, various forms of optical and electronic spectroscopy, and laser beam methods) directly under catalytic conditions (*in situ*).

II. Methods of study

The rapid development of the theory of catalysis is impossible without the development of new methods of study, especially *in situ* (under reaction conditions). Optical (IR, UV) and microwave spectroscopic (EPR) methods for the study of the surfaces of catalysts were applied in the 1950's–1960's. X-Ray and photoelectron spectroscopic methods, low energy electron diffraction, secondary ion mass spectrometry, the method based on the fine structure of X-ray absorption (EXAFS), and a number of other methods were applied in the 1970's–1980's. Automatic apparatus for the testing of catalysts and computer techniques have been rapidly improved. New methods are appearing annually.

Unfortunately in the majority of studies the new research methods are used to compare different properties of the catalyst before or after the reaction—at best under catalytic conditions but in a stationary state. Nevertheless, in order to construct a theory of catalysis, it is essential to perform direct measurements of the duration of the dynamic processes on the surfaces. This can be done with the aid of non-stationary methods: the use of the so-called transient regimes, pulsed influences, abrupt changes in the temperature and pressure of the gas, abrupt alteration of the ratio of the components of the catalytic reaction, etc. It is essential to be able to measure both the rate of the catalytic reaction under non-stationary conditions and the rate of change of the concentrations of the absorbed substances and in the structure and various properties of the catalyst itself under the reaction conditions. These processes have to be investigated over all time scales.

Budar[1] drew attention to the fact that the turnover number of the reaction $n = r/N$ (r is the rate of reaction referred to the number N of active centres on the surface) is in the range from 10^{-2} to 10^{2} s^{-1} for many heterogeneous-catalytic reactions. The characteristic reaction times $\tau = 1/n$ are correspondingly between 10^{2} and 10^{-2} s. For such reaction times and turnover numbers, the reaction products are in fact formed in amounts which can be measured analytically in the usual catalytic experiments. In the analysis of the times taken to achieve various elementary stages of the process, it is therefore necessary to examine in the first place whether they fall within the range from 10^{-2} to 10^{2} s, i.e. whether they can influence significantly the rate of catalysis.

We examined[2] the characteristic times of heterogeneous processes occurring in catalysis. Many elementary processes fall within the time range indicated: adsorption and desorption, the majority of chemical stages on the surface, surface diffusion, phase transitions, and electron capture by the so called slow states. The bulk-phase diffusion in the solid catalyst is in most cases a slower process and its rate influences not so much the rate of the catalytic reaction as a whole as the change in the activity of the solid. On the other hand, the exchange of the energy of atoms and molecules with the surface (translational, vibrational, and rotational relaxation, spontaneous phase transition, and electron capture by the so called fast states on the surface) are as a rule faster processes with characteristic times of $10^{-12}-10^{-6}$ s. The electronic excitations can relax even faster, over a period of $10^{-15}-10^{-13}$ s. However, these short characteristic times must also be known in order to construct a complete dynamic picture of the catalytic process.

The methods for the measurement of the characteristic times of all heterogenous processes important for catalysis, both rapid and slow, have therefore assumed major importance. Naturally, the measurement of short times is a more difficult task.

It is necessary to investigate the dynamics of the changes in both the composition of the gas phase and in the concentration of the surface compounds and in the catalyst structure *in situ*. The jump methods are commonest. For example, after the attainment of a stationary state in a flow system, the pressure of one of the components is diminished abruptly and the variation of the pressures of the reactants and reaction products is investigated. In certain cases, it is possible to reject a particular proposed reaction mechanism. The interaction of an alcohol with an aldehyde on MgO,[3] the oxidation of CO on MnO_2 and Cr_2O_3,[4] and the decomposition of HCOOH on ZnO and metals[5] have been studied by this method. The characteristic times amounted to minutes and tens of minutes in the above investigations.

The minimum characteristic times which can be measured using the kinetic flow regime combined with chromatographic analysis are $10-10^{3}$ s. Using cold traps, it is possible to shorten this range somewhat. The pulse type of kinetic study using a katharometer for gas analysis makes it possible to measure times in the range $1-0.1$ s, while without the resolution of peaks in experiments using a katharometer or a flame-ionisation detector it is possible to attain also 10^{-2} s. Mass spectrometric analysis permits the measurement of even shorter times ($0.1-1$ s) in the flow regime at atmospheric pressure and $10^{-3}-10^{-4}$ s in the flow vacuum version.

Further shortening of the measurable characteristic times is limited by the distance from the surface of the catalyst to the sampling site. Unique procedures have been developed for the removal of samples at short distances from the catalyst (less than 1 mm).[6] It has been possible to improve the time resolution to $<10^{-3}$ s. Gleaves et al.[6] called their method the time analysis of products (TAP). The rates of adsorption, desorption, and intracrystal diffusion of acrolein during the oxidation of C_3H_6 on bismuth molybdate and the mechanism of the activation of the reactants in the oxidation of ethylene on silver, in the oxidation of butane on $(VO)_2P_2O_7$, and in the oxidative ammonolysis of methanol on $Mn_2P_2O_7$ were investigated by the TAP method.

In order to understand the mechanism, it is essential to determine simultaneously the composition of the gas phase and the spectroscopic characteristics under the conditions of non-stationary catalysis. Tamaru[7] was one of the first to investigate the rates of reaction of surface compounds on oxide catalysts by IR spectroscopy. Together with the investigation of the dependence of the rate of reaction under stationary conditions on the concentration of a particular surface form, the response of the system to rapid changes in the reaction conditions, for example, the alteration of the isotopic composition of one of the reactants or a change in temperature or pressure, was analysed. Investigators have called this procedure the dynamic approach to the study of chemisorption states.

A set of physical methods for the study of catalysis *in situ* has been developed at the Institute of Chemical Physics of the USSR Academy of Sciences.[8] Catalytic reactors which serve simultaneously as cells for IR, UV, and Raman spectroscopy, as cameras for the study of the X-ray structure, as tubes for EPR measurements, and as cells for the Mössbauer spectrometer were devised. The mechanisms of the interaction of NO with CO on metals,[9] of the oxidation of NH_3 on metals and oxides,[10] and of the partial oxidation of isobutene on complex oxides[11] were investigated with the aid of IR spectroscopy. Raman spectroscopy was applied *in situ* to the study of the high-temperature oxidative condensation of methane on alkaline earth and lanthanide oxides.[12] A new method, namely the spectroscopy of surface electromagnetic waves,[13] has been used to study the oxidation of methane on the same catalysts at a lower temperature. The changes in phase composition in the catalyst on partial oxidation of propene on the Bi–Co–Fe–Mo–O catalyst and in the Fischer–Tropsch synthesis on iron catalysts were studied by X-ray phase analysis and by Mössbauer spectroscopy *in situ*.[14,15] The oxidation of allyl alcohol to acrolein on the V–Mo–O_3 catalyst was investigated by EPR.[16]

In all the studies listed above, the process kinetics were analysed from the change in the intensity of one line in the spectrum (or on the X-ray diffraction pattern). The kinetics of the change in the composition of the gas phase were investigated simultaneously by gas chromatography. This did not ensure satisfactory time resolutions, the measured characteristic times amounting to several seconds and more. The application of mass spectrometric analysis of the gas phase helped to shorten the measured characteristic times.

In the study of reactions of surface compounds alone without the analysis of the gas phase, it is possible to measure also shorter times. The commonest method for the study of surface compounds is IR spectroscopy. It ensures a high resolution with respect to energy and can be used at any pressure of the gas phase. However, the existing versions of IR spectroscopy do not permit the attainment of a time resolution better than to within 1 min.[17] For example, when the FTIR method (Fourier transform IR spectroscopy) was used to study surface compounds in the autooscillatory process involving the oxidation of CO on platinum, the resolution was to within 1 min.

New versions of IR spectroscopy ensure a higher sensitivity, a better time resolution, and in many instances also a better spectroscopic resolution. For example, using the IRAR method (infrared absorption reflection) and sensitive detectors, it has been

possible to increase the sensitivity of the measurement to within 10^{13} cm^{-2} or 0.01 of a monolayer of adsorbed molecules on the face of a single crystal.[19] The method of emission IR spectroscopy permits the investigation with a high sensitivity of catalytic reactions at a high temperature,[10] while diffuse reflectance IR spectroscopy increases significantly the possibility of detecting surface compounds in the spectral range 2000–4000 cm^{-1}.[20] The spectra obtained by the method of surface electromagnetic waves (SEW) exhibit an unusually high spectra resolution especially if one uses powerful light sources such as lasers.[13] According to Shafranovskii, et al.,[21] the SEW method is at least four times more sensitive than the IRAR method.

A disadvantage of the electronic and photoelectron spectroscopic methods, whose sensitivity is extremely high and which give rise to an extremely good time resolution, is the impossibility of using them at high pressures. The kinetics of reactions on the faces of single crystals were investigated by X-ray photoelectron spectroscopy (XPES) and measurements were made of the changes in the concentrations of surface compounds. The kinetics of the oxidation of NH_3 on platinum were investigated[22] on the basis of the Auger spectra of the adsorbed oxygen. The oxidation of hydrogen on platinum has also been studied by Auger spectroscopy. It proceeds via the formation of surface OH groups.[23] The measured characteristic times of surface processes in the above studies exceeded 1 s.

The application of vibrational LEES (low energy electron scattering) spectroscopy, which is highly sensitive, ensures a satisfactory time resolution and the possibility of measuring the vibrational spectra of isotopically-substituted molecules, to the study of surface reactions is developing rapidly. The disadvantages of the method are a low spectra resolution (compared with IR spectroscopy), a non-linear dependence of the line intensities on concentration, and, what is most important, the necessity to carry out measurements under vacuum conditions. The kinetics of the $C_6H_6 + D_2$ deuterium exchange on Pt(111) were investigated by this method.[24] At 314–346 K, the characteristic process time was 30–120 min and the resolution was to within ~5 min.

The application of multichannel detectors appreciably increases the sensitivity of the LEES method and hence the time resolution. In the study of the decomposition of N_2O on Si(110) by the LEES method, a time resolution of 5 ms was attained.[25] Similar resolutions were achieved in the study of the adsorption and desorption of CO on Ni(110), Rh(100), and Cu(100), the dissociation of NO on Rh(100), the decomposition of CH_3OH on Ni(100) and Fe(100), and the oxidation of hydrogen on Rh(100).[17] In the adsorption of CO on Ni(111), the resolution was improved as far as 20 μs.[26] The use of electron pulses makes it possible to reduce the resolution time to 1 μs. Owing to the disadvantages of the LEES method mentioned above, there has been a marked diminution of its application in very recent times in the study of the kinetics of reactions of surface compounds, the procedure being replaced by optical methods.

The measurement of even shorter times involves the use of laser techniques. By virtue of the high monochromaticity and high power of the laser radiation one can (1) ensure the independent excitation of various vibrations of the reactant molecules in order to drive the reaction in the required direction, (2) one can detect with a high degree of sensitivity and indentify the reaction intermediates and the energy state of the molecule in the gas phase can be determined with respect to all degrees of freedom—translational, rotational, and vibrational, and (3) the lifetime of the excited states on the surface can be determined.[27]

The laser spectroscopy of species in the gas phase, which has been rapidly developing in recent years, has been used in particular for the determination of the degree of excitation to various energy levels of the desorbed molecules.[28–30] For this purpose, the laser beam is passed in the immediate vicinity of the catalyst. Among the methods employed, we may mention the intracavity laser spectroscopy (ICLS),[31] which is characterised by a sensitivity of 10^8-10^{10} cm^{-3} and a time resolution of 10^{-6} s, laser magnetic resonance (LMR)[32] with a sensitivity of 10^8-10^{10} cm^{-3} and a time resolution of $10^{-2}-10^{-1}$ s, and laser-induced fluorescence (LIF)[33] with a sensitivity of 10^6-10^{10} cm^{-3} and a time resolution of $10^{-8}-10^{-9}$ s. The multiphoton ionisation (MPI) method exhibits the greatest sensitivity (10^3 cm^{-3}) and is most general.[34] Its time resolution is $10^{-8}-10^{-9}$ s and its spectra resolution is 10^{-3} cm^{-1}. The MPI method has been used successfuly to investigate the quantum state of the desorbed molecules.[35,36]

Other laser techniques—coherent anti-Stokes Raman spectroscopy (CARS),[37] opto-acoustic spectroscopy,[31] multiphoton excitation,[38] and high-resolution sub-Doppler laser spectroscopy[39]—still await their application in the study of the quantum kinetics in gas–solid systems. The electron beam-induced fluorescence (EBIF) method, which provides information about electronically excited states, has been used to investigate the desorption of the N_2 molecule.[40] The IR luminescence method involving the application of a Fourier spectrometer, i.e. the emission of radiation characteristic of excited states, has been employed[41] to identify the vibrational and rotational states of CO_2 as the product of the oxidation of CO on platinum. The time resolution of the method is 10^{-6} s.

Laser methods have been used more rarely for the determination of the kinetic constants of surface processes. The laser-stimulated desorption (LSD) method[42] made it possible to determine the constants for a series of catalytic reactions which are difficult to determine by other procedures. In principle it is possible to attain a picosecond (10^{-12} s) time resolution with the aid of the LSD method.[17]

In order to determine the true lifetime of the ultrashort-lived excited state on the surface, the pulsed picosecond laser technique has begun to be used recently. The specimen is usually irradiated by a laser pulse (for example, a pulse from the neodymium laser) lasting several picoseconds and is probed by the laser before, during, and after the laser flash. The lifetimes of the vibrationally excited states of the OH groups on a series of adsorbents[43,44] and of the CO group in the adsorption of CO on metals and complexes[45] have been measured by this (direct) method. It proved to be $10^{-10}-10^{-11}$ s.

The lifetimes of the electronically-excited states on the surface, measured with the aid of laser picosecond photoelectron spectroscopy (LPS),[46] are about 70 ps. There are as yet very few data on the lifetimes of the electronically excited states and they all lie within a very broad range—from 10^{-5} to 10^{-15} s.[28]

A new method for the study of surfaces has appeared recently—the spectroscopy of second harmonic generation of laser radiation (SGSLR).[47–50] When the pulse technique and a photon counter were employed, unique time resolution, amounting to 100 femtoseconds (10^{-13} s), was achieved, i.e. a time of the order of magnitude of the period of a single vibration. The exceptional sensitivity of the SGSLR method is due to the fact that it makes it possible to measure forbidden transitions in a centrosymmetrical system. Within the bulk of a solid, such symmetry predominates, whilst on the surface it is usually disturbed and the restrictions on

the manifestation of the signal are eased. The kinetics of the adsorption of O_2 on Rh(111)[51] and on Si(111),[52] the kinetics of the dehydrogenation of benzene,[53] etc. have been investigated by the SSGLR method. In the study of two-dimensional phase transitions on the Si(111) face, it was found that, as a result of the exposure of the Si(111) surface to laser radiation, the (7 × 7) structure disappears over a period shorter than 150 fs. During this period, the evaporation of atoms cannot take place: it is easy to calculate that the Si atom ejected at a thermal velocity travels only 0.1 nm during this period. The authors[54] justifiably assume that during such a short period only electronic excitation takes place in the forbidden gap of silicon and that Si atoms move slightly away from the ordered positions. In 1989 yet another short wave femtosecond range began to be used in spectroscopy and a resolution as far as 10^{-14} s was achieved. This makes it possible to investigate the properties of the transition state (activated complex) not by calculation but by means of direct measurements. It is difficult to overestimate the importance of transition state spectroscopy for chemical kinetics and catalysis. Although very simple reactions of the type[55]

$$IHg+I^{\bullet}\rightarrow I+HgI^{\bullet},$$

were investigated in the first studies, there are no fundamental obstacles to extention of this method also to complex, including heterogeneous-catalytic, processes.

The rate of transport of current carriers in a semiconductor has been investigated with the aid of laser pulses lasting 6 fs.[56] Laser pulses having an energy of 2 eV and a duration of 200 fs have been used to desorb NO from the Pd(111) face. Translationally and vibrationally excited NO molecules are desorbed. On the other hand, on exposure to nanosecond pulses, unexcited NO molecules are desorbed.[57]

The rates of phase transformations on the surface and in the bulk phase during adsorption and catalysis can be investigated by dynamic structural methods *in situ*. Numerous studies on the structures of two-dimensional phases of adsorbates and adsorbent surfaces have been performed by the slow electron diffraction (SED) method. This method was also used for kinetic purposes[58] and it is then referred to as dynamic SED or video-SED. In the study of the oxidation of CO on Pt(100) by the video-SED method, the movement of diffraction waves on the surface for a constant interconversion of the Co(1 × 1) and CO(*hex*) structures and diffusion of CO between the phases was observed. The time resolution of video-SED method is about 1 s.

Approximately the same time resolution is attained also when scanning tunnel microscopy (STM) is employed.[59–67] This new very highly sensitive method makes it possible to obtain a direct image of the surface atoms with a spatial resolution less than 0.1 nm, i.e. not only at the atomic but also at a subatomic level. The STM method provides a very detailed photographic picture of chemisorption. The high degree of localisation of the method is to some extent a disadvantage, since the minute details of the region investigated thus revealed are difficult to relate to real atoms and surface orbitals.[66] There are no fundamental reasons to prevent the application of electron microscopy *in situ* to investigate catalysts under a controlled atmosphere.[66] The adsorption of H_2 on Si, of S on Re(001),[62] of O_2 on GaAs,[63] and of NH_3 on Si(111)[65] were investigated by the STM method.

In the method based on the extended fine structure of X-ray absorption (EXAFS), a powerful source of X-rays, usually a synchrotron source, with an energy of 1–25 keV is used. With the aid of these X-rays, the fluorescence or emission of Auger electrons is excited, this being accompanied by the formation of holes in deep levels. The EXAFS method reflects fairly accurately the local structure of the surface and makes it possible to measure the distances between the atoms of the adsorbate and the surface or between the surface atoms. The usual time resolution in the EXAFS method is 10^{-6} s. New highly intense sources of soft X-rays (0.1–3 keV) make it possible to obtain nanosecond (10^{-9} s) pulses. Numerous studies on catalysts and their genesis have been carried out with the aid fo the EXAFS method.[68] The application of the method to the study of the real dynamics of a catalytic process is so far in its initial stage[69] and will undoubtedly expand. In one of the latest studies,[70] the spectra of the Pt/Al_2O_3 catalyst were investigated under the conditions of the reforming of hydrocarbons at 20 atm and 400 °C.

Various physical methods have been applied to investigate the changes in the bulk-phase structure of the catalyst during the catalytic process. We have already mentioned the use of the Mössbauer effect for the analysis of the phase composition of the catalyst *in situ*. In the instruments used hitherto,[14] the power of the γ-radiation sources was low and the measurement of a satisfactory spectrum required a long time, which was necessary to accumulate data. For this reason, only very long characteristic times, of the order of minutes and tens of minutes, can be measured by this method.

In many cases the phase transformations of the catalyst take place relatively slowly and determine not so much the rate of the catalytic step proper as the rate of deactivation or activation, i.e. processes involving the formation and ageing of the catalyst. The diffusion of oxygen from the surface into the bulk of the oxide catalyst and back again can be the rate-determining stage of the catalysis proper in oxidation-reduction reactions. This has been demonstrated by the EPR method *in situ* in relation to oxidation reactions on $V-MoO_3$ catalysts.[16] The measured characteristic times are in the range 1–10 s.

The first studies on the application of NMR spectroscopy *in situ* to the investigation of the structure of a catalyst and its changes have been published.[71,72]

Spontaneous phase transitions can occur as a result of the shift of the lattice by fractions of interatomic distances, in which the diffusion of species in the solid plays a subsidiary role. The formation of nuclei and growth of crystals do not take place. A method of measurement of the highest rates of phase transitions has been developed.[73] Using a pulse source of X-rays with a current of tens of kiloamperes, the authors investigated the structural transformations occurring under the influence of a shock wave. In each experiment, the apparatus was completely disrupted. The minimum measurement time was 10^{-8} s and the transformation was completed over a period shorter than 1 μs. The conversion of α-cobalt into another modification was achieved over a period of 2×10^{-8} s. Thus in spontaneous transformations the rearrangement of the entire lattice can be completed over an unusually short time. For this reason, the further development of the X-ray phase analysis (XPA) method requires the development of powerful sources of X-rays and sensitive detectors. The use of synchroton radiation ("X-ray cinema") is promising.

The molecular beam method occupies a special place in studies of the dynamics of the interaction of molecules with surfaces and of the exchange of energy between the molecules and the surface in order to elucidate the elementary stages in chemisorption and catalysis.[28,74,75] A stream of reactant molecules emitted from a high-pressure

chamber via a small aperture into a vacuum chamber strikes a target (the catalyst). In the beam, the collisions of molecules with one another or with the wall are impossible. Diffusional limitations are also excluded. With the aid of the molecular beam method, it is possible to determine (1) the minimum lifetime of the reactant molecule on the surface required for the occurrence of the reaction, (2) the probability of the reaction in a single collision with the surface, (3) the dependence of the rate of reaction on the energy of the molecules in the beam and on the surface temperature, (4) the distribution of the energy (translational, vibrational, and rotational) between the surface, reactant, and the reaction products, (5) the dependence of the rate of reaction on the surface coverage by measured amounts of the adsorbent, (6) the probability of the deactivation of the excited molecules, and (7) the angular distribution of the desorbed and scattered molecules.

The energy of the molecules in the beam is determined by the design of the source. In thermal Knudsen sources, the gas is maintained at a temperature between 77 and 3000 K. These sources yield beams having an atomic flux density of $(2-4) \times 10^{14}$ s^{-1} cm^{-2} and energies from 0.008 to 0.32 eV. The temperature of the beam is frequently also referred to. However, the estimation of the energy of the molecules in the beam in degrees Kelvin is useful only in the case of a Maxwell–Boltzmann distribution.

The application of an ultrasonic beam makes it possible to narrow the distribution with respect to velocity by a factor of 100 compared with the Maxwell distribution in thermal sources. Despite the high density, the molecules in the ultrasonic beam travel parallel to one another and do not collide. By applying a high pressure (>0.1 MPa), it is possible to attain flux densities of $10^{16}-10^{18}$ s^{-1} cm^{-2} for energies of 1–2 eV. By diluting heavy gases with light ones, which move rapidly, for example, helium, it is possible to raise the kinetic energy to 10 eV. By combining the heating of the molecules in the source with ultrasonic flow, it is possible to obtain molecular beams with equal translational and vibrational energies. If a low pressure of a neutral gas is established in the space between the source and the target, it is possible to preserve the vibrational excitation in the molecules having quenched the translational excitation.

The method of modulated molecular beams for the relaxation spectroscopy of molecular beams (RSMB) is used to investigate the kinetics of heterogeneous-catalytic reactions. The interruption of the beam and the application of pulses of the reactants to the target-catalyst greatly increases the signal/noise ratio. The method makes it possible to measure characteristic times up to 10^{-4} s.

The method of molecular beams has found an interesting application in the investigation of real catalytic reactions at a high pressure.[76] The reaction is studied on the face of a single crystal cleaned in an ultrahigh vacuum. After the reaction, the pressure is rapidly reduced and the face of the single crystal is exposed to the molecular beam. Attempts have also been made to obtain high-density molecular beams simulating a high pressure.

Together with the molecular beam method, the method of ion beams has also been developing.[27,77] The theory shows that ion beams are rapidly neutralised on interaction with the surfaces of metals, forming neutral molecules in a vibrationally or electronically excited state. Thus experiments with ion beams can yield information about the interaction with the surfaces of solids of neutral molecules in the ground or weakly excited states, which corresponds approximately to the information obtained by the method of molecular beams. One of the simple ways of studying the interaction of atomic and molecular ions with the surface involves the acceleration of the ions by means of ionic cyclotron resonance.[78]

In our analysis of the research methods listed above, we drew attention mainly to their dynamic and kinetic applications and their time resolution. However, many of the methods being developed are designed primarily for the determination of the structures of catalysts, the structures of the surface and the active centres, and their energy levels.

III. Dynamics of the elementary step in catalysis

Over a long period, the rates of the elementary processes on the surface have come to be estimated from the standpoint of the transition state theory proposed in the 1930's. In this theory, the real dynamics of the motion of nuclei is not considered and account is taken only of the fundamental characteristics of the potential energy surface for the system and of the thermodynamic equilibrium between the reactants and the transition state (activated complex) at the apex of the potential barrier. The ranges of values of the pre-exponential factor k_0 in the Arrhenius equation for different surface processes have been calculated.[79–81]

Very fine experiments are needed for the determination of the exact values of k_0 and clearly there are not enough such experiments. Furthermore, it has been stated recently in a number of instances that transition state theory is inadequate and is subject to limitations when applied to the processes on surfaces: the tunnelling of nuclei at low temperatures, the possibility of a non-adiabatic course of the reaction, and the need to introduce corrections associated with non-equilibrium effects.[81] For example, in adsorption kinetics the factor k_0 is only partly determined by the laws of equilibrium thermodynamics; its other component (the sticking coefficient) is determined by local non-equilibrium effects.[66] The sticking coefficient is usually much smaller than unity.

The non-equilibrium effects in adsorption and catalysis have been examined in a monograph.[28] Several questions have been posed.

1. Are excited molecules formed in exothermic processes on the surface?
2. What is the lifetime of excited molecules on the surface?
3. What is their reactivity?
4. Is the concentration of the active centres related to the characteristics of the mechanism of catalytic reaction?
5. What is the lifetime of the excited states of the solid catalyst?

An accurate answer to the majority of the questions formulated requires a detailed knowledge of the dynamics of the elementary step. In particular, it is necessary to have detailed information about the potential energy surface. Calculations on the dynamics of the interaction have encountered considerable difficulties and can be performed only in the simplest cases. For example, a simplified trajectory method has been used[82] to describe the interaction of NO with the Pt(111) surface. The calculation, in which account was taken of 19 surface platinum atoms, made it possible to find the dependence of the rotational excitation of the desorbed NO molecules on the initial velocity of the molecules incident on the platinum surface. The majority of the answers to the questions posed above have been obtained experimentally.

The most important result of experiments carried out by the molecular beam method is the frequently observed extremely narrow angular distribution of the scattered molecules. The same thing frequently happens in the desorption of the molecules formed in the catalytic reaction. Thus analysis of the angular distribution of the

CO_2 molecules formed in the reaction of the adsorbed CO and O molecules on platinum showed that the intensity varies in accordance with the $\cos^n\varphi$ law, where $n = 6-40$.[83] The very narrow distribution of the desorbed or scattered molecules indicates their translational excitation.

Three reactions have been investigated on platinum by the thermal desorption method:[84,85]

$$N_2O+CO\rightarrow N_2+CO_2,$$
$$2NO\rightarrow N_2+O_2,$$
$$C_{ads}+O_{ads}\rightarrow CO_g.$$

In all three cases, a narrow angular distribution of the reaction products was observed, i.e. they were translationally excited. It is of interest to note that, after the adsorption of the CO molecules on platinum and the subsequent desorption, the angular distribution obeyed the $\cos\varphi$ law, which corresponds to complete thermal accommodation. Evidently the CO molecules desorbed after the equilibrium adsorption and those formed in the C + O reaction on the surface have different structures. In the second case, the CO molecule is not at the bottom of the potential well before escaping into the gas phase. This suggests the need to revise a series of mechanisms of heterogeneous catalysis according to which the reaction proceeds via adsorption interaction on the surface and desorption. Cases in which the reaction of a molecule continues also after its escape from the surface into the gas phase are apparently possible in catalysis.

The application of modern detection methods has made it possible to record the variation of the vibrational and rotational energies of the scattered and desorbed molecules. It was found that in many exothermic catalytic reactions vibrationally excited molecules are formed on the surface. Such reactions include the recombination of H atoms on copper,[86] the oxidation of CO on platinum and palladium,[87,88] the oxidation of carbon on copper,[89] the oxidation of H_2 on platinum,[90] etc. This indicates the energy of the catalytic reaction can be utilised for its possible acceleration.

The formation of vibrationally excited species in the endothermic NH_3 decomposition reaction on platinum has been observed.[91] On excitation of certain N_2 molecules, the 9th vibrational level proved to be occupied (energy of 2.4 eV). When the mechanism of this reaction was considered, only one exothermic stage was discovered:

$$NH_{ads}+NH_{ads}\rightarrow N_2^*+2H_{ads}+2.4\text{ eV}.$$

This may excite the molecule to the 9th vibrational level.

The phenomena involving the "cooling" of the molecule after catalytic reaction were also observed. The formation of translationally cold molecules with a temperature below the surface temperature after the $D_2 + O_2$ reaction on platinum was explained by the fact that the rate of desorption exceeds the rate of the thermal excitation of the reaction product (D_2O) adsorbed on the surface.[92] "Rotational cooling", i.e. a decrease in the "rotational temperature" of the molecules compared with the surface temperature, is frequently observed in the adsorption and desorption of NO on platinum,[93] nickel,[94] and palladium[95] and in the oxidation of NH_3 to NO on germanium.[96] The "rotational cooling" can be explained by the transfer of the energy of the rotation of the NO molecule before desorption to the translational energy on desorption. The interesting phenomenon of the different probabilities of the adsorption of NO from molecular beams oriented with the N or O atoms pointing towards the surface has been investigated.[97]

The explanation of the observed relations is in its initial stage. With the aid of trajectory calculations, attempts have been made[98] to relate the excitation of the molecules on desorption to the characteristics of the potential energy surface. In the thermal desorption of H_2 from Ni(111), one of the observed peaks corresponds to the predominantly vibrational excitation of the desorbed molecule, while the other corresponds to the predominantly translational excitation. In the former case (surface coverage $\theta > 0.5$), the desorption process is limited by the passage of the molecules through the "inlet" potential barrier, while in the latter case ($\theta < 0.5$) it is limited by their passage through the "outlet" potential barrier. Calculations of a similar kind have shown which part of the energy of adsorption and catalysis is transmitted to the surface and consumed on heating the latter and which is distributed in the form of the translational, vibrational, and rotational energies of the reaction product.[99]

On recombination of the N atoms on metals, electronically excited nitrogen molecules were detected.[100,101] The formation of singlet oxygen O_2 ($^1\Delta_g$) was observed in the oxidative dehydrogenation of butane on the Li–Sn–P oxide catalyst.[102]

Thus the formation of excited molecules in catalysis is an established experimental fact. The task for the immediate future is to find the general rules governing this phenomenon and to discover the relation between the formation of excited molecules and the characteristic features of the mechanism of the elementary step.

If during catalysis and desorption excited molecules are formed in conformity with the detailed equilibrium principle, it is to be expected that the excitation of the molecules reacting on the surface will also influence their reactivity. This phenomenon has been investigated in a number of studies on molecular beams.

In a large number of investigations of the interaction of molecular beams having different energies with the surface, a change in the probability of adsorption was observed as a function of the kinetic energy of the molecules in the beam (see, for example, the studies on the adsorption of H_2 on palladium[103] and nickel,[104] of N_2 on tungsten,[105] of O_2 on platinum,[106] etc.). The sticking coefficient s_0 usually increased with increase of the kinetic energy E_i of the molecules in the beam (the usual range is $E_i \simeq 0.5-10$ eV). The sharp changes in this relation for certain values of E_i are usually explained by the existence of an activation barrier to adsorption, while smoother relations are accounted for by the non-uniformity of the surface, i.e. the distribution of the activation barrier with respect to energy.

However, for very low energies of the beam, for example in the adsorption of O_2 on W(100) for $E_i < 0.03$ eV,[106] s_0 diminishes and does not increase with increasing energy. In this case the dependence of s_0 on the surface temperature T_s is much more marked than the dependence of s_0 on T_i. This can be explained by the occurrence not of direct adsorption but of adsorption via a precursor—a presorption state. Before passing to the chemisorbed state, the molecule can exist for a certain time in a weakly bound presorption state and can migrate in this state along the surface. The concept of a precursor and of its role in chemisorption was first put forward by Langmuir and its role in catalysis was examined in detail as early as the 1930's by Roginskii and Zel'dovich.[107] Prolonged debates concerning the question whether the presorption state is a "myth or reality"[106] were terminated, as a result of experiments with molecular beams, by an unambiguous answer: the precursor is real. Controversy continues concerning the nature of the presorption state: some workers believe that it is a physically

adsorbed molecule while others postulate that it is a short-lived excited state. It may be that both cases occur.

Whereas experiments with beams having differing energies have demonstrated incontrovertibly the influence of the translational energy on activated chemisorption, the available data on the translational excitation are fairly contradictory and do not permit a final conclusion. The appreciable increase in the probability of the dissociative adsorption of CO_2 ($\rightarrow CO + O$) on Ni(100) when CO_2 molecules are heated in a source of an ultrasonic beam has been attributed[108] to the involvement of the vibrationally excited molecules in the adsorption process. According to the authors,[108] distorted (bent) CO_2 molecules participate in the dissociation $CO_2 \rightarrow CO + O$.

Controversy concerning the mechanism of the activation of methane and other paraffins in their interaction with metals has continued for a long time. The large isotope effect, observed in the dissociative adsorption of CH_4 and CD_4 on rhodium, has been explained by the translational excitation of these molecules on passing from the presorption state to the chemisorbed state.[109] The subsequent data were fairly contradictory. Lo and Ehrlich,[110] who investigated the adsorption of CH_4 on W(211), adhere to their previous standpoint,[109] i.e. they explain the activation of CH_4 by vibrational excitation. On the other hand, it is believed that the activation of CH_4 on W(110) is caused by translational excitation with subsequent tunnelling of the H atom on chemisorption.[111] The dependence of the sticking coefficients s_0 of methane, ethane, propane, and butane on Ir(110) on the molecular beam energy has been attributed to the direct translational activation of the molecules colliding with the surface.[112] A deficiency of the above studies has been the lack of accurate data concerning the distribution of energy between different levels in the initial molecules.

Direct selective excitation of one of the bonds in the molecule by a laser makes it possible, in principle, to obtain molecules in a definite vibrational state and thus to achieve selective catalysis. The number of studies in this field is extremely large (see the relevant reviews[113–115]), but the results are not so far convincing. Most experiments have been carried out using irradiation by the IR CO_2 laser of various adsorbed compounds with light corresponding to an absorption band of the OH vibrations. The observed desorption was explained by the selective excitation of the bonds in the adsorbed molecule. However, as noted by Chuang,[116] in reality this explanation is doubtful, since there is no clear-cut dependence of the yield on the vibration frequency. The "translational temperature" of the desorbed molecules is usually low and close to T_s. These phenomena have been explained by "indirect" or "resonance" heating.[117] Phonons are emitted from the intermediate vibrational excitation levels, which leads to the heating of the specimen.

These considerations apply also to various data concerning the effect of the laser on catalytic reactions. The reported[118] acceleration of the oxidation of NH_3 on platinum following exposure to the light from a laser at a frequency of 933 cm^{-1} (vibrations of the N–H bond) was not confirmed in a subsequent test.[28]

More definite positive results have been obtained in the study of the electronic excitation of a solid and of adsorbed molecules by laser radiation in the visible and UV ranges. Thus the desorption of oxygen in the form of O_2 and O from the ZnO surface has been observed on exposure to laser light at the frequency corresponding to the forbidden gap in ZnO (λ = 354 nm).[119]

The use of short ($< 10^{-8}$ s) low-power laser pulses and the study of the process at a low temperature are most promising. By applying very short nanosecond (5 ns) laser pulses with a very low power (0.1–1 mW cm^{-2}), with an energy of 4.6–5.3 eV, Natzle, et al.[120] observed the selective desorption of NO from the Ag(111) surface at a low temperature (25–50 K).

The problem of direct detection of vibrationally excited molecules on the surface in chemisorption and catalysis has not so far been solved. Infrared adsorboluminescence might be used as a direct method for their detection. However, experiments and calculations have shown that, during the period taken by adsorption, the molecules have sufficient time to be virtually completely thermalised and the observed glow is simply a result of the heating of the specimen due to the heat of adsorption.[28] An IR laser has been used[121] for the vibrational excitation of physically adsorbed layers of CO on NaCl(100) at 22 K. The infrared adsorboluminescence observed subsequently was characterised by lifetimes of 2–12 μs.

The lifetimes of excited chemisorbed species on the surface have been measured directly in only one group of studies.[43,44] The lifetimes were calculated from the fluorescence decay time by means of the pulse excitation with a laser of the local vibration of the adsorbed molecule. In a number of studies, the lifetime of the vibrationally excited molecules on the surface was also determined by an indirect procedure—from the width of the lines in the IR spectra. For example, the experimental width of the absorption band of CO on Ni(100) and Ni(111), namely $\Delta\nu$ = 10 cm^{-1}, corresponds to the two-phonon breakdown of the C–O vibrations predicted by the theory.[122] The determination of the vibrational relaxation times from SEW spectra has been examined.[123]

Although the measured lifetimes of the vibrationally excited states are fairly short ($\sim 10^{-10}$ s), the excited species presumably participate in catalytic processes.

As regards the stages of the chemical interaction proper in a catalytic reaction, it is usual to distinguish two extreme cases; the Langmuir–Hinshelwood (OH) or surface interaction mechanism and the Eley–Rideal (ER) or impact mechanism. In the former case, the reaction proceeds between the species of two chemisorbed substances, while in the latter it occurs between a chemisorbed species and a species from the gas phase. The oxidation of CO on platinum and palladium has been investigated in greatest detail.[81,124] If the LH mechanism is valid, the elementary stage is the reaction

$$CO_{ads} + O_{ads} \rightarrow CO_2$$

while in the case where the impact (ER) mechanism operates the elementary stage is the reaction

$$O_{ads} + CO_g \rightarrow CO_2$$

or

$$CO_{ads} + O_{2g} \rightarrow CO_2 + O_{ads}.$$

Strictly speaking, both names are incorrect. In reality both the impact and surface mechanisms had been proposed by Langmuir.

The study of the oxidation of CO on Pt(111) by the relaxation spectroscopy of molecular beams[125] showed that the LH mechanism is valid. When CO molecules were admitted onto the Pt(111) surface coated by adsorbed oxygen, an arrest in the release of CO molecules was observed ($< 6 \times 10^{-4}$ s). The lifetime τ of CO molecules on the surface depends not only on the rate of the surface reaction but also on the rate of desorption of CO. On the other hand, when the ER mechanism operates, there should be no arrest and $\tau = 0$. In certain cases, the ER mechanism apparently also operates in a pure

form. Examples of the translational activation of molecules in dissociative reactions following direct impact against the surface (in the presence of the necessary activation energy) were quoted above. Catalytic reactions involving methane proceed as a result of the direct activation of the CH_4 on impact against the surface:[126]

$$CH_4 \rightarrow CH_3 + H_{ads}$$

In reality the LH and ER mechanisms represent certain limiting cases. In the intermediate (and probably the common) version, chemisorbed molecules and mobile weakly adsorbed species in the presorption state (see above) participate in the reaction.

In the oxidation of H_2 on metal single crystals,[127,128] several surface stages were observed:

$$O_{ads} + H_{ads} \rightarrow OH_{ads},$$

$$OH_{ads} + H_{ads} \rightarrow H_2O.$$

The rate of reaction depends on the surface coverage. The repulsive interaction between neighbouring like species exerts the greatest influence. Such interaction has been examined from the standpoint of the lattice gas theory.[81]

Yet another type of elementary process on the surface has been examined.[129,130] In the dehydrogenation of cyclohexane on platinum,[131] the adsorbed labelled benzene readily exchanges with cyclohexane in the gas phase so that labelled benzene is evolved into the gas phase:

$$Pt \cdot {}^{14}C_6H_6 + C_6H_{12} = Pt{:}C_6H_{12} + {}^{14}C_6H_6.$$

A similar exchange of an alcohol with the Al_2O_3 surface hydroxyl has been observed for the dehydration of the alcohol on Al_2O_3:[129]

$$(OH)_{surf} + ROH \rightleftarrows (OHROH)_{surf} \rightleftarrows (OR)_{surf} + H_2O.$$

Thus the dehydration of the alcohol involves adsorption substitution. According to an estimate,[129] the rate of the associative desorption exceeds by many orders of magnitude the rate of the direct desorption (for example, the evolution of water on dehydration of a surface OH group).

An associative complex has been detected by the direct IR spectroscopic method *in situ* in a study of the selective oxidation of isobutene to methylacrolein on a complex oxide catalyst.[11] It has been demonstrated[132] that associative substitution processes and, in a more general form, reactions involving strongly chemisorbed species occur widely. In the reactions mentioned above,[129–131] the activated complex included one strongly and one weakly chemisorbed species. Subsequently this phenomenon was "rediscovered" and was called "adsorption-induced desorption"[133] without referring to earlier investigations.[129,130]

Processes involving the migration of the reactants on the surface (surface diffusion), where one of the reactants diffuses towards the other which is adsorbed more strongly, or towards an active centre at which it reacts also occur extensively in catalytic surface reactions.

It is noteworthy that the surface migration process proceeds as a significantly activated process, its activation energy being appreciably smaller than the activation energy for desorption. Since the species on the surface are far from free in their migrations, in many cases the local concentrations can be replaced by average concentrations when surface diffusion is considered.[28,134]

There exist many examples of the experimental determination of the surface diffusion coefficients by the method of electronic[135,136] and ionic[137] projectors. However, the choice of objects is small and is determined by the possibility of obtaining an image of a section of the surface of the metal in an electronic projector or of individual species in an ionic projector. The diffusion of metal[137] and oxygen[135] atoms and CO molecules[136] on the surfaces of metals has been investigated by this procedure. A method for the determination of the surface diffusion coefficients by studying the desorption induced by the rapid heating of a section of the catalyst has been developed at the Institute of Chemical Physics.[138] Measurements have shown that the activation energy for surface migration is 0.1–0.3 of the activation energy for desorption or 20–60 kJ mol^{-1}, while the pre-exponential factor is between 10^{-2} and 10^{-4} cm^2 s^{-1}.

A model of surface diffusion as a process involving the migration of species both via jumps between centres and in the energy space as a result of the absorption and emission of phonons has been investigated in detail.[134] The possibility of the migration of species over large distances in a single jump has been demonstrated. Allowance for such a jump, which covers many lattice periods, leads to the appearance of characteristic relations in the kinetics of surface reactions, in particular, in the time variation of the rate constant.

The number of measured rate constants for surface diffusion is still very small. It is also essential to know the rate constants for the diffusion of the reaction components into the bulk of the catalyst or into its micropores. In oxidative catalysis, the elementary stage of the process may be the diffusion of oxygen atoms (ions) into the bulk of the oxide catalyst. In selective oxidation catalysts such as bismuth molybdates, the diffusion coefficients of oxygen at the catalytic temperatures can reach $10^{-4}-10^{-6}$ cm^2 s^{-1}. The usual mechanisms of the diffusion of atoms in a solid via vacancies or interstices do not explain such high diffusion coefficients.[139] In order to obtain an explanation of this kind, it is essential to consider cooperative mechanisms (see the next section).

Despite the enormous practical importance of real studies on diffusion in ultraporous catalysts of the type of zeolites, they were begun only recently. At the temperatures of catalytic cracking, the diffusion coefficients of ethane and heptane in the HT-zeolite are respectively $10^{-11}-10^{-12}$ and $10^{-13}-10^{-15}$ cm^2 s^{-1}.[140] MAS–NMR (NMR with magic angle spinning) methods are used to investigate the diffusion in zeolites.[141] Trajectory calculations of the diffusion coefficients of molecules in zeolite pores using data for the real geometry and for the movements of the atoms constituting the zeolites are extremely interesting.[142]

There also exist a further two types of elementary processes in catalysis; electron transfer and proton transfer between two reactants or between reactants and the catalyst.

There have been an enormous number of studies in which the rates of transfer of an electron between the surface and the bulk of a solid were considered, in particular between the adsorbed molecules and a solid. These investigations are in the main associated with the development of microelectronics.[143] "Fast" surface states with capture cross-sections $\sigma \simeq 10^{-13}-10^{-15}$ cm^2 (the corresponding electron or hole capture times are $10^{-8}-10^{-10}$ s) and "slow" surface states with $\sigma \simeq 10^{-18}-10^{-21}$ cm^2 (capture times $10^{-4}-10^{-1}$ s) have been observed. "Ultraslow" traps, characterised by capture cross-sections of $10^{-20}-10^{-30}$ cm^2, which are apparently associated with adsorbed states have also been noted. These ultraslow slow stages in fact determine in many instances the charge and potential of the

surface. The capture times vary in this instance within the range $10^{-1}-10^{3}$ s at low temperatures, i.e. they are equal to or exceed the characteristic times of the catalytic reaction.

It has also been demonstrated[143] that the so called electronic theory of catalysis on semiconductors,[144] in which considerable importance is attributed to the equilibrium Fermi level in the semiconductor as a criterion of its adsorption and catalytic activity, is inconsistent with the experimental data. Owing to the relatively low rate of transport of species on the surface and in the surface layer of the adsorbent and the catalyst, non-equilibrium processes occur.

It has been shown in a number of studies[145,146] that, under the conditions of adsorption and catalysis, the electron and hole transport to adsorbed molecules is effected over large distances from the bulk of the solid. Adsorption requires the obligatory direct overlap of the orbitals of the molecule being adsorbed and the surface atom—active centre. Pure charge transfer is overtaken by the subsequent movement of atomic species, for example, the diffusion of oxygen in the oxide, which frequently limits the rate of the catalytic oxidation.

For example, in the oxidation of allyl alcohol on V/MoO_3, investigated by the EPR method *in situ*,[146] the alcohol molecule initially interacts with the surface oxygen ions O_s^{2-}:

$$CH_2{=}CHCH_2OH+O_s^{2-}\rightarrow CH_2{=}CHCHO+H_2O+\square_s^{2-}.$$

After this, the electron rapidly passes from the surface into the bulk phase, which leads to the reduction of the vanadium ion which is observed by EPR:

$$\square_s^{2-}+V_v^{5+}\cdots O^{-}\rightarrow \square_s^{-}+V^{4+}\cdots O^{-}.$$

Next follows a slow stage—the diffusion of oxygen to the surface (or the reverse diffusion of a vacancy into the bulk of the catalyst):

$$\square_s^{-}+V^{4+}\cdots O^{-}\rightarrow V^{4+}\square_v+O_s^{-}.$$

Under the conditions of stationary catalysis, the movement of electrons into the bulk of the catalyst and from the bulk to the surface and the corresponding movement of oxygen ions reach equilibrium and a surface layer only a few angstroms thick actually "works".

At low temperatures, the electron moves over distances up to 1–2 nm via a tunnel mechanism. The reaction has a low activation energy. At a higher temperature, charge is transferred via the polaron or band mechanism. At still higher temperatures, the main catalyst lattice is oxidised and reduced.

In acid–base catalysis, the most probable elementary stage is proton transfer to the adsorbed molecule with formation of a positive ion (a carbonium ion in the case of hydrocarbons: $C_nH_m + H^+\rightarrow C_nH_{m+1}^+$) or a proton is split off with formation of a negative ion (a carbanion in the case of hydrocarbons: $C_nH_m\rightarrow C_nH_{m-1}^- + H^+$). The carbonium and carbanion mechanims of catalysis have been recognised by most investigators who have studied the reactions of hydrocarbons on oxide catalysts.[147] However, in reality there are very few examples of the spectroscopic detection of carbonium ions on the surface and under catalytic conditions there have been almost none.

Attempts have been made to use the NMR method for this purpose. For example, the kinetics of the conversion of methanol into hydrocarbons on the H-ZSM-5 zeolite were investigated on the basis of the MAS–NMR spectra *in situ*.[141] The formation of protonated methyl ether $(CH_3)_2OH^+$ is apparently an intermediate stage. In the latest study,[148] it was possible to determine the mobility of the protons of the hydroxy-groups of oxides from the width of the NMR line. It was found that the range corresponding to a sharp increase in the mobility of protons on catalysts such as γ-Al_2O_3, Al_2O_3.HF, and others coincides with the region corresponding to the rapid increase in catalytic activity in the dehydration of alcohols. The average residence time of the protons in the equilibrium state is of the order of 10^{-6} s. The authors[148] concluded that the transport of protons ensures more effective interaction with the adsorbed molecules than the transport of the molecules themselves to the hydroxy-groups (under these conditions, we have $\sim 10^{-4}$ s).

The dynamics of proton transfer in the adsorption of molecules with participation of the hydroxy-groups of the surfaces of the oxides has been examined.[149] By analysing the changes in the IR spectra (specially overtones of the OH vibrations) during adsorption, the author[149] concluded that the potential barrier to proton transfer may be lowered.

In subsequent studies, it was shown that proton transfer processes in cyclic complexes of the reactants with the catalyst occur widely in heterogeneous catalysis.[150] The transfer of a proton (or protons) in a single cyclic complex appreciably reduces the activation energy. Such cyclic complexes were first proposed to account for the catalysis of acid reacitons on Al_2O_3 as early as 1938 in studies by Shilov.[151] It remained only to demonstrate their involvement in catalysis by direct spectroscopic measurements.

IV. Macrodynamics of the catalytic process

Together with the concept of chemical kinetics as the science of the rate and mechanisms of chemical reactions, the term "dynamics" of chemical reactions has been increasingly applied in recent times. The term dynamics is applied to the theory of the general evolution of chemical systems on the basis of kinetic equations and dynamic equations of mathematical physics.[152,153] The methods developed by mathematicians for the study of dynamic systems have been vigorously applied in recent years to heterogeneous catalysis.

The kinetic description of heterogeneous-catalytic processes is based on the ideal adsorbed layer model developed by Langmuir.[154] According to this model, all the sections on the surface are uniform and on each of them equilibrium adsorption is observed. The catalytic reaction takes place on interaction of the reversibly adsorbed species. Further development of the formal kinetics of catalytic processes showed that fractional orders, which do not arise from the simple Langmuir kinetics, are frequently encountered in the kinetic equations.

The concept of the kinetics of catalytic processes on non-uniform surfaces was therefore developed in the studied of Roginskii, Zel'dovich, and Temkin.[155] According to this concept, the existence of biographic or induced non-uniformities is postulated and either a distribution function for the centres with respect to heats of adsorption or the law governing the interaction of the species on adsorption is introduced. The idea of a non-uniform surface or of the interaction of the adsorbed species made it possible to explain numerous kinetic relations observed in the study of adsorption and catalytic processes.

Studies in the recent decades have shown that the real picture is still more complex. It has been observed with the aid of physical methods that even on ideal atomically clean single crystal surfaces the kinetics of adsorption and of the reaction are not described by simple Langmuir equations.[156] We may also note the problem of the so called "pressure gap" in studies on catalysis, which are usually carried out at a pressure of 1 atm, and in studies on the physics of surfaces where the kinetics of the elementary heterogeneous processes are investigated under high vacuum conditions ($10^{-6}-10^{-2}$ Pa). In some investigations, attempts have been made to fill this gap. For example, the oxidation of CO on Pd/Al_2O_3 has been investigated[157] in the pressure range from 10^{-4} to 10^{4} Pa. The difference between the turnover numbers at low and high pressures of almost an order of magnitude indicates the operation of different mechanisms of the reaction under these conditions.

Numerous studies have shown that deviations from the Langmuir kinetics may be induced not only by the non-uniformity of the surface on interaction between the molecules but also by entirely trivial causes; mass and heat transfer and non-isothermal conditions in the catalyst bed. Among the non-trivial causes associated with the dynamics of the catalytic process itself we may note the following:

(1) phase and structural rearrangement of the catalyst;

(2) phase transformations of the two-dimensional adsorbed layer;

(3) diffusion of the reactants and intermediates between the active centres (kinetics with a precursor);

(4) diffusion of the reactants and intermediates between the different phases in a complex catalyst (spill-over);

(5) exchange of material between the surface and the bulk of the catalyst under the conditions of the catalytic reaction mixture;

(6) the possibility of the extension of the reaction to the gas phase (heterogeneous-homogeneous processes);

(7) the non-equilibrium nature of the process and the influence of the energy exchange on the reaction kinetics;

(8) radical-chain processes on the catalyst surface;

(9) complex autocatalytic and coupled reactions.

For a complete kinetic and dynamic description of the catalytic reaction, it is essential to divide all the relaxation processes into rapid and slow, to elucidate the question of the existence and of the number of stationary states, to carry out studies under conditions remote from equilibrium, and to construct phase portraits of the system (in terms of the "concentration–concentration" or "concentration–temperature" variables).[152] Kinetic models have been devised with three, four, and more independent variables in which account is taken of the catalytic stage proper and the interactions, listed above, which complicate the process dynamics. Even the superposition of two processes with similar characteristics can give rise to a fairly complex overall picture of the dynamic behaviour of the system.[124] The non-linearity arising under these conditions greatly hinder the description of the catalytic reaction.

Theories in which account is taken of the lateral interaction of the nearest molecules on the surface are used for the description of the kinetics of adsorption, desorption, and the reaction on the catalyst surface. These are the Ising[157] and lattice gas[81] models.

The CO oxidation reaction on metals has been subjected to the most comprehensive and detailed investigation. Most workers tend to the view that the main reaction proceeds via the Langmuir–Hinshelwood mechanism. The "non-linearity" of the kinetic equations, caused by the interaction between the adsorbed susbtances, leads to a series of unusual features in the dynamic behaviour of the system.[124,158] Critical phenomena, a multiplicity of stationary states, and autooscillations arise. It has been shown[124] that the slow relaxation, observed in the oxidation of CO on metals, i.e. the anomalously long period of the transition from the initial to the stationary state, can be induced by purely kinetic causes arising from the Langmuir–Hinshelwood mechanism. It had been believed previously that such phenomena are caused by extraneous factors, for example by the slow diffusion of substances on the surface or in the bulk of the catalyst.

At the microscopic level, new approaches to the description of the dynamics of catalytic processes with allowance for the interaction between the reaction medium and the catalyst have been developing on a wide scale. Such processes are considered from the standpoint of the thermodynamics of irreversible processes[159] and synergistic effects.[160]

The application of the concept of reaction affinity, introduced by De Done and borrowed from the thermodynamics of irreversible processes, made it possible to determine the directions of the transformations in a system of complex consecutive reactions.[161] For the occurrence of the reaction, it is essential that the affinities of all the stages in the chain of consecutive reactions are positive. Hence it was concluded that thermodynamic coupling (i.e. the occurrence of a thermodynamically unfavourable reaction after another more favourable one) is impossible. However, in chain or catalytic reactions there is a possibility of kinetic coupling: this requires that the concentration of the intermediate should be higher than the "equilibrium" concentration, if the concentrations refer to the number of reactants (i.e. the species on the left-hand side of the chemical equation of the given stage), or is below the "equilibrium" concentration if the concentrations refer to the number of reaction products (the species on the right-hand side of the equation). At high concentrations of the intermediate, there is a possibility of highly endothermic stages, for example, the desorption stage, which is almost always thermodynamically unfavourable. For example, in the decomposition of NH_3 on tungsten and molybdenum film, the stationary surface coverage by nitrogen atoms under catalytic conditions is much higher than the equilibrium concentration (i.e. the concentration in the absence of catalysis involving the reaction $N_2 \rightleftarrows 2N_{ads}$). The high concentration of nitrogen atoms ensures the occurrence of both the endothermic desorption of N_2 and of the catalytic reaction as a whole.[162]

Thus the widely used concept of the decrease in activation energy on catalysis compared with the non-catalytic reaction as the main cause of catalysis is incorrect or at any rate inadequate. Catalysis is also characterised by the formation of superequilibrium concentrations of intermediates, which is necessary to overcome the endothermicity of the unfavourable stages.

Whereas for small deviations from equilibrium it is possible to make do with linear mechanisms, for large deviations the breakdown of linearity cannot be disregarded. New stationary states arise and are stabilised as a result of energy exchange with the medium. They are organised in both space and time. Prigogine[159] called such structures dissipative. Dissipative structures are formed in open systems under the conditions of exchange of material or energy with the medium and for the cooperative occurrence of microscopic processes.

Four types of dissipative structures have been observed;[163] (1) spatially non-uniform; (2) periodic in time (autooscillations); (3) spatial-temporal (autowaves); (4) bistable or polystable (of the "trigger" type). An increasing number of observations of dissipative structures accumulate in heterogeneous catalysis every year, which

suggests that the observed phenomena are general in character. This applies particularly to complex catalytic systems.

Among spatially non-uniform structures—dissipative structures of the first type, two-dimensional phases have been investigated in greatest detail. In the study of low-temperature adsorption in single crystals of metals and oxides, an enormous number of two-dimensional phases have been discovered.[164,165] Their role in catalysis was also studied, in particular the possibility of a reaction between two adsorbed susbtances forming different phases has been examined. The oxidation of CO on single crystals of platinum group metals has been studied in greatest detail (and continues to be studied). The phases of the adsorbed CO and O on the Pd(111) face and the possible mechanisms of the interaction between them have been investigated by the video-SED method.[165,166] At low coverages, isolated portions of the two-dimensional O_{ads} and CO_{ads} phases are observed and reaction between them is possible as a result of surface diffusion. At moderate coverages, the phases come into contact and the reaction can proceed at the interface. Finally, at coverages close to one monolayer, mixed two-dimensional phases are formed in which each adsorbed CO molecule has a neighbouring O atom and can react with it.

In our studies,[167] the topochemical model of the formation and growth of nuclei was used to describe the kinetics of two-dimensional phase transformations. This model made it possible to explain a series of anomalous phenomena in the kinetics of heterogeneous catalytic reactions. The initial nuclei are formed more readily on dislocations, edges, and other defects. There are also data showing that the reactions of two-dimensional phases can proceed via a cooperative pathway as a result of shifts in linear series. For example, the conversion of the (1 × 1) structure into the hexagonal structure (*hex*) on Pt(100) is a result of the shift of atomic layers through a disordered state.[168]

The so called kinetic phase transitions[169] and their role in heterogeneous catalysis are widely investigated. The ZGB (Ziff, Gulari, and Barshad) model[170] has been used in very numerous investigations. The authors[170] examined similar kinetic transitions in relation to the oxidation of CO on a square uniform lattice. The probability of adsorption in each collision of the molecule with an active centre was assumed to be unity and the probability of reaction in each entry of a CO molecule and an O atom into neighbouring centres was also assumed to be unity. The very fact that the CO molecule occupies one centre on the surface while the O_2 molecule occupies two centres leads to sharp breaks on the curve describing the dependence of the surface coverage on the composition of the gas mixture and to corresponding changes in the reaction rates. Conditions were found under which periodic interaction of the metal alternately with CO and O_2 ensures a higher yield of the product than the interaction with a CO + O_2 mixture. Such sharp breaks were called kinetic first- and second-order phase transitions.

In subsequent studies,[171–174] the ZGB model was developed further: other types of lattices were examined, for example, the hexagonal lattice, and account was taken of the influence of the rates of desorption and diffusion and of the finite probability of reaction (< 1). In all cases, stationary oxidation of CO is possible only in the middle range of coverages θ_{CO} (in the simplest case from 0.33 to 0.52). At the edges of this range, the catalytic activity changes abruptly and a "kinetic phase transition" takes place. Much importance has been attributed to the formation of clusters under the conditions of low coverages θ_{CO} and θ_O and to subsequent percolation in the same CO oxidation reaction on platinum.[175]

The study of the role of two-dimensional and adsorption phases in catalysis is in its initial stages. The application of the video-SED method in catalysis suffers from an evident disadvantage; with its aid, it is possible to determine the structure of the surface only in a high vacuum. Furthermore, the majority of studies have been carried out with an abrupt transformation of the equilibrium phase into a non-equilibrium one by the rapid increase or decrease in temperature, which hinders the study of the initial stage of phase formation. The rapid development of tunnelling electron microscopy, which can be used at a high pressure and even in a liquid, will make it possible to carry out investigations during catalysis *in situ*.

The question of three-dimensional phase transformations and of their role in catalysis has been elucidated to the greatest extent. This problem has been examined in greatest detail in connection with oxidation-reduction reactions of oxidation catalysts. For example, the stability of the catalytic oxidation reactions involving the formation and decomposition of the oxidised and reduced phases has been discussed:

$$M+{}^1/_2O_2=MO, \quad MO+R=RO+M,$$

where M is the metallic phase, MO the oxide phase, and R the oxidised substance. On the basis of the phase rule, some workers[176,177] suggested that under stationary conditions the catalyst should consist of only one phase, M or MO, and that phase transformations cannot serve as stages in a catalytic reaction occurring under stationary conditions.

Further investigations demonstrated that these considerations are erroneous. In reality, during the reaction the catalyst exists in a non-equilibrium state. After oxidation and reduction under catalytic conditions, several phases usually coexist. In particular, it was shown that in the stationary state the oxidised and reduced phases can coexist in the catalyst.[178] On the other hand, under certain external conditions none of these phases can exist.

The existence of non-equilibrium phases in a series of catalytic reactions has been observed at the Institute of Chemical Physics by X-ray phase analysis *in situ*. Thus, in the selective oxidation of propene on the complex Bi–Mo–Co–Fe oxide catalyst, a non-equilibrium iron molybdate phase is formed in which there is a high concentration of vacancies and there iron exists in a state intermediate between Fe^{2+} and Fe^{3+}.[179] After extensive oxidation of methane on Pt/V_2O_5, the formation of a phase having the stoichiometric composition V_2O_4 was observed but with a crystal structure corresponding to that of the initial V_2O_5, i.e. having an enormous number of vacancies.[180] The non-equilibrium phases observed in the above investigations[179,180] facilitate the transport of oxygen via the lattice, which in the given instance is a stage of the overall catalytic process. Under the conditions of the Fischer–Tropsch synthesis on an iron oxide catalyst, a layered structure consisting of alternating fairly thin (20–30 Å) layers of iron oxide and carbide, is formed.[181]

The question of the catalytic transformations occurring in the vicinity of the phase transition point is also of interest. It has been shown that the ferroelectric $BaCO_3$ phase, which is inactive in the oxidation of CO, is converted at the Curie point (403 K) into a catalytically active paraelectric phase.[182] The Curie point of barium titanate shifts by several degrees following the adsorption of various gases; electron acceptors (NO and oxygen) increase it, whilst the electron donor CO and propene reduce it. Hence it follows that not only the phase transition but also, conversely, adsorption and catalysis influence the phase transition point.

Dissipative structures of the second type consist of auto-oscillations. In the 1970's–1980's studies on autooscillations in heterogeneous catalysis developed in an avalanche-like fashion mainly in relation to catalytic oxidation. We may note for example, studies on the autooscillations in the oxidation of cyclohexane on the NaY[183] and KY[184] zeolites, the oxidation of propene on $Co_xMg_{1-x}O$,[185] and the oxidation of CO on palladium-containing zeolites.[186]

Autooscillations are a striking manifestation of the self-organisation and non-equilibrium phenomena in catalysis. In order to account for autooscillations, various kinetic models are used, including negative feedback, non-linearity, and the presence of buffer stages (see the relevant reviews[187,188]). Common explanations include the change in the activation energy for the reaction with surface coverage (for example, as a result of the charging of the surface and the formation of an oxide layer on metals[186]), the thermokinetic mechanism which presupposes the heating and cooling of the system (provided that its heat capacity is high), a heterogeneous-homogeneous mechanism,[189] the existence of two and more surface forms, and the existence of two different phases (for example, oxidised and reduced).

A series of studies in which two-centre and two-phase models of autooscillations in heterogeneous catalysis were confirmed have been published recently. Thus it has been shown that the autooscillations in the H_2 oxidation reaction on different catalysts can be explained by the existence on the surface of Z and Z* centres having different activities and by the transfer of adsorbed species on the surface from one set of centres to another.[190] The autooscillations in the CO oxidation reaction on Pt(100), investigated by means of direct observations of the surface structure using the video-SED method[191] and scanning photoemission spectroscopy,[192] are induced by the coexistence of two structures—a square (1 × 1) structure and a hexagonal (*hex*) structure—of two-dimensional phases. For a coverage $\theta_{CO} < 0.5$, the *hex* structure is stable, whilst for higher values of θ_{CO} the (1 × 1) phase induce a decrease in θ_{CO}, as a result of which the phase transition takes place again and the oscillatory cycle is repeated. The mechanism of this phase transition was investigated with the aid of scanning tunnelling microscopy. It involves the formation of isolated groups (nuclei) comprising adsorbed CO and the subsequent diffusion of the CO species into the layer over the isolated groups.[193] Such isolated groups are much larger than atomic groups but smaller than the area of the single crystal face (90 μm^2).[194]

On Pt(110), autooscillations are observed in the oxidation of CO over a narrower temperature range and are sensitive to small oscillations in pressure. Here too, as on Pt(100), the autooscillations are induced by the presence of two surface phases, but, in contrast to the process on Pt(100), synchronisation is acheived not as a result of the propagation of surface waves of phase transformations but apparently occurs via the gas phase.[195] The synchronisation of autooscillations on the (110) faces of two separate small palladium crystals is achieved very rapidly, over a period of several seconds.[196] On the other hand, on the Pd(111) and Pd(100) faces of the single crystal such synchronisation has not been observed.[197]

The very important problem of the synchronisation of autooscillations in catalysis is still far from being solved. Rigorously periodic autooscillations are frequently observed not only on single crystals but also on powders containing a large number of grains and microcrystals. An attempt has been made[198] to explain the synchronisation of the autooscillations in the oxidation of CO on a palladium-containing zeolite by phase transitions accompanying the oxidation of palladium in combination with thermal effects. The strong heating occurring in the exothermic reaction

$$O_{ads} + CO_{ads} \rightarrow CO_2$$

leads to the diffusion of oxygen and further to the Pd→PdO phase transition. It has been shown[198] that, for small sizes of the palladium crystals, all the oscillations are averaged out and the reaction proceeds in a stationary regime. An increase in the size of the small crystals facilitates the diffusion of O_2 between them and increases the thermal conductivity, which in fact leads to the synchronisation of the autooscillations.[199]

Among other oscillatory regimes in liquid-phase reactions, apparent non-periodic oscillations or chaos have been observed.[200] Deterministic chaos is described in terms of the so called strange attractor in which all the trajectories are attached to a definite region in the three-dimensional phase space. The transition from regular autooscillations to chaotic ones and back again has been observed in the oxidation of CO on Pt(110).[201] The transition to deterministic chaos took place via a stage involving the doubling of the period of the oscillations.

Autooscillations have been observed also in non-oxidative heterogeneous-catalytic reactions: in the interaction of NO with CO on Pt(100),[202] in the decomposition of CH_3NH_2 on platinum,[203] and in the hydrogenation of nitrobenzene on deposited copper and nickel catalysts.[204]

Dissipative structures of the third type—spatial-temporal periodic structures or autowaves—are observed on smooth catalyst surfaces in the same cases as autooscillations.

Travelling waves have been observed in the oxidation of NH_3 on a platinum filament.[205] After brief heating of a small section of the filamental catalyst and after the transition of the reaction on this section from the initial kinetic regime (from a state with a low catalyst activity) to the diffusional regime (to a highly active state), it is possible to obtain a travelling wave in which sections having a high activity alternate with those having a low activity. The travelling wave can be obtained also by the converse procedure involving the rapid cooling of one of the surface sections.

The autowaves arising in the oxidation of CO on the Pt(100) face have been investigated by the video-SED method with scanning of the surface.[206] Autowaves are generated by the alternation of the (1 × 1) and *hex* structures with diffusion of the CO between the phases. Irradiation of a small spot on the Pt(100) surface with laser light induces the desorption of CO in the spot and the propagation of chemical waves at a rate of 2 mm min^{-1} at 480 K.[207]

The problem of the existence of stationary periodic structures or Turing structures in heterogeneous catalysis is separate. In liquid-phase reactions, such structures arise for certain ratios of the rates of reaction and diffusion. They can be observed when the autooscillatory Belousov–Zhabotinskii reaction is carried out in a layer of chromatographic gel.[208]

Dissipative structures of the fourth type, which arise when there are two and more stationary regimes corresponding to the same parameters and with an abrupt transition between them, have long been known in heterogeneous catalysis. The critical phenomena observed in the oxidation of CO and hydrocarbons on metals[209] have been sometimes explained by the self-heating of the catalyst with transfer of the reaction to the diffusional region. Further investigations demonstrated, however, a non-thermal cause of the observed phenomena. The existence of two stationary regimes in the oxidation of CO on platinum—one at high CO concentrations and

the other at high O_2 concentrations—can be explained by the competition between the adsorption and impact mechanisms.[124,153] The ZGB model mentioned above, according to which the critical phenomena in catalysis are caused by kinetic two-dimensional phase transitions, was later used[210] to explain such bistability.

Critical phenomena of this kind have been observed in the study of the oxidation of ammonia on fine platinum filaments.[205,211] The thermographic method developed by Berelko, et al.[205] made it possible to achieve the compensation of the heat evolution in the reaction over a very short period of 10^{-4} s. This procedure made it possible to demonstrate that the rapid transition from the low-temperature stationary regime to the high-temperature regime is induced by kinetic causes and not by a "thermal explosion". Critical phenomena have been observed also in a calorimetric study of the oxidation of propene on the deposited catalyst MoO_3/MgO.[212] The sharp increase in the rate of reaction after the attainment of a certain degree of surface coverage by oxygen was explained by the formation of a more active surface phase.

Hysteresis phenomena have been observed in many critical reactions. These involve the occurrence of the reaction via different stationary states depending on whether the reaction takes place with rising or falling tempertures or depending on the direction in which the reactant concentration varies. Hysteresis has been observed in the oxidation of methane on Pt/V_2O_5 [180] and of NH_3 on platinum.[211] This phenomenon has been usually explained by phase transformations and by changes in the structure of the catalyst on the surface.

In the extensive oxidation of propene on the $CuO/Cu_2O/Cu$ or NiO/Ni catalyst, the hysteresis loop was observed under conditions where the temperature of the O_2 pressure was varied in the forward or reverse directions.[213] These phenomena were attributed to catalyst oxidation and reduction processes. According to Greger, et al.,[213] the removal of oxygen from the catalyst and the absorption of O_2 are independent processes which are influenced by the particle size, the morphology of the particles, and the presence of impurities. Over a wide range of external parameters, two catalyst phases coexist: oxidised and reduced.

The critical phenomena in catalysis have also been attributed to the appearance of a branched chain reaction involving the formation of active centres.[211] An attempt to explain the "catalytic explosion" observed in the decomposition of HCOOH on Pt(110) by the occurrence of a branched chain reaction has in fact been made.[214] However, all the attempts to accelerate the decomposition by introducing the possible intermediate active species formed in the decomposition of HCOOH (hydrogen atoms, CO, and others) yielded a negative result.

There are general relations between catalysis and chain reactions.[215] In heterogeneous catalysis, there is a possibility of the formation of active species: free atoms and radicals escaping from the surface of the gas phase, quasi-free species propagating the chain reaction in the adsorbed layer, and also excited molecules. The commonest case is, however, the formation of non-equilibrium centres of the catalyst itself, similar to the species involved in a gas-phase chain reaction. Examination of the simplest kinetic schemes for A→B catalytic reactions showed that the catalyst activation stage

$$A+Z\rightarrow A+Z^*,$$

where Z is an active centre, is analogous to the chain reaction initiation stage, the catalytic stage proper

$$A+Z^*\rightarrow B+Z$$

is analogous to the propagation of a chain reaction, while the catalyst deactivation stage $Z^*\rightarrow Z$ is analogous to linear chain termination. The possible mechanisms of the formation of new active centres in catalysis, analogous to the occurrence of a branched chain reaction, have also been examined.

The kinetic differences between catalysis and a chain reaction are apparently not very significant. However, there are so far few chain mechanisms in catalysis whose reality has been demonstrated. There have been studies indicating a chain mechanism of the oxidation of CO on V_2O_5/SiO_2,[216] of the isomerisation of olefins on MoO_3,[217] of the Fischer–Tropsch synthesis on iron catalysts,[218] and of the synthesis of hydrocarbons from methanol on zeolites.[219] Further development of physical methods will make it possible to detect more reliably the intermediate species characteristic of chain mechanisms in catalysis.

Here we should like to draw attention to a number of features characteristic of a chain reaction which are frequently observed in catalysis: (a) the alternation of the formation and destruction of active centres (the occupation and liberation of the centres on the surface); (b) the attainment of superequilibrium concentrations of intermediates helping to overcome the endothermicity of unfavourable stages; (c) the attainment of the maximum rate of the reaction after some time has elapsed from its start.

The occurrence of heterogeneous-homogeneous catalysis, where the active species are desorbed from the surface and propagate the chain reaction in space, also constitutes indirect evidence in support of a chain mechanism. The phenomenon of heterogeneous-homogeneous catalysis was discovered in the 1930's and was investigated mainly by the method involving separate calorimetric measurements on the catalyst and the gas phase, which served as the principal means of detecting the homogeneous chain propagation of the heterogeneous-catalytic reaction.[220]

A series of data showing that not only free radicals but also excited molecules can escape from the surface in exothermic catalytic reactions have appeared recently. We have already quoted a number of examples of the narrow angular distribution of the desorbed molecules, indicating their translational excitation. For example, in the decomposition of hydrazine, i.e.

$$N_2H_4\rightarrow N_2+2H_2$$

on Ir(110) the entire evolved nitrogen is distributed within the limits of 7° around the normal to the surface and is translationally hot.[221] In an earlier study[222] of the catalytic decomposition of N_2H_4 by the method of separate calorimetric measurements, the heating of the gas phase relative to the catalyst was explained by the radical-chain propagation in the gas phase of the reaction initiated on the surface. In the light of new data,[221] this result can be explained also by the escape from the catalyst of excited molecules, which are subsequently deactivated in the gas phase with evolution of heat.

In the course of the oxidative dehydrogenation of butene on the Li–Sn–P oxide catalyst, the formation of an electronically excited molecule—singlet oxygen $O_2(^1\Delta_g)$—was observed.[223] It may be that the flow of the gas phase observed in certain catalytic oxidation reactions at 400–500 °C is caused by the formation of electronically excited molecules.

The heterogeneous-homogeneous mechanism of catalysis is apparently the principal mechanism of catalysis at high temperatures. Depending on the nature of the molecules and catalysts, ionic mechanisms of the electrophilic or nucleophilic substitution type, common in liquid-phase organic processes, predominate at low

temperatures (200–500 °C) and acid–base interaction plays an important role. Homolytic mechanisms involving the formation of free radicals and excited molecules predominate at a high temperature.

The transition from the measurement of macrocharacteristics (separate calorimetric measurements, increase in the free volume of the gas over the catalyst) to the direct detection of intermediate species became a new stage in the study of the mechanism of heterogeneous-homogeneous catalysis. The method involving the freezing out of radicals in a matrix beyond the layer of catalyst with their subsequent detection by EPR, which was devised at the Institute of Chemical Physics in Erevan[224] and subsequently developed further,[225] played a major role. The direct detection of free radicals in the gas phase beyond the catalyst without freezing out, for example, by laser magnetic resonance[226] and multiphoton ionisation[227] methods, has given rise to some prospects.

The oxidative condensation of methane on various oxide catalysts has been studied in particularly great detail in recent years:[225,228]

$$2CH_4+O_2=C_2H_4+2H_2O.$$

In this reaction, free radicals are formed on interaction of a methane molecule with the surface oxygen O_s:

$$O_s+CH_4\rightarrow CH_3^{\bullet}+OH_s.$$

The recombination of the radical from the gas phase, i.e.

$$2CH_3^{\bullet}\rightarrow C_2H_6$$

leads to the formation of an ethane molecule (and subsequently, on oxidative dehydrogenation, of ethylene). Although the reactivity is determined by the properties of the catalyst, the selectivity depends on the equilibrium in the gas phase:

$$CH_3^{\bullet}+O_2\rightleftarrows CH_3O_2^{\bullet}.$$

At a low temperature, the $CH_3O_2^{\bullet}$ radical undergoes further extensive oxidation to CO_2 and H_2O, while at temperatures above 600 °C the equilibrium is displaced towards methyl radicals and the selectivity in the formation of their C_2 product increases as the temperature rises. If the activation energy E for the interaction of methane with the catalyst, i.e.

$$CH_4+Cat\rightarrow CH_3^{\bullet}+Cat-H$$

is plotted against the energy Q of the bond between hydrogen and the catalyst Cat–H, then the points corresponding to the case where the acceptor (Acc) is the catalyst lie on a single straight line with the corresponding points for a homogeneous radical reaction:

$$CH_4+Acc\rightarrow CH_3^{\bullet}+Acc-H.$$

The Polanyi–Semenov relation holds:[228]

$$E=E_0-\alpha Q.$$

Heterogeneous-homogeneous radical processes also probably play a definite role in other high-temperature catalytic reactions (vapour phase conversion of methane, oxidation of ammonia, the synthesis of HCN). These should in fact be sought. The study of high-temperature catalysis is in the initial stage and the discovery of new reactions may be expected.

When the macrodynamics of catalytic reactions is examined, it is desirable to pay special attention to the organisation of the process on multicomponent and especially multiphase catalysts. The high reactivity and selectivity of such catalysts is attained as a result of the separation of the process in space: each stage of the catalytic reaction proceeds on a separate phase.

The principle of the separation of a complex reaction into stages each of which is accelerated by its own catalysts was proposed by Lebedev already about 60 years ago;[229] thus a selective catalyst was chosen for the synthesis of butadiene from alcohol:

$$2C_2H_5OH\rightarrow C_4H_6+2H_2O+H_2.$$

Dehydration, dehydrogenation, and condensation stages were isolated in this reaction and for each its own catalyst was selected. Subsequently a complex catalyst consisting of oxide phases accelerating the above stages was devised.

One of the advantages of multiphase catalysis is the possibility of displacing an unfavourable equilibrium as a result of the removal of an intermediate from one phase to another. Weisz,[230] who investigated in detail the conversion of hydrocarbons on the so called bifunctional catalysts, was one of the first to understand this. It was shown that in the reforming reaction on Pt/Al_2O_3 dehydrogenation of n-paraffins (A) is effected on platinum while the subsequent skeletal isomerisation of the n-olefin (B) to the iso-olefin (C) takes place on Al_2O_3 or aluminosilicate: $A\rightleftarrows B\rightarrow C$. By selecting a catalyst, it is possible to accelerate the removal of the substance B from one phase to another and to displace the equilibrium $A\rightleftarrows B$. An increase in the diffusion coefficient and a decrease in the distances between the species promoted the shift of the reaction towards complete conversion. In particular this can be achieved by the mechanical displacement of phases.

The shift of an unfavourable equilibrium can be achieved also in a simple catalytic reaction $A\rightleftarrows B + C$ without intermediates.[231] For this purpose, it is necessary to remove the reaction products constantly to other surface centres, which adsorb it more strongly. The occurrence of the reaction in the so called chromatographic regime was discovered in relation to the dehydrogenation of cyclohexane to benzene. The thermodynamically unfavourable reaction (at a low temperature)

$$C_6H_{12}\rightleftarrows C_6H_6+3H_2$$

can be effected by carrying it out under pulsed conditions with constant removal of products.

In such cases, a multiphase structure is always useful. The activity and selectivity in certain reactions can be increased by using special adsorbents for the reaction products. Thus, zeolites have been used for the removal of water in certain condensation reactions and for the removal of lower alcohols in the exchange of alcohols with esters.[232] Under real conditions of stationary heterogeneous catalysis, not only the concentration gradients of the intermediate compounds diffusing in the pores between the particles of different catalyst phases but also stationary gradients of the catalyst composition within each phase can be established.

The principle of the constant removal of the product from the reaction zone in order to increase the selectivity of the catalysis has been used in metallic membrane catalysts. The application of

palladium alloys in the form of membranes increases their selectivity in the dehydrogenation of butane to butadiene as a result of the removal of hydrogen to the other side of the membrane.[233,234] The involvement of hydrogen in another catalytic reaction (hydrogenation, oxidation) on the other side of the membrane increases the yield of butadiene still further.

The role of the multiphase structure of the partial oxidation catalyst was examined in detail in our investigations[14,235] based on the study of their structure by X-ray phase analysis and Mössbauer spectroscopy *in situ*. It was found that under the reaction conditions the complex Bi–Co–Fe–Mo–O catalyst consists of five main phases: (1) the β-$FeMoO_4$ phase necessary for the adsorption of oxygen; (2) the β-$CoMoO_4$ phase stabilising the β-$FeMeO_4$ phase by virtue of the coherence of the lattices; (3) the non-equilibrium partially reduced $Fe_2(MoO_4)_3$ phase through which oxygen atoms are transported from the oxygen adsorption centres to propene adsorption centres; (4) the $Bi_2(MoO_4)_3$ phase necessary for the adsorption and activation of propene; (5) the MoO_3 phase ensuring the maintenance of stoichiometric relations in the reduction of iron molybdate. The active centres are located near the interface. Non-equilibrium concentrations of vacancies and stationary hydrogen concentration gradients are created in the catalyst.

In oxidative catalysis there is a possibility also of separation in space of centres within a single phase.[236] The study of the oxidation of allyl alcohol to acrolein[16] on the MoO_3 catalyst with added vanadium by EPR *in situ* showed that organic molecules are adsorbed on the outer surface of the catalyst. On the other hand, oxidation and reduction processes occur on the V^{4+}/V^{5+} active centres within the bulk of the catalyst. Constant exchange of oxygen and electrons takes place between the surface and the bulk phase.

The separation of the active centres in space is apparently a general rule for complex catalytic processes. The theory of these processes has been inadequately developed. It must take into account the shifts of the equilibrium, the coupling of stages, and the transport processes between the centres, phases, or particles.

The role of surface and bulk-phase diffusion in heterogeneous catalysis is apparently much greater than has been thought hitherto. The phenomenon of the interphase diffusion of adsorbed species has been called spill-over. The spill-over of hydrogen, first observed in the adsorption of hydrogen on Pt/WO_3,[237] ensures the transfer of hydrogen atoms from the metal to the oxide. In the absence of the metal, there is no adsorption of hydrogen on the oxide. The spill-over phenomenon must play a major role in reactions involving hydrogen, displacing the equilibrium by virtue of the removal of hydrogen atoms.

The mechanism of spill-over is different in different systems. The exchange of D_2 with the hydrogen of the OH groups on Pt/SiO_2 has been investigated[238] by IR spectroscopy with Fourier analysis *in situ*. It was found that deuterium diffuses from the metal to the carrier in a weakly bound state on top of strongly bound OH groups on SiO_2 and exchanges with them. The driving force of spill-over is the concentration gradient between different states of deuterium. The spill-over of hydrogen atoms across an oxide film has been observed.[239] Platinum deposited on silicon and fully coated by a layer of the inert SiO_2 exhibits activity in the dehydrogenation of cyclohexane. The activity of the catalyst decreases exponentially with increase in the thickness of the film from zero to 30 nm and becomes constant for thicknesses in the range 30–2200 nm. The spill-over of hydrogen in the H_2-D_2 exchange and C_2H_4 hydrogenation reactions has been observed without direct contact between the oxide (SiO_2, Al_2O_3) and the metal (Pt/SiO_2, Pt/Al_2O_3), i.e. through the gas phase.[240] According to different data,[241] atomic and ionic species can participate in spill-over. The diffusion coefficients of the H and D atoms in the Pt/SiO_2 and Pt/Al_2O_3 systems proved to be unexpectedly very high: $10^{-3}-10^{-6}$ cm^2 s^{-1}.

The "spill-over of oxygen"—the diffusion of oxygen atoms across an oxide lattice from one active centre to others—was already mentioned above. The phenomenon of the spill-over of the NCO species from the surface of a metal (Pt, Rh) on to a carrier (γ-Al_2O_3) and conversely under the conditions of the reaction of NO with CO has been observed.[242] It has been shown by IR spectroscopy *in situ* that the NCO species participate in the reaction as intermediates.

Synergistic phenomena—the superadditive increase in the activity of the catalyst on mechanical mixing of the components—can be explained by the transfer of material between phases, diffusion, and spill-over. The conversion of propene in its oxidation on the mixed catalyst $CoMoO_4$ + MoO_3 or $CoMoO_4$ + $Bi_2(MoO_4)_3$ was found to be higher than the sum of the conversions on each component separately.[243] This can be explained by the fact that on one or both phases intermediates of possibly free-radical character are formed and after being released into space are adsorbed on another phase and undergo further reaction.

Numerous instances of synergism in partial oxidation reactions have been listed in a review.[244] A new term has been proposed for the designation of the synergistic intensification of catalysis in mixtures—remote control.[245] Synergistic effects have been noted in the hydrogenolysis of thiophene on (MoS_2 + CoS)/γ-Al_2O_3, in the oxidation of isobutene to methylacrolein on SnO_2 + Sb_2O_4, and in the dehydration of *N*-methylformamide on MoO_3 + Sb_2O_4; the influence of platinum on the reduction of Ni is associated with these effects.[245] The operation of the remote control mechanism makes it useful to introduce the catalyst in the form of several layers consisting of different materials.

The overall organisation of the process via parallel or consecutive mechanisms is very important in the dynamics of complex catalytic reactions. This determines, in particular, the selectivity of the catalyst—its ability to accelerate only one of several reactions occurring simultaneously. The principal factors influencing selectivity, namely the bond energy, the ligand effect, the ensemble effect, steric effects, and multiphase structure were examined in the present author's previous review.[235]

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Translated from Uspekhi Khimii 60 1875–1897 (1991) U.D.C. 541.11 547.458.81

Thermochemistry of the dissolution and characteristics of the solvation of cellulose, polysaccharides, and their derivatives

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ABSTRACT. The results of thermochemical studies on solutions of cellulose, its derivatives, and other polysaccharides are surveyed and treated systematically. The existing ideas about the energy effects due to the amorphous-crystalline structure of polysaccharides, including cellulose, are analysed. It is shown that the enthalpies of solution under the conditions of thermodynamic equilibrium are thermodynamically most preferred. Attention is concentrated on the establishment of a relation between the heats of solution and the electron-donating capacities of the solvent and the polymer. New approaches to the quantitative estimation of the thermochemical parameters of solvation processes in solutions of cellulose and its ethers and esters, based on multiparameter correlations of the enthalpies of solution and transfer with the physicochemical properties of the solvents, are described.

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I. Introduction

By virtue of their universality, thermochemical methods are widely used in the study of the solvation, dissolution, and interactions of cellulose and its derivatives in solutions.[1–5] The concept of electron donor–acceptor (EDA) complex formation is nowadays of fundamental significance, explaining the nature of the interaction of various organic solvent systems with polysaccharides.[6–8] According to this concept, the energy relations of the EDA interaction in the solution are determined by the electron-donating and electron-accepting capacities of the corresponding centres of the polymer and solvent molecules. The calorimetric method for the study of the specific solvation of cellulose and its derivatives in solutions therefore helps in the development of criteria for the solvent power of non-aqueous solvents on the basis of correlations between the enthalpies of solution and the EDA properties of the liquids.

There exist numerous data for the heats of wetting, swelling, and interaction of cellulose with various liquids, but the question of the elucidation of the relation between the enthalpies of reaction and the EDA capacities of the solvents were considered in only a few studies.[9–11] In our view, no account was taken of the following factors in these investigations.

The data on the heats of reaction of cellulose and its derivatives with solvents refer to non-equilibrium processes occurring in a heterogeneous medium.[1,42] The interpretation of such experimental data is difficult as a consequence of their thermodynamic indefiniteness. Enthalpy of solution data characterising the energy relations of the dissolution process at the molecular level, are best.

In the discussion of experimental results, use was made in the above investigations[9,10] of ether the electron-donating or the electron-accepting capacities of the solvents. The amphoteric nature of the functional groups of cellulose and its derivatives needs to be taken into account when the electron-donating and the electron-accepting properties of liquids are considered jointly.

There are few literature data on the heats of solution of polysaccharides, so that further investigations in the field of the calorimetry of solution of cellulose and its derivatives are essential.

II. Thermochemistry of the wetting, swelling, and interaction of cellulose with individual solvents, electrolyte solutions, and ionic complexes

Numerous studies have been devoted to the thermochemistry of the interaction of cellulose with liquids and solutions of electrolytes and complexes.[9–11,13–41] A considerable proportion of these studies dealt with the investigation of the heats of wetting, swelling, sorption, and interaction of cellulose with water.[12,13–28]

As a hydrophilic polymer, cellulose exhibits an enhanced affinity for water. However, water molecules are sorbed only by amorphous regions without the disruption of the crystalline regions of cellulose.[9,13] Consequently the enthalpies of reaction with water to a certain extent characterise the ratio of the crystalline and amorphous regions of cellulose, which depend on the previous history of the specimen and the methods of processing and preparation. The integral heats of reaction of the amorphous regions of cellulose with water have been calculated from the ethalpies of reaction of celluloses having different degrees of crystallinity with water.[14,15]

The second decisive factor is the moisture content of the initial specimen. The heats of reaction approach zero for a water content in the specimen corresponding to $P/P_0 \simeq 0.65$. To illustrate this, Fig. 1 presents the variation of the integral enthalpies of reaction with water of specimens of cotton (*1*), wood (*2*), mercerised cotton (*3*), and regenerated (*4*) cellulose and its amorphous regions (*5*) with different moisture contents,[14] the different degrees of crystallinity X of which are respectively 0.70, 0.65, 0.54, and 0.40.

Thermodynamic analysis[14] has shown that, with decrease in the moisture content, the compatibility between the amorphous regions of cellulose and water is determined by the changes in both the enthalpy and entropy of the system. With increase in the water content, the contribution of the enthalpy to the free energy of formation of the system becomes dominant. The appreciable exothermicity of the process is due to the specific interaction between the components with formation of hydrogen bonds.

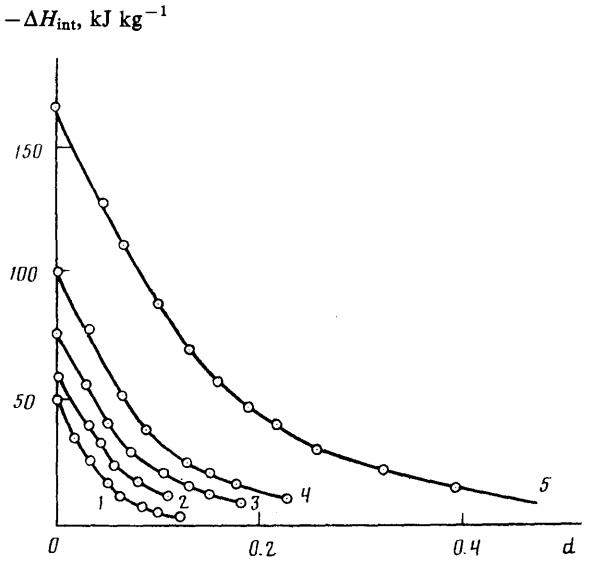


Figure 1. Dependence of the integral enthalpies of reaction with water on the water content in the initial specimens: (*1*)–(*5*) see text.

Among the communications devoted to the study of the cellulose–water system, mention should be made of an investigation[21] in which it was assumed that the thermal effects due to three processes contribute to the enthalpy of interaction (ΔH_{int}): the exothermic effect of the solvation of cellulose by water; the endothermic effect of the rupture of the intramolecular and intermolecular hydrogen bonds of cellulose on sorption of water; the exothermic effect of the solvation by water of the free hydroxy-groups formed on dissociation of the hydrogen bonds of cellulose.

The enthalpies of reaction of cellulose with solvents are determined by the nature of the EDA interaction in the systems.[9,10,29–32] As a rule, solvents with inadequate EDA interaction (water, alcohols, nitriles, ethers, and ketones, etc.) mix only with the amorphous component of cellulose. In our view, a general criterion of the solvating capacities of solvents was not put forward in the studies mentioned above.[9,10] Bearing in mind the polyfunctionality of polysaccharides, it is necessary to use jointly the parameters of the electron-donating and electron-accepting properties of the liquids for this purpose. The enthalpies of reaction of wood cellulose with individual liquids are listed in Table 1. The sharp increase in the absolute values of ΔH_{int} for certain primary amines and strong acids indicates the disruption of the crystalline regions of cellulose and of the specific solvation in the system. However, analysis of the data in Table 1 shows that there is no correlation between the absolute values of ΔH_{int} and the electron-donating properties of amines. Despite the high electron-donating capacity characteristic of bases such as piperidine (DN = 60.9), diethylamine (DN = 56.1), and triethylamine (DN = 60.1), they are characterised by low enthalpies of reaction with cellulose.

Table 1. Enthalpies of the interaction ($-\Delta H_{int}$) of wood cellulose with solvents and empirical parameters of the solvent polarities.

Solvent	$-\Delta H_{int}$, kJ mol^{-1}		DN	AN	$\frac{DN+AN}{2}$
	1 : 25	1 : 10			
Water	9.6	9.2	18.0	54.8	36.4
Methanol	–	5.0	19.0	41.3	30.15
N-Methylformamide	11.1	11.3	24.6 *	31.1 *	28.35
Dimethylformamide	10.1	10.0	26.6	16.0	21.3
Dimethyl sulphoxide	13.5	13.4	29.8	19.3	25.55
Piperidine	1.80	1.7	60.9 *	–	
Pyridine	2.71	–	33.1	14.2	23.65
Diethylamine	2.51	–	56.1 *	9.4 *	
Morpholine	3.72	–			
Tetramethylurea	1.55	–	29.6		
Triethylamine	1.35	–	60.1 *	1.4 *	
Monoethanolamine	15.5	15.5			
Butylamine	24.3	–	47.0 *	–	
Hexamethylenediamine (318 K)	39.4	–			
Diethylenetriamine	40.4	–			
Ethylene diamine	42.0	41.8	55.0 *	20.9 *	
Hydrazine (95 wt.%)	–	44.3			
Acetic acid	–	5.0	12.7 *	52.9	
CF_3COOH	–	36.8	0	105.3	52.65
Phosphoric acid (85 wt.%)	–	19.2	–	–	
Nitric acid	–	82.8	–	–	

Note. The enthalpies of reaction are listed for 1:25 and 1:10 component ratios (by weight).
*Calculation based on the data of Makitra et al.;[33] in the remaining cases, the data quoted by Burger[68] were used.

It has been suggested[34] that, for effective interaction with cellulose, organic solvents should possess a favourable set of polar, basic, and steric properties. Since the available ΔH_{int} data refer to non-equilibrium conditions, the establishment of a relation between the heat effects and EDA properties of solvents constitutes an insoluble problem. The enthalpy of solution (ΔH_{soln}) data, characterising the specific solvation process at a molecular level, i.e. under conditions ensuring the complete utilisation of the EDA properties of the solvents, are in this sense preferable for the description of the influence of the solvent on the thermal effects.

Calorimetric data for the interaction of cellulose with aqueous solutions of bases, acids, and salts have been published.[10,11,35–39] The EDA capacity of aqueous electrolyte solutions increases with increase in their concentration. At a certain electrolyte concentration, the exothermicity of the interaction increases owing to the disruption of the crystalline regions of the polymer and the solvation of the macromolecules (Figs. 2 and 3).

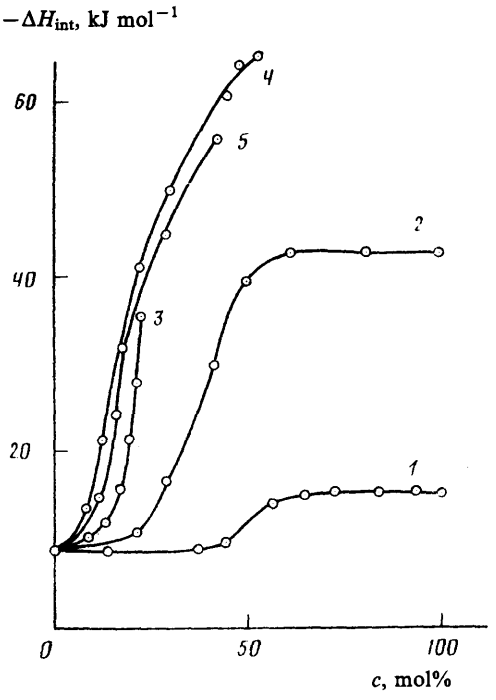


Figure 2. Dependence of the enthalpies of reaction of cellulose with aqueous solutions of monoethanolamine (curve *1*), ethylenediamine (curve *2*), and zinc chloride (curve *3*) at 298 K and with sodium hydroxide solutions at 333 K (curve *4*) and 298 K (curve *5*) on the concentrations of the bases and salts.

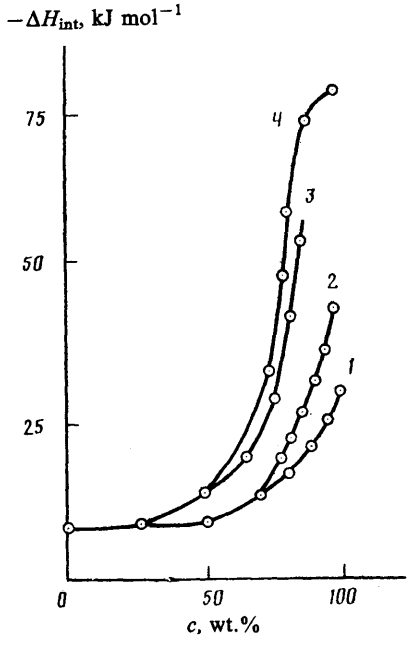


Figure 3. Dependence of the enthalpies of reaction of wood cellulose with aqueous solutions of trifluoroacetic (curve *1*), phosphoric (curve 2), sulphuric (curve *3*), and nitric (curve *4*) acids at 298 K on the acid concentration.

We may note that the interaction of cellulose with reactive compounds in solutions leads to the formation of cellulose derivatives. The thermochemical properties of concentrated solutions of metal hydroxides were attributed[11] to the formation of cellulose alkoxides, whilst in other studies[35] they were attributed to inclusion compounds. The interaction of cellulose with strong acid solutions is as a rule accompanied by the formation of the corresponding esters.[40,41] The enthalpies of reaction include additional contributions due to the exchange of the hyroxy-groups for ester groups, the dissolution of the water formed under these conditions in the solution, and the solvation of the product in the solution.

It follows from the data presented that, in a thermochemical study of the swelling, interaction, and dissolution of polysaccharides, it is essential to take into account the additional energy effect associated with the phase state of different regions of the polysaccharides, it is essential to take into account the additional energy effect associated with the phase state of different regions of the polymer.[4,9–11,17,42] The dissolution of polysaccharides having an amorphous-crystalline structure has been represented[42] in the form of three stages. The first involves the transition of the solid polymer to a hypothetical liquid amorphous state, the second is associated with the dissolution and solvation of macromolecules, and the third involves the mixing of the solvated polymer molecules with the solvent to give an infinitely dilute solution. The integral enthalpy of solution ΔH_{soln} is then regarded as the sum of contributions:

$$\Delta H_{soln} = \Delta H_m + \Delta H_g + \Delta H_{int} + \Delta H_{mix}. \quad (1)$$

The first stage characterises the enthalpy of fusion of crystalline regions (ΔH_m) and the enthalpy of the transition of the amorphous component from the vitreous to the highly elastic (ΔH_g) state. The second entails the interaction (ΔH_{int}) between the polymer and solvent molecules as a consequence of the solvation of the components. The third stage combines all the thermochemical effects of the mixing process (ΔH_{mix}) which occur on dilution (for example, the heats of conformational changes).

Analogous expressions have been proposed[9,10] for the enthalpies of the reactions of cellulose with solvents:

for systems in which the crystalline regions are not disrupted:

$$\Delta H_{int} = \Delta H_g N_a + \Delta H_{mix} N_a; \quad (2)$$

for systems in which the crystalline regions are disrupted:

$$\Delta H_{int} = \Delta H_m N_c + \Delta H_{mix}, \quad (3)$$

where N_c and N_a are the contents of the crystalline and amorphous (vitreous) cellulose (in mole fractions).

The quantities ΔH_g, characterising the transition of the vitreous component of the polysaccharide to the highly elastic state under the influence of the solvent, are particularly large for natural polar polymers with a high glass point T_g (T_g = 493 K for cellulose[13]). Thus, according to Tsvetkov et al.,[10] $\Delta H_g = -12.6 \pm 8$ kJ mol^{-1} unit^{-1} or -77.5 J g^{-1} for the fully amorphous vitreous cellulose.

The enthalpy of fusion of the crystalline regions of cellulose can be estimated in different ways. It has been suggested[10] that ΔH_m be estimated from the enthalpies of solution of laevoglucosan (a compound modelling cellulose) over a wide concentration range. It is assumed that the enthalpy of fusion of crystalline regions of

cellulose is equal to the hypothetical enthalpy of fusion of laevoglucosan and amounts to 14.2 kJ mol^{-1} or 87.3 J g^{-1}.

We believe that the most reliable values of ΔH_m have been obtained from measurements of the enthalpies of solution of cellulose specimens in different solvents.[43,44] The following relation has been used[43] in the determination of the degree of crystallinity:

$$\Delta H_{soln} = -X(\Delta H_c) + + \Delta H_a, \quad (4)$$

where X is the fraction of the crystalline phase in the specimen, ΔH_c the enthalpy of crystallisation, and ΔH_a the enthalpy of solution of the amorphous cellulose. In the calculation of ΔH_c, the degrees of crystallinity obtained by X-ray diffraction were used. ΔH_c is -15.6 kJ mol^{-1} (-96 J g^{-1}) for cellulose (I) and -19.2 kJ mol^{-1} (-118 J g^{-1}) for cellulose (II).

The enthalpy of fusion ΔH_m for cellulose crystallites has been calculated[44] from the equation

$$\Delta H_m = \Delta H_{inta}(\Delta H_{soln1} - \Delta H_{soln2})/(\Delta H_{int2} - \Delta H_{int1}), \quad (5)$$

where $\Delta H_{int\,a}$ is the enthalpy of reaction with water of the amorphous regions of cellulose, amounting to -168 J/g of cellulose at 298 K,[15] $\Delta H_{soln\,1}$ and $\Delta H_{soln\,2}$ are the enthalpies of solution of two cellulose specimens comprising the same crystalline modification, and $\Delta H_{int\,1}$ and $\Delta H_{int\,2}$ are the enthalpies of reaction with water of the same specimens. The quantity ΔH_m was found to be 36.4 kJ mol^{-1} (224 J g^{-1}) for cellulose (I) crystallites and 45.0 kJ mol^{-1} (277 J g^{-1}) for cellulose (II) crystallites. These results indicate a greater energetic stability of the cellulose (II) crystallites compared with cellulose (I) crystallites.

Various approaches have been used[10,43,44] for the estimation of the enthalpies of fusion of the crystalline regions of cellulose. However, it is noteworthy that the absence of systematic studies and the necessity to take into account the type of crystalline modification of the polymer preclude at the present time an unambiguous solution of the problem of the reliability of the available literature values of ΔH_m.

We therefore believe that it is essential to pose the problem of the determination of a common standard state in comparing thermodynamic data for processes involving the dissolution and solvation of cellulose and its derivatives. Since the polysaccharides are involatile, the use of an ideal gas as the standard state is excluded. The pure polymers, having an amorphous-crystalline structure, are also unsuitable for this purpose, because it has been shown that the phase state of the polymer plays an important role in the dissolution process. The lack of reliable thermodynamic data for the devitrification and fusion of the polysaccharides precludes an unambiguous solution of this problem. However, bearing in mind that the contributions of ΔH_g and ΔH_m have different signs in the range of degrees of crystallinity 0.5–0.7, cancelling out to an appreciable extent, the enthalpies of solution of such specimens of cellulose and its derivatives characterise mainly the specific solvation of the polymer.

The results of the estimation of the enthalpies of reaction from experimental enthalpies of solution of model oxygen- and hydroxyl-containing cellulose compounds in different solvents are of definite interest.[9,10,45–50]

Table 2 shows that the interaction of the model compounds in electron-donating solvents (ethylenediamine, aqueous NaOH solution) takes place preferentially via hydroxy-groups, while in electron-accepting solvents (acids) it involves mainly ester groups.

It has been established from thermochemical data for solutions of cellulose in the ferric sodium tartrate complex (FeTNa),[43,45,47,51] cadoxen,[46,50] and the copper–ammonia complex[52] that the interaction proceeds via two secondary hydroxy-groups. It is noteworthy that the enthalpies of reaction of cellulose and other hydroxylated compounds with FeTNa and cadoxen calculated per hydroxy-group, are close, amounting to 10.9–12.1 kJ/mol of OH groups.[47,50]

Table 2. Enthalpies of the interaction ($-\Delta H_{int}$) of cellulose and model compounds with solvents at 298 K (kJ mol^{-1}) (1:40 ratio by weight).[9]

Compound	NaOH (20 wt.%) (ref. 10)	Ethylene-diamine (ref. 10)	MMO*·H_2O (ref. 9)	FeTNa (ref. 45)	H_3PO_4 (83 wt.%) (ref. 10, 48)	CF_3COOH (ref. 48)
Wood cellulose	25.5	41.8	24.1	22.2	19.2	36.8
Laevoglucosan	8.4	17.6	−3.5	–	0	–
Methanol	6.3	9.6	–	6.3	8.8	14.6
Ethylene glycol	11.7	19.2	12.4	9.2	12.5	22.2
Diethylene glycol	18.4	20.1	14.8	16.0	24.2	36.8
Glycerol	15.9	28.2	21.4	13.0	15.9	27.2
Triethylene glycol	24.2	21.7	12.2	–	34.3	51.4

*Methylmorpholine *N*-oxide monohydrate (353 K).

To a first approximation, the enthalpies of mixing of the highly elastic amorphous cellulose with solvents can be estimated as the sum of the enthalpies of reaction via three hydroxy-groups and two oxygen atoms of cellulose. A common approach to the estimation of the values of ΔH_{mix} from ΔH_{soln} for model compounds is based on the hypothesis of the additivity of the intermolecular interactions of the functional groups which do not interact strongly with one another. In the case of cellulose, the mutual influence of the functional groups and the steric features of the macromolecular chain alter appreciably the EDA properties of the acetal oxygen atoms and hydroxy-groups.

It has been suggested that[9] the following assumptions be made in the calculation of ΔH_{mix}. The electron-donating capacity of the oxygen atoms of cellulose is equivalent to that of one oxygen atom of the cellulose ether group in model compounds, while the electron-accepting capacity of the hydroxy-groups of the glucopyranose cellulose unit is equivalent to that of four groups of low-molecular-weight alcohols, for example glycerol and ethanol. The enthalpies of reaction of wood cellulose (degree of crystallinity 0.7) with solutions of sodium hydroxide, EDTA, methylmorpholine *N*-oxide, and phosphoric and trifluoroacetic acids calculated on the basis of such a scheme (-23.5, -33.3, -24.6, -31.6, and -51.0 kJ mol^{-1} respectively) are close in order of magnitude to the values calculated by Eqn. (3) (-19.9, -36.2, -18.5, -13.6, and -31.2 kJ mol^{-1} respectively). For acids, the values of ΔH_{int} exceed significantly the experimental values in terms of absolute magnitude. Evidently the approach examined is promising for the qualitative estimation of the enthalpies of reaction of cellulose in solvents of different chemical types. However, more rigorous quantitative calculations require the

development of fundamentally new approaches taking into account all the characteristic features of the intermolecular interactions of both model compounds and of the functional groups in polysaccharide molecules.

When the interaction is of the electron donor–acceptor type, it is essential to take into account the EDA properties of all the system components.[12] Thus the influence of the EDA capacity of the functional groups of the polysaccharide molecules on the solvating capacity of the polymer can be followed by comparing the enthalpies of reaction of cellulose, chitin, and chitosan[53] with organic solvents. The replacement of hydroxy-groups by electron-donating groups (the acetamide group in chitin and the amino-group in chitosan) diminishes the aboslute values of ΔH_{int} in solutions of bases and increases them in solutions of acids. It has been established on the basis of thermochemical data[9] that the electron-donating capacity of the functional groups of cellulose derivatives in solutions diminishes in the sequence chitosan > chitin > cellulose diacetate > nitrocellulose > monocarboxycellulose.

Thus the following conclusions can be drawn from the analysis of thermochemical data for the enthalpies of reaction (wetting, swelling). In the interpretation of the values of ΔH_{int}, it is essential to take into account the structural features of various regions of the polymer, the previous history of the specimen, and the presence of impurities. The absolute values of ΔH_{int} for cellulose and its derivatives in solutions are determined by the EDA capacity of the functional groups of the polymer and the solvent. However, the establishment of a relationship between ΔH_{int} and the EDA properties of solvents is possible only at a qualitative level. For a successful solution of this problem on a quantitative basis, it is necessry to accumulate systematic data for the enthalpies of solution of cellulose and other polysaccharides in non-aqueous solvents.

III. Thermochemistry of the dissolution and characteristic features of the solvation of cellulose, other polysaccharides, and their derivatives in solutions

The experimental data available at present for the thermochemical properties of solutions of polysaccharides refer mainly to the enthalpies of solution of dextrans,[42,54,55] certain cellulose derivatives (nitrocellulose, cellulose acetates),[56–58] cellulose in solutions of ionic ferric sodium tartrate and cadmium-ethylenediamine (cadoxen) complexes, etc.[43–46,50,51]

Depending on the conditions of their preparation, dextrans undergo structural changes. The experimental densities and heats of solution of dextrans in water and 10% aqueous NaOH solution[54] indicate the polymorphism of polysaccharides.

As in the case of ΔH_{int} for cellulose materials,[15] a decrease in the absolute magnitude of the enthalpies of solution of dextrans with increase in the degree of crystallinity is observed.

One of the important problems in the thermochemistry of the dissolution of polymers is that of the influence of the molecular weight on the heat change. The enthalpies of solution and dilution of certain low-molecular-weight carbohydrates (saccharides) and dextrans with different molecular weights in water and dimethyl sulphoxide (DMSO) have been determined.[42] The values of ΔH_{soln} increased with the increase in the molecular weight (M) to 1000, while for the fraction with M > 1000 they remained almost unchanged on further increase in M. The enthalpies of dilution had the opposite character. The independence of the enthalpies of dilution of the molecular weight for M > 2000 demonstrates very small changes in the helical conformation of dextran and the absence of association in dilute and moderately concentrated solutions.

Table 3. The densities and enthalpies of solution of various modifications of dextran.[54]

Modification	Density of preparation		$-\Delta H_{soln}$, kJ mol^{-1}		Degree of crystallinity, %
	unground	ground	in 10% NaOH	in H_2O	
Current state of dextran —amorphous					
–	1.304	1.303	44.9	29.5	–
Current state of dextran —crystalline					
I	1.372	–	37.5	27.2	15.0
I	1.536	1.341	34.5	9.76	28.6
II	1.473	1.360	39.6	–	23.2

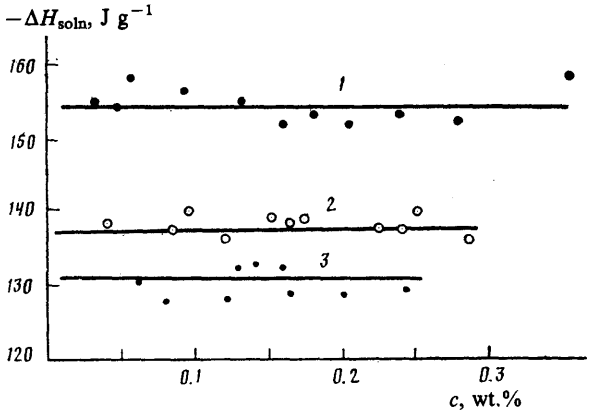


Figure 4. Dependence of the enthalpies of solution of dextran with M = 110000 in DMSO (*1*), water (*2*), and formamide (*3*) on the dextran concentration at 298.15 K.

We measured experimentally the integral enthalpies of solution of dextrans with $M = 2 \times 10^4$, 4×10^4, 7×10^4, and 11×10^4 in water, formamide (FA), DMSO, and their mixtures at 298.15 K.

It was found that an increase in the degree of polymerisation (DP) of dextrans from 100 to 680 does not lead to a significant alteration of ΔH_{soln}. This agrees with the theoretical idea that the degree of polymerisation (for specimens with DP > 10) has an insignificant influence on ΔH_{soln} for flexible-chain amorphous polymers.

Fig. 4 presents the variation of ΔH_{soln} for dextran with M = 110000 in individual solvents.[55]

At least three processes can contribute to the enthalpy of solution of fully amorphous dextran in a liquid:

$$\Delta H_{soln} = \Delta H_g + \Delta H_{conf} + \Delta H_{soln}. \quad (6)$$

The first (ΔH_g) is the transition of the amorphous polymer from the vitreous to the highly elastic state in solution. ΔH_g for amorphous dextran is 11.7 kJ mol^{-1} or 72.1 J g^{-1}.[10] The second (ΔH_{conf}) involves conformational transformations of the polysaccharide molecules in solution. Since the conformers of dextran in solutions have the same energies,[59] the quantity ΔH_{conf} can be assumed equal to zero. The third (ΔH_{solv}) is the solvation of a hypothetical liquid dextran by the solvent and is determined by the intermolecular interactions between the solution components. The presence of a multiplicity of hydroxy-groups in the dextran molecule leads to the formation of a stable solvation shell via polymer–solvent hydrogen bonds. The specific features of the solvation are responsible for the large negative values of ΔH_{solv} (from −54.8 J g^{-1} in formamide to −82.1 J g^{-1} in DMSO).

The exothermicity of the solvation of dextran increases in the sequence formamide ⩽ water < dimethyl sulphoxide. The values of ΔH_{solv} in formamide and water are close in absolute magnitude, which is apparently due to the characteristics of the individual solvents. The need to take into account both electron-donating and electron-accepting properties of the liquids in the solvation of a polysaccharide arises from the bifunctional nature of the hydroxy-groups of dextran. It has been suggested[60] that half the sum of their *DN* and *AN* numbers be used as a criterion of the donor–acceptor capacity of the solvent. Formamide and water are characterised by similar values of (*DN* + *AN*)/2—31.9 and 36.4 respectively. Furthermore, formamide and water are highly associated liquids with similar FA–FA, water–water, and FA–water hydrogen bond energies (~15.5 kJ mol^{-1}).[61]

The greater exothermicity of the solvation of dextran in DMSO compared with water and formamide is due to the complex influence of a set of factors. Thus the Flory parameter of the dextran–DMSO interaction is an order of magnitude higher than for the dextran–water interaction,[42] while according to ^{13}C NMR data[62] the conformational mobility of dextran micromolecules in water is greater than in DMSO. The endothermic contribution to ΔH_{solv} associated with the rupture of the solvent–solvent bonds is smallest in DMSO among all the liquids investigated.

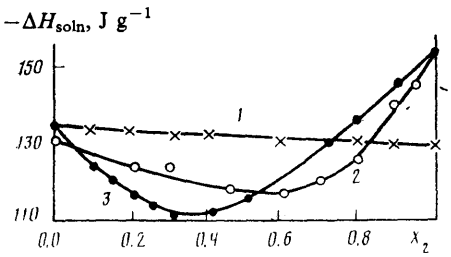


Figure 5. Enthalpies of solution of dextran with M = 110000 in water–formamide (curve *1*), formamide–DMSO (curve *2*), and water–DMSO (curve 3) mixtures at 298.15 K (X_2 = mole fraction of the second mixture component).

Fig. 5 presents the dependence of the integral enthalpies of solution of dextran with M = 110000 in water–formamide, water–DMSO, and formamide–DMSO mixtures on the composition of the mixed solvent at 298.15 K. The nature of the dependences of ΔH°_{soln} on the mixed solvent composition is various. The dependence of ΔH°_{soln} for dextran on the composition of the water–formamide mixture is linear. The water–DMSO and formamide–DMSO systems are characterised by an extremum in the $\Delta H^\circ_{soln} = f(X)$ relation. The nature of the observed dependences of ΔH°_{soln} for the polysaccharide on the solvent composition is associated with the characteristic features of the donor–acceptor interaction between the mixture components. In the range of compositions where an exothermic minimum is observed in ΔH°_{soln}, the molecular interaction of the solvent components is strongest. This confirms the similarity of the variations of the enthalpies of solution of dextran in solvent mixtures and of the enthalpies of mixing of the components of the binary solvent.[61] The formation of mixed associated species comprising the molecules of low-molecular-weight substances over the entire range of compositions weakens the solvation of dextrans and hence diminishes the exothermicity of the dissolution process.

Fig. 6 presents the dependences of the enthalpies of transfer of dextran from DMSO in water–DMSO and formamide–DMSO mixtures on the DMSO mole fraction, which characterise the enthalpy component of the solvation of dextran in the systems investigated. The figure shows that the dependence of ΔH°_{trans} for the water–DMSO system is characterised by a concavity on the descending section of the extremum for X_{DMSO} > 0.5 (mole fraction). The similar form of the relations for solutions of low-molecular-weight saccharides and polyhydric alcohols indicates the occurrence of selective solvation.[63] In the present instance, this implies that the hydroxy-groups of dextran are selectively solvated by water in the water–DMSO mixture. This conclusion agrees with those of an investigation[64] whose authors demonstrated the occurrence of the selective solvation of dextrans in a water–DMSO mixed solvent by gel-permeation chromatography.

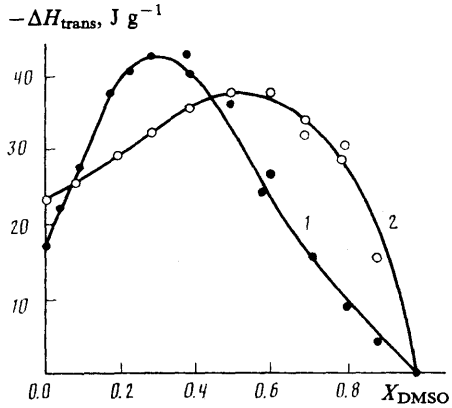


Figure 6. Enthalpies of transfer of dextran from DMSO in water–DMSO (curve *1*) and formamide–DMSO (curve *2*) mixtures at 298.15 K.

Comparison of the $\Delta H^\circ_{trans} = f(X)$ relations shows that, in contrast to the water–DMSO system, in the non-aqueous formamide–DMSO mixed solvent there is no selective solvation of the macromolecules. This is due to the difference between the

mechanisms of the formation of hydrogen bonds in the aqueous organic and composite non-aqueous solvents with dextran macromolecules.

Fig. 7 presents the dependences of the enthalpies of solution of cellulose (C), cellulose acetate (CA), cellulose diacetate (CDA), and cellulose triacetate (CTA) on the degree of substitution γ of the hydroxy-groups by acetate groups in non-aqueous individual and mixed solvents at 298.15 K. Evidently, for all the solvents investigated, there is a linear relation between the enthalpies of solution and the amount of bound acetic acid in cellulose acetates. The increase in the exothermicity of the dissolution of cellulose acetates in non-aqueous solvents with decrease in the degree of substitution is caused by the increased EDA capacity of the polymers.

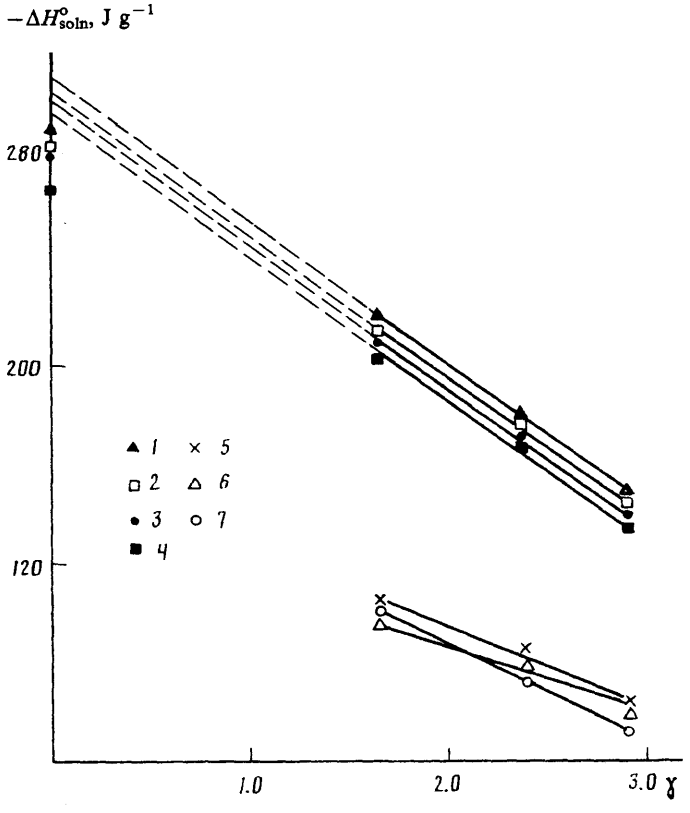


Figure 7. Dependence of the integral enthalpies of solution of cellulose, cellulose acetate, cellulose diacetate, and cellulose triacetate on the degree of substitution of hydroxy-groups by acetate groups in different solvents at 298.15 K: *1*, $CF_3COOH + C_2H_4Cl_2$; *2*, $CF_3COOH + CH_2Cl_2$; *3*, $CF_3COOH + CHCl_3$; *4*, CF_3COOH; *5*, DMSO; *6*, DMF; *7*, DMA.

In a thermochemical study of the dissolution of cellulose and its derivatives, it is essential to take into account the energy contributions associated with the fusion of the crystalline regions of the polymers (ΔH_m) and the transition of their vitreous regions to the highly elastic state under the influence of solvents (ΔH_g). The quantities ΔH_m and ΔH_g for cellulose are respectively 13.4 and 12.6 kJ mol^{-1} unit^{-1},[10] i.e. in the case of specimens with a degree of crystallinity of 0.59 the contributions of ΔH_m and ΔH_g to a large extent cancel out. In our view, the foregoing consideration can be applied also to cellulose acetate specimens. Thus the values of ΔH°_{soln} characterise mainly the specific solvation of the polymers and their absolute values are determined by the donor–acceptor properties of the solution components.

The results of the thermochemical measurements agree with data for the rotational mobility of molecular NMR-relaxation probes.[65] 1,4-Diazabicyclo[2.2.2]octane (DABO) was used in the present study as an active probe capable of competing with the solvent for the formation of hydrogen bonds with the molecules of cellulose acetates. A linear increase in the rate of spin–lattice relaxation W accompanied by a decrease in the degree of substitution γ has been found for DABO, indicating the restriction of its rotational mobility as a consequence of the formation of hydrogen bonds with the unsubstituted OH groups of cellulose acetates. Like the $\Delta H^{\circ}_{soln} = f(\gamma)$ relation, the $W = f(\gamma)$ relation constitutes proof of the formation of hydrogen-bonded complexes and of the intensification of the specific intermolecular interactions of the polymer with the solvent as the degree of substitution diminishes. The relation between the thermochemical and microdynamic properties of solutions of cellulose acetates in DMSO is illustrated by the linear correlation between ΔH°_{soln} and W (Fig. 8). On extrapolation of the linear relations between ΔH°_{soln} and the degree of substitution to zero values of the latter for solutions of cellulose acetates in trifluoroacetic acid and its mixtures with chlorinated hydrocarbons, the hypothetical enthalpies of solution of cellulose in these solvents were obtained (Fig. 7). The extrapolated and experimental values of ΔH°_{soln} are close in absolute magnitude (the difference is not more than 15 J g^{-1}). This is due to the differences between the degrees of crystallinity of specimens of wood cellulose and cellulose acetates.

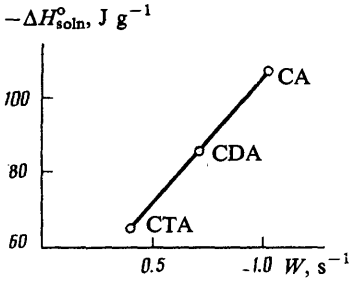


Figure 8. Dependence of the integral enthalpies of solution of cellulose acetates with different degrees of substitution on the rate of the spin–lattice relaxation of the ^{13}C nuclei in low-molecular-weight probes.

Using the literature values of the heats of fusion of cellulose[10] and the difference between the degrees of crystallinity, we estimated the endothermic contribution to ΔH°_{soln} associated with the fusion of additional regions of cellulose. It proved to be 15 J g^{-1}. Thus the validity of the linear extrapolation to the zero degree of substitution

was confirmed and the retention of this type of dependence of ΔH°_{soln} on the latter factor was demonstrated.

The amount of acetic acid bound in cellulose acetates can be determined calorimetrically on the basis of the observed dependence of the heats of solution of cellulose and its acetates in various solvents on the degree of substitution. The experimental data permit a comparative analysis of the influences of the nature and composition of the solvents on ΔH°_{soln} for cellulose acetates with a definite degree of substitution.

The addition of chlorinated hydrocarbons $C_xH_yCl_z$ to trifluoroacetic acid increases the solvent power of the mixtures in relation to cellulose and its acetates,[66] which is accompanied by an increase in the absolute values of ΔH°_{soln} in the sequence $CF_3COOH < CF_3COOH + CHCl_3 < CF_3COOH + CH_2Cl_2 < CF_3COOH + C_2H_4Cl_2$. This fact can be explained by the influence of chlorinated hydrocarbons on the self-association of the acid[67] and the formation of reactive acid monomers, which increases, in turn, the electron-accepting properties of the CF_3COOH-based mixtures in relation to the polymers.

In the series of individual solvents, an increase in the exothermicity for cellulose acetates is observed: dimethylacetamide (DMA) < dimethylformaide (DMF) < DMSO < trifluoroacetic acid. On solvation of cellulose and its derivatives, it is essential to take into account the mixed donor–acceptor capacity of the solvents.

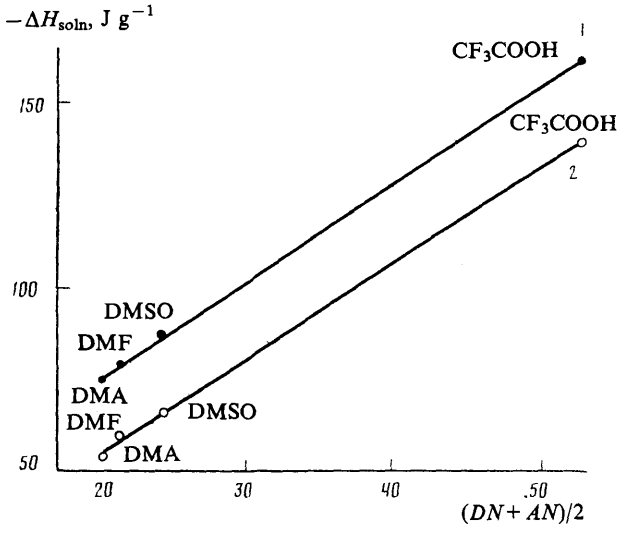


Figure 9. Dependence of the integral enthalpies of solution of cellulose diacetate (line *1*) and cellulose triacetate (line *2*) on half the sum of the donor and acceptor numbers of the individual solvents at 298.15 K.

The decisive role of specific solvation in the dissolution of the acetates is confirmed by the linear relation between ΔH°_{soln} for cellulose diacetate and triacetate and half the sum of the donor and acceptor numbers $(DN + AN)/2$ for the solvents investigated (Fig. 9). Such linear correlation makes it possible to combine the result of the determination of ΔH°_{soln} for cellulose acetates in solvents of different nature, differing significantly in their electron-donating and electron-accepting properties—ranging from the proton donating CF_3COOH to the dipolar aprotic solvents DMA, DMF, and DMSO.

We have thus shown that in dilute solutions of cellulose and its derivatives, the donor–acceptor interaction between the components is decisive. On the other hand, one can postulate that in the case of concentrated solutions of the polysaccharides it is not legitimate to relate the thermodynamic characteristics of the dissolution process to any one physicochemical parameter of the solvent. The limitations of simple correlations necessitate the application of more complex models.[68] The choice of a multiparameter model is determined by the type of the process in which particular physicochemical properties of the solvents predominate. Analysis of the available information about the structural-thermodynamic characteristics of solutions of cellulose and its derivatives[3] leads to the conclusion that the enthalpy contribution predominates over the entropy contribution. Processes of this kind are described satisfactorily by the Gutmann–Mayer and Krigovskii–Fossett models.[68] We confirmed the fruitfulness of this approach in a study of concentrated solutions of hydroxypropylcellulose in different solvents.

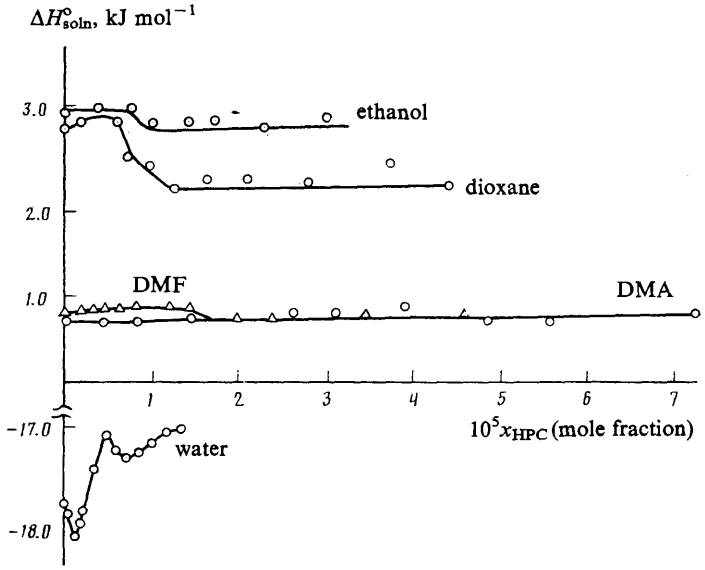


Figure 10. Dependence of the integral enthalpies of solution of DMSO in solutions of hydroxypropylcellulose on the mole fraction of hydroxypropylcellulose.

The experimental determination of the enthalpies of solution of cellulose ethers is difficult in view of the long time required for the attainment of equilibrium in dissolution processes. In order to find the thermochemical parameters of the solvation of hydroxypropylcellulose (HPC) and other cellulose ethers, it appears useful to introduce into the binary polymer–solvent system a third component—a liquid non-electrolyte—as a "probe" for solvation processes. Such a methodological procedure is extremely fruitful in the study of solvation processes in liquids.

We determined the enthalpies of solution of DMSO in solutions of hydroxypropylcellulose in water, ethanol, DMA, DMF, and dioxane (DO). The results of the thermochemical studies are presented in Fig. 10. Evidently the concentration of hydroxypropylcellulose does not exert a significant influence on ΔH°_{soln} for DMSO in the HPC–DMA and HPC–DMF systems. On the other hand, the influence of the hydroxypropylcellulose concentration on the enthalpy of solution of DMSO in water and certain non-aqueous solvents (dioxane and ethanol) is clearly manifested. Furthermore, the increase in ΔH°_{soln} for DMSO can be seen in the series of solvents water < DMA < DMF < DO < ethanol.

The enthalpies of solution of DMSO in ethanol, DMA, and DMF were determined for the first time. The enthalpies ΔH°_{soln} for DMSO in water and dioxane agree well with the literature values.[61,69]

The enthalpies of solution of DMSO in aqueous solutions of hydroxypropylcellulose are exothermic, while in non-aqueous solutions they are endothermic. These results can be explained from the standpoint of the donor–acceptor properties of the solvents.

It is known that the mixing of two electron-donating liquids is accompanied by an endothermic effect.[70] A similar effect occurs on mixing DMSO with ethanol. This phenomenon can be accounted for by a change in the electron-donating capacity of ethanol in the associated state, which is indicated by the donor numbers: DN_{SbCl_5} = 18.5,[68] DN_{bulk} = 27.8 according to Marcus,[71] and DN_{bulk} = 32 according to Gutmann.[71]

The first stage in the study of the characteristic features of solvation in the solvent (I)–solvent (II)–polymer systems was the determination of ΔH°_{soln} for DMSO (solvent I) in the individual solvents II. On passing from DMSO–solvent II mixtures to the hydroxypropylcellulose–solvent II systems, the values of ΔH°_{soln} for DMSO change owing to polymer solvation processes in the solution. It is known that,[57] when the concentrations of cellulose and its ethers are greater than 1 wt.%, the polymer molecules interact with formation of a fluctuating network of hydrogen bonds. In our case, this is manifested in the range of hydroxypropylcellulose concentrations in the solutions $X_{HPC} > 125 \times 10^{-7}$ (mole fraction), while the enthalpy of solution of DMSO does not change with increase in the polymer concentration.

The extremum in the $\Delta H^{\circ}_{soln} = f(X_{HPC})$ relation is probably associated with the change in the structure of the solutions. The increase in the exothermicity of the dissolution of DMSO in an aqueous HPC solution for a mole fraction of 7.5×10^{-7} is a result of the disruptive effect of polymer molecules on the water structure. A further increase in the hydroxypropylcellulose concentration leads to the stabilisation of the aqueous solutions.[72] In the region of the concentrations corresponding to the second minimum, several factors are superimposed: the simultaneous strengthening of the intermolecular hydrogen bonds between the molecules of the dissolved polymer and the transolvation of the dissolved hyroxypropylcellulose molecules by water molecules induced by this factor. The general trend towards a decrease in the exothermicity of the interaction with DMSO with increase in the hydroxypropylcellulose concentration in the aqueous solution is probably associated with the stabilisation of the structure of the solution as a result of the formation of cooperative HPC–HPC and HPC–water hydrogen bonds.

In non-aqueous solutions for X_{HPC} up to a mole fraction of 125×10^{-7}, ΔH°_{soln} for DMSO remains constant within the limits of experimental error. Bearing in mind that ethanol, dioxane, DMF, and DMA are associated liquids, one can postulate the retention of the primary structure of the solvent after the introduction of small amounts of added polymer.

The enthalpies of the transfer of the test substance from one solvent to another can be conveniently used as a thermochemical characteristic of the solvation of atomic-molecular species in a series of individual solvents. We used the enthalpies of transfer (ΔH°_{trans}) of DMSO from an individual solvent to a concentrated polymer solution as thermochemical characteristics sensitive to solvation processes. Fig. 11 presents the dependence of ΔH°_{trans} on the ratio of the donor and acceptor numbers of the solvents. The relation is non-linear with a minimum in the exothermicity of the enthalpies of transfer of DMSO corresponding to the region of equal donor and acceptor numbers (DN/AN = 1).

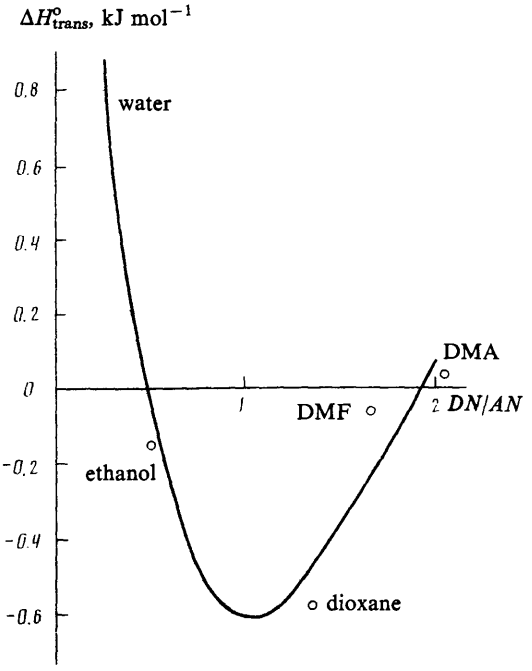


Figure 11. Dependence of the enthalpies of transfer of DMSO from the individual solvents to concentrated solutions of hydroxypropylcellulose on the ratio of the donor and acceptor numbers of the solvents.

In order to establish the relation between the phyisochemical properties of the solvents and the experimental thermochemical parameters [ΔH°_{soln} for DMSO, and the enthalpy of the transfer of the latter (ΔH°_{trans}) from the solvent to hydroxypropylcellulose solutions], methods of mathematical statistics were employed. The calculations were performed on an EC 1060 computer. The parameters of the solvents for such analysis are presented in Table 4. Pair and multiple regression analyses of ΔH°_{trans}, $\Delta H^{\circ}_{trans}/\Delta^{\circ}_{soln}$, and the physicochemical properties of the solvents were carried out.

The results of the calculation of the coefficients of the pair correlation of ΔH°_{trans} and $\Delta H^{\circ}_{trans}/\Delta H^{\circ}_{soln}$, on the one hand, and the properties of the solvents, on the other, are presented in Table 5.

Table 4. Physicochemical parameters of the solvents.

Parameter	Water	Ethanol	DMA	DMF	1,4-Dioxane	References
$\frac{n^2-1}{n^2+2}$	0.2054	0.2214	0.2647	0.2584	0.2543	[33]
$\frac{\varepsilon-1}{2\varepsilon+1}$	0.490	0.470	0.480	0.480	0.223	[33]
B, cm^{-1}	–	235	343	291	237	[33]
E_T^1, Kj mol^{-1}	264.1	217.3	183.0	183.4	150.7	[33]
Z^1, kJ mol^{-1}	296.0	333.2	280.0	286.7	270.4	[33]
$DN^2_{SbCl_5}$	18	19.2	27.8	26.6	14.8	[68, 73]
AN	54.8	37.1	13.6	16.0	10.8	[68, 73]
π^*	1.09	0.54	0.88	0.88	0.55	[75]
ε	78.3	25.2	37.8	36.7	2.21	[75]
$\mu(D)$	1.84	1.69	3.81	3.86	0.4	[75]
$\overline{V}$, cm^3 mol^{-1}	18.07	58.69	92.98	81.12	85.71	
ρ, g cm^{-3}	0.997	0.785	0.937	0.901	1.028	[76]
δ, J m^{-3}	98.08	54.33	46.55	50.86	41.90	[76]

Note. The following parameters of the solvents are listed: the polarisability $(n^2 - 1)/(n^2 + 2)$, the polarity $(\varepsilon - 1)/(2\varepsilon + 1)$, the basicity B, the Richardt–Dimroth electrophilicity parameter E_T, the Kosower electrophilicity parameter Z, the Kamlet–Taft dipolarity parameter π^*, the dielectric constant ε, the dipole moment μ, the molar volume $\overline{V}$, the density ρ, the three-dimensional solubility parameter δ, and the Hildenbrandt parameter.

Table 5. Coefficients of the pair correlations of ΔH°_{trans} and $\Delta H^\circ_{trans}/\Delta H^\circ_{soln}$ with the physicochemical properties of the solvents.

Solvent parameter	$r\Delta H^\circ_{trans}$	$r\Delta H^\circ_{trans}/\Delta H^\circ_{soln}$
$(DN+AN)/2$	0.70	0.61
δ	0.74	0.53
$\overline{V}$	−0.63	−0.46
μ	0.32	0.47
ε	0.90	0.66
π^*	0.65	0.59
Z	0.68	0.52
E_T	0.71	0.59

Comparison of the correlations of ΔH°_{trans} and $\Delta H^\circ_{trans}/\Delta H^\circ_{soln}$ makes evident the advantages of using absolute rather than relative heats of transfer for the estimation of the influence of the solvent. The most significant parameters influencing ΔH°_{trans} are the dielectric constant, the Hildebrandt parameters, the Richardt–Dimroth electrophilicity parameter, and the sum of the donor and acceptor numbers of the solvents. The regression coefficients decrease in the above series from 0.9 to 0.7. Since there is a high degree of correlation between ΔH°_{trans} and ε, it is useful to employ a linear regression model of the type

$$\Delta H^\circ_{trans} = A + B\varepsilon, \qquad (7)$$

The coefficients of this model are presented in Table 6.

Table 6. Experimental and calculated heats of transfer of DMSO from the solvent to the hydroxypropylcellulose solution (kJ mol^{-1}) obtained with the aid of the linear model (7) and by fitting the multiple agreesion equation (8).

Solvent	ΔH°_{trans} (experiment)	ΔH°_{trans} [calc. by Eqn. (7)]	ΔH°_{trans} (expt)−ΔH°_{trans} [calc. by Eqn. (7)]	ΔH°_{trans} [calc. by Eqn. (8)]	ΔH°_{trans} (expt)−ΔH°_{trans} [calc. by Eqn. (8)]
Water	0.870	0.825	0.045	0.874	−0.004
Ethanol	−0.164	−0.196	0.032	−0.168	0.004
DMA	0.021	0.046	−0.025	−0.003	0.024
DMF	−0.069	0.025	−0.094	−0.050	−0.019
1,4-Dioxane	−0.596	−0.638	0.042	−0.591	−0.005

Note. The following parameters were adopted in the calculation by Eqn. (7): $A = -0.6809 \pm 0.0669$ and $R = 0.01924 \pm 0.00153$; the following parameters were adopted in the calculation by Eqn. (8): $A_0 = 0.1953 \pm 0.0396$, $A_1 = 0.6517 \pm 0.0446$, $A_2 = 0.7687 \pm 0.2491$, and $A_3 = -0.6753 \pm 0.2517$.

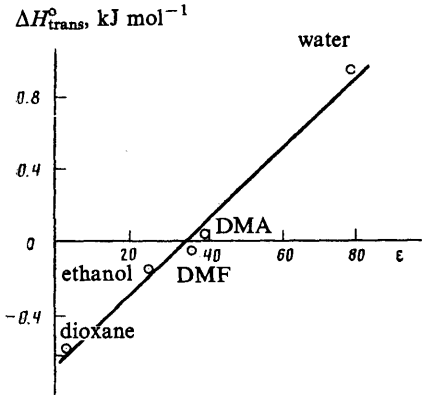


Figure 12. Dependence of ΔH°_{trans} on the dielectric constants of the solvents.

Comparison of the results of the calculation with experimental data shows that the absolute error in the fitting of Eqn. (7) is not more than 0.094 kJ mol^{-1}. The criterion of the linear fit F, defined as the ratio of the variance of the average value of ΔH°_{trans} to the variance of the calculated values, is 39.9. It characterises the quality of the proposed model (Fig. 12). Since a decrease in the pair correlation coefficients is observed for other physicochemical parameters (Table 5), they cannot be used to construct a one-parameter linear model similar to that defined by Eqn. (7). In constructing models with the aid of multiple regression, singular analysis of an undefined system of equations,[77] and computer methods, the following best fit was obtained:

$$\Delta H^\circ_{trans} = A_0 + A_1X_1 + A_2X_2 + A_3X_3,$$
$$X_1 = \frac{\varepsilon-40}{38}, \quad X_2 = \frac{E_T-50}{74}, \quad X_3 = \frac{(DN+AN)/2-24}{12}. \qquad (8)$$

The coefficients of this equation, the results of the calculation, and the experimental data are presented in Table 6. The criterion F is 292 and the error of the calculation does not exceed 0.024, which indicates a high accuracy of the multiparameter fit. All the coefficients of Eqn. (8) are significant at a level of fiducial probability exceeding 95% (Fig. 13).

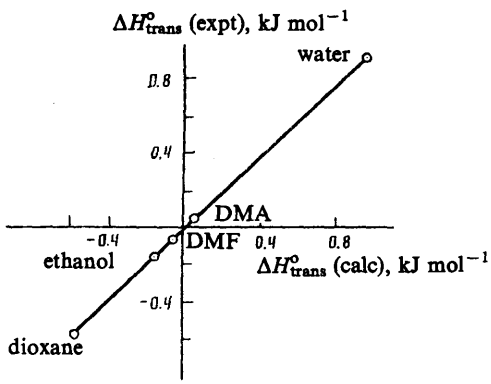


Figure 13. Experimental and calculated [by Eqn. (8)] enthalpies of transfer of DMSO from the solvent to the hydroxy propylcellulose solution.

The model developed is analogous to the Krigovskii–Fossett model,[68] which is applicable to the description of the influence of the solvent on the thermodynamics of solvation processes characterised by a significant contribution of the enthalpy factor.

Analysis of the significance of the coefficients of Eqn. (8) shows that the most significant contribution to the enthalpy characteristic of the solvation of DMSO in the hydroxypropylcellulose–solvent I–solvent II system is determined by the dielectric properties of the non-aqueous solvents. This agrees with the data of Solomonov et al.,[78] indicating a significant contribution of non-specific solvation to the enthalpies of solvation of organic non-electrolytes.

The characteristic features of the proposed model are determined by the necessity to take into account the combination of the donor and acceptor numbers of the non-aqueous solvents under the conditions of the specific solvation of the hydroxy-groups in the cellulose macromolecules (which have both electron-donating and electron-accepting properties).

With the aim of further development of the proposed approach to the study of concentrated solutions of cellulose derivatives, we measured the enthalpies of solution of poly(ethylene glycol) (a high-molecular-weight probe) with $M = 400 \pm 20$ in solutions of cellulose acetates with different degrees of substitution in DMSO. The results of the thermochemical measurements are presented in Fig. 14. The dissolution of poly(ethylene glycol) in the test systems is characterised by negative values of ΔH°_{soln}. Analysis of the observed concentration variations of the enthalpies of solution reveals their varied character. For solutions of cellulose acetates with $\gamma = 0.63$, there is virtually no dependence of ΔH°_{soln} for poly(ethylene glycol) on the cellulose acetate concentration in solution. In the case of individual cellulose acetates, the exothermicity of the dissolution of poly(ethylene glycol) increases in the range of concentrations from 1 to 2 wt.%, which indicates the occurrence of the poly(ethylene glycol)–cellulose acetate interaction.

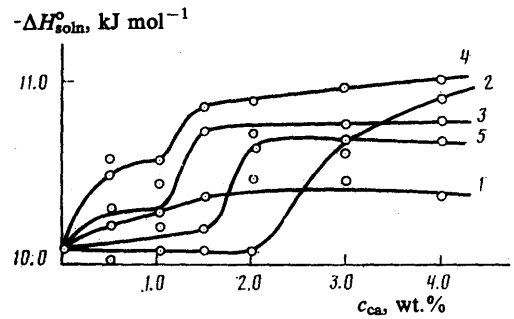


Figure 14. Dependence of the enthalpies of solution of poly(ethylene glycol) in solutions of cellulose acetate with different degrees of substitution γ in DMSO on the polymer concentration (c_{CA}, wt.%): *1*, 0.63; *2*, 0.96; *3*, 1.55; *4*, 2.43; *5*, 2.90.

Fig. 15 illustrates the dependence of the initial concentration at which the absolute values of ΔH°_{soln} for poly(ethylene glycol) increase in solutions of cellulose acetate on the degree of substitution γ. This dependence clearly illustrates the tendency towards a decrease in c_{init} with increase in γ for cellulose acetate, which is apparently due to the formation of a fluctuation network of intramolecular and intermolecular bonds in cellulose acetate.[3]

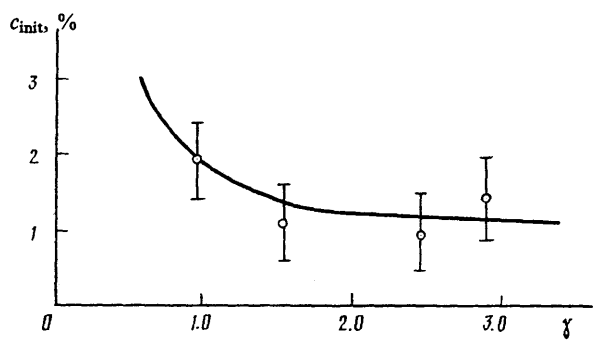


Figure 15. Dependence of the initial concentration corresponding to the onset of the change in ΔH°_{soln} for poly(ethylene glycol) in solutions of cellulose acetates on the degree of substitution.

Fig. 16 presents the dependence of the enthalpies of transfer of poly(ethylene glycol) from DMSO to a cellulose acetate solution at the initial concentration c_{init} on the degree of substitution γ. In the range $0.6 < \gamma < 1.0$, an abrupt increase in the exothermicity of the

transfer process is observed, which is associated with the intensification of the poly(ethylene glycol)–cellulose acetate intermolecular interactions. For $\gamma \geqslant 1.0$, the absolute values of ΔH°_{trans} for poly(ethylene glycol) hardly depend on the degree of substitution. The similarity of the values of ΔH°_{trans} for poly(ethylene glycol) in terms of absolute magnitude in solutions of cellulose acetate indicates the insignificant influence of the degree of substitution of the hydroxy-groups of cellulose by acetate groups on the poly(ethylene glycol)–cellulose ether interaction. For cellulose acetate with $\gamma \geqslant 0.63$, the poly(ethylene glycol)–cellulose acetate interaction is hindered. One of the possible causes of this is, in our view, the enhancement of the solvation of the cellulose acetate macromolecules with increase in the number of unsubstituted OH groups in the polymer.

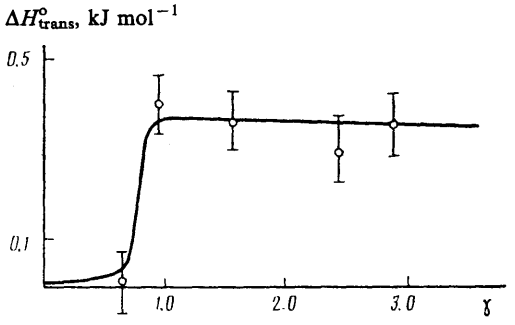


Figure 16. Dependence of the enthalpy of transfer of poly(ethylene glycol) from DMSO to a solution of cellulose acetates at the initial concentration c_{init} on the degree of substitution γ.

Thus the experimental enthalpy of solution data presented make it possible to consider the thermochemical characteristics of non-aqueous solutions of cellulose and its derivatives from a single standpoint based on the allowance for the EDA capacity of the polymer and the solvent and also to discover the principal characteristics of the influence of the physicochemical properties of the solvents on the enthalpies of transfer of the probes in concentrated solutions of cellulose ethers.

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The chemistry of processes which create dielectric layers with functional group substituents on semiconductors by impurity thermo-oxidation

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ABSTRACT. Processes are examined which involve the growth of film layers with dielectric properties on the surfaces of semiconductors during thermo-oxidation in the presence of impurity compounds specially introduced into the system. It is shown in relation to the thermo-oxidation of silicon and gallium arsenide that impurities influence significantly the kinetics and mechanism of the formation of dielectric oxide layers, accelerating the process, lowering the duration of the high-temperature treatment, and altering within wide limits the composition and properties of the resulting films. The rules governing processes involving the impurity thermo-oxidation of semiconductors, determined by the class of impurity compounds introduced, were discovered. The principal criteria governing the selection of the impurities influencing specifically the oxidation process are discussed, the methods for their introduction into the system are examined, and the experimental results concerning the kinetics and mechanisms of such processes are analysed.

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I. Introduction

Thin films are used in various branches of modern technology: microelectronics, optoelectronics, laser techniques, etc. This has given rise to a new flow of information about various aspects of the creation of thin-film materials, their structure and properties, the conditions governing their preparation, and the possibility of their practical application. The development of such research has been assisted to a considerable degree by the creation of modern powerful physical instrumental methods such as electronic Auger spectroscopy (EAS), X-ray electron spectroscopy (XES) and mass spectrometric analytical methods (MSAM), including local X-ray spectroscopic micro-analysis (LXSMA), infrared spectroscopy (IRS), secondary ion mass spectrometry (SIMS), X-ray spectroscopic analysis (XSA), and other electronic-probe and optical methods. The development of studies in the field of thin films has appreciably stimulated the development of new accurate physical methods for the monitoring of the composition, structures, and properties of materials. The study of processes leading to the formation of thin films with a wide variety of properties on the surfaces of solids has greatly promoted the development of ideas about the kinetics and mechanisms of heterogeneous reactions of the solid–gas and solid–solid types.

In the investigation of the kinetics and mechanism of the formation of thin oxide films on the surfaces of solids, it was established that phenomena involving the mass transfer (diffusion and electromigration) of species through a growing film play an appreciable role in these processes. In this connection, "physical" models of the growth of films appeared, in which stress is laid on the elucidation of the nature of the diffusing species and the determination of the rate and mechanism of the mass transfer. However, the chemical aspect of the problem—the role of the chemical interaction of the components in the formation and growth of thin films—has been to some extent neglected in such research. Nevertheless, on the basis of one of the key ideas in modern chemistry, namely the dependence of the composition and properties of substances on the conditions governing their preparation and the nature of the chemical bond in them, one can solve the main problem in this science, i.e. that of the creation of new materials with specified properties.

The establishment of correlations (and ultimately of causal links) between the preparation conditions (the process conditions and process kinetics and mechanism) and the composition and properties of thin films and heterogeneous thin film structures makes it possible not only to expand the ideas concerning the chemistry of the processes but also to obtain materials with a wide range of properties. In the creation of dielectric films on the surfaces of semiconductors during their thermo-oxidation, one of the methods for the solution of this problem involves the introduction into the oxidation atmosphere or onto the surface of the support of specific specially selected impurities which, by exerting a radical influence on the kinetics and mechanism of the film growth process, can ultimately alter the composition and properties of the films in the required direction. This method can be referred to as the impurity thermo-oxidation of semiconductors. It was found that the role of the impurities introduced is unusual and that it is extremely important for it is determined not only (and not largely) by their concentration but also by their nature, i.e. one can speak of a specific effect of various impurities. This effect consists primarily in the alteration of the nature of the chemical reactions responsible for film growth, but the incorporation of impurities in the layer formed naturally influences also the kinetics of the mass transfer of the oxidant in it. Certain general rules governing the impurity thermo-oxidation processes, which were found to be universal and permitted the use of a simple approach to the creation of dielectric layers and

various semiconducting materials, were discovered and formulated in the course of the study.

Investigation of the impurity thermo-oxidation processes is based on the combination of formal kinetic studies and modern instrumental physical and physicochemical methods, which permit an unambiguous establishment of the composition of the reaction products formed, of the distribution of the components within the thickness of the layer, and of the change in the composition and structure of the layers and supports, and hence one can obtain comprehensive information about the dependence of the film composition on the formation conditions and the process kinetics and mechanisms. The application of chemical etching methods and the study of voltage–capacitance and dynamic voltage–current characteristics make it possible to establish the relation between the metal/dielectric surface structures (MDS) based on them (electrical strength, mobility of charge carriers, density of surface states, effective surface and space charges, etc.).

II. Oxidation of silicon under the influence of impurity compounds

Silicon is so far the main material in the technology of semiconductor devices and integrated circuits (IS), while SiO_2 possesses a unique combination of physicochemical and dielectric properties which gives rise to its wide scale application in microelectronics as a universal multifunctional dielectric. The formation of heterogeneous Si/SiO_2 structures can serve as a model process in the chemistry of heterogeneous reactions by virtue of the following factors:

1. The highly symmetrical structure of silicon permitting a comparatively simple modelling of the oxidation process at the atomic level.

2. The high degree of stoichiometry of SiO_2 and hence its satisfactory reproducibility with different conditions in its preparation.

3. The tendency of SiO_2 to form glasses, which rules out side effects such as the diffusion of the oxidant via intercrystallite boundaries, the segregation of impurities, etc.

4. The absence of a flux of atoms from the support to the film; as a result the oxidation proper takes place only on the moving internal interface and the silicon atoms not linked to oxygen (sometimes detected in the film).[1] This arises owing to its rapid movement and "toppling" within the support. On the other hand, when layers are deposited, the increment in thickness is ensured by the movement of exclusively the outer interface, while the support influences only the initial stages of the process (adsorption and nucleus formation). In subsequent stages, its nature does not have an effect, which permits the construction of universal models.

5. A fairly high degree of ideality of the silicon/dielectric interface and the small thickness of the transition layer. These make possible the application of the "sharp transition" model to the Si/SiO_2 heterostructure.[2]

6. The thermal silicon oxide on silicon, grown under "clean" conditions, is a kind of reference standard against which the oxide layers obtained by any other method are compared.

The thermo-oxidation of silicon itself is described by the fairly simple model of Deal and Grove[3] and also by revised models,[4–13] which yield similar kinetic equations. According to general ideas, at high temperatures film growth on a surface coated by a natural oxide ($\sim$3 nm) initially obeys a linear law where the rate-limiting stage is assumed to be the chemical reaction at the Si/SiO_2 interface. Consequently the layer of natural oxides hardly constitutes a barrier to the diffusion of oxidant species. With increase in the thickness of the natural oxide film, its barrier functions become more marked and the rates of reaction and diffusion become comparable, which corresponds to a linear-parabolic oxidation regime. Subsequently diffusion becomes the limiting factor and parabolic oxidation takes place.

However, purely mathematical difficulties, associated with the determination of the contribution of the surface reaction and diffusion to the overall process, arise even in such description. As a result of this, the effective activation energy (EAE) is assumed to be an integral characteristic of the entire process. On the other hand, the hypothesis of an abrupt change to diffusional control of the reaction is a fairly rough approximation, because under real conditions the transition from one type of control to another takes place continuously and gradually. A formal model, reflecting this gradual transition and making it possible to determine the range of temperatures and times corresponding to the change in the controlling stage and the contribution of each component within the limits of these ranges, has been proposed.[14]

Yet another problem is to incorporate as completely as possible the factors influencing the above process components. These are the nature of the diffusing species, the field and deformation stresses near the interface and in the bulk of the oxide, the generation of defects in the course of the oxidation, the influence of the degree of doping of the support, etc. Such factors have been taken into account most fully in Tiller's studies.[10–13] The establishment of the types of all the diffusing species responsible for the growth of the thickness of the layer is important.

Since fluxes of both neutral and charged oxidant species occur in the film,[8,15] it is legitimate to consider a general case—mixed diffusion and electromigration. However, such study sometimes leads to cumbersome expressions even for the oxidation of silicon itself,[16] which are relatively unsuitable for more complex processes. Despite the allowance for varying numbers of factors in different studies, the final equations describe in the general case the linear-parabolic oxidation and differ only in their coefficients.

The opposite approach proved to be extremely productive: it involves the formal kinetic description of the process on the basis of a formalised kinetic equation generalised to the maximum extent:

$$d=k^n\tau^n, \qquad (1)$$

where d is the thickness of the layer, τ the duration of its formation process, and k the integral process rate constant.

This equation does not take into account the specific mechanisms of the individual stages and characterises the process as a whole. For the oxidation of silicon itself, the exponent n varies in the range 1–0.5, reflecting the gradual transition to the diffusional control of the reaction. This relation makes it possible to describe any new layer formation processes on any supports and to carry out a comparative formal kinetic analysis.

The need to search for new dielectric layer formation processes on silicon is not at first sight dictated by practical requirements, since silicon oxide itself in general satisfies the requirements of the technology of semiconductor devices and integrated circuits. However, on passing to a flexible technology, it becomes evident that, instead of a universal multipurpose dielectric, it is in many cases useful to employ layers with properties modified for a particular purpose. The problem of reducing the duration of the

high-temperature treatment of supports and heterostructures, which makes it possible to reduce the diffusional "spreading" of the elements of the integrated circuit, remains no less timely.

The first studies on the oxidation of highly doped silicon[17,18] already demonstrated the dependence of the kinetics of the growth of films on the level of doping. Naturally, the process mechanism and hence also the properties of the films change under these conditions. Systematic study of the oxidation of diffusionally and ionically doped supports[19–29] led to the discovery of the influence of impurities in an elemental state on the kinetics and mechanism of the oxidation process and the properties and composition of the oxide layers.

Overall, the kinetic relations for the thermo-oxidation of both diffusionally and ionically doped supports are similar to the familiar relations for the weakly doped reference silicon. In all cases, the oxidation proceeds either in the linear-parabolic or the parabolic regime but its rate changes consistently: $v_{ref} < v_d < v_i$ (the subscripts ref, d, and i refer respectively to the reference process and to diffusionally and ionically doped layers of silicon). The acceleration of the process in the last two cases (by a factor of 1.5–3) promotes also the more rapid transition from the linear-parabolic to parabolic oxidation, compared with the reference standard.

The change in mechanism is manifested particularly distinctly in the oxidation in the H_2O (vapour) + O_2 mixture, where regular layers are formed in very short time intervals. Compared with ion implantation, diffusional doping does not induce appreciable disturbances in the structure of the support and one can therefore assume that the acceleration of the process is caused in this case mainly by the influence of the impurities, while in the case of ionic doping it is caused by the combined influence of the impurity and radiation defects. However, it has been established[25] that the nature of the impurity itself exerts the main influence on the rate of the process and that radiation defects are an accelerating factor only in the initial instant of the oxidation. The implantation in silicon of a chemically neutral impurity (Ar^+) hardly alters the rate of its oxidation compared with the reference standard as a consequence of the rapid annealing of the radiation defects. Furthermore, on double implantation ($Ar^+ + As^+$ or $Ar^+ + Sb^+$) the overall concentration of radiation defects is higher than in ionic doping by only one active impurity, but the rate of the process is a maximum for singly implantation.

In the cases considered, the role of the impurity reduces to the transfer of oxygen from its oxidised forms to silicon and the process is faster than the direct oxidation of the support. Interactions of the type

$$2E_xO_y + ySi = ySiO_2 + 2xE \qquad (2)$$

have been called transit interactions.[30,31] In the oxidation of doped silicon, they are most significant at low temperatures and for short process times, where the contribution of the reaction component is high and the surface concentration of the impurity is a maximum.

The similarity of the kinetics of the above processes and of the reference process is confirmed by the similarity of the exponents in the kinetic equation (1) and of the effective activation energies. There is an analogy in the process mechanisms; the increase in the complexity of the mechanism on passing from reference supports to doped and implanted supports consist only in the appearance of the parallel transit oxidation with participation of the impurity. The flux of oxidant species diffusing across the film on the inner interface (or in its vicinity) is "divided" into two: the first interacts directly with the support, whilst the second interacts via the initial oxidation of the impurity with subsequent transfer of oxygen to silicon.

The similarity of the kinetics and mechanisms of the oxidation of doped and reference supports leads to a similarity of the compositions and properties of the films obtained. They consist of virtually pure SiO_2 slightly doped by the corresponding impurity (~1–3 at.%; XSA, EAS), whose physical characteristics are also similar to those of the reference standard.

The characteristic features of the growth of films in these processes are associated with the physicochemical nature of the impurity. Thus the influence of the electron-donating and electron-accepting impurities implanted in silicon on the nature of the time variation of the process is different. Electron-donating impurities (phosphorus, arsenic, antimony) accelerate the growth of films predominantly in the initial stage, i.e. they influence mainly the reaction component. An electron-accepting impurity (boron) gives rise to a relative stability of the acceleration of the process and of the effective activation energies, which can be explained by the value of the partition coefficient of boron between silicon and SiO_2 [9] and by the possibility of not only the reaction component but also the diffusion component of the process being acted upon. This also accounts for the continuous variation of the parabolic oxidation rate constant (calculated on the basis of the model of Deal and Grove[3]) with temperature, the linear dependence of the oxidation rate on the concentration of the incorporated impurity at all stages of the process, and the difference between the kinetics of etching of the grown oxide layers compared with those for the reference standard.

The observed acceleration of the process cannot be attributed to the catalytic effect, because the latter presupposes a decrease in activation energy together with an increase in the rate. On the other hand, in the cases considered an appreciable decrease in the activation energy was not observed.

Thus the chemical effect of the impurity (the transfer of oxygen to silicon as a result of the transit interaction) plays a decisive role in the acceleration of the thermal oxidation of silicon. The impurity was introduced in the elemental form, which in fact made it possible to discover the influence of a specific element on the kinetics and mechanism of the oxidation reaction. One of the criteria governing the selection of the accelerating impurity element is the possibility of the spontaneous occurrence of the transit interaction (2), which can be assessed thermodynamically.[32] At the same time, it is necessary to take into account also the probability of other reactions competing with the transit interaction. For example, thermodynamic calculation has shown[30] that the oxides of a series of transition metals are capable of transferring oxygen to silicon. However, the metal segregated under these conditions forms silicides with the support as a result of which the reoxidation of the metal with renewal of transit is impossible. On the other hand, the introduction of the same metal directly into the support immediately leads to the formation of silicide phases. It is for this very reason that, despite the fact that the typical oxidation catalysts are in fact certain transition metals and their oxides, in the given instance it is hardly possible to identify the catalytic effect. For this reason, the results of a number of studies[33,34] in which a strong catalytic action of transition metals (Pt, Pd, etc.) was allegedly noted, are susceptible also to another interpretation: the formation of silicide phases and the breakdown of the laminarity of the flow when silicon is in close contact with the metallic needle.

The use of impurities in the form of binary compounds is more fruitful, because we then have the possibility of the action of both components of the impurity—the cation- and anion-forming agents—on the kinetics and mehanism of the process, and their effects can be not only independent but also cooperative. By selecting different classes of compounds with the same cation-forming agent (or anion-forming agent), it is possible to discover the general features characteristic of the given class as well as the characteristic features determined by each component of the impurity separately, which permits the modification of the properties of SiO_2 in several ways at once. Oxides participate in the transit interaction and when they are used as impurities it is possible to obtain a kind of reference standard for the elucidation of the role of the anion. Furthermore, the oxygen anion is one of the few species whereby the impurity can be introduced into the system in two ways: via the gas phase (unlimited source of impurity) and by deposition on the oxidisable surface of a layer whose thickness can be regulated (limited source). This is necessary to elucidate the influence of the method of introduction of the impurity into the system on the kinetics and mechanism of the growth of layers.

It has been established that, when oxides are introduced into the system, the transit interaction in a pure form determines the acceleration of the process only in those cases where the impurity oxide is indifferent with respect to the growing SiO_2 layer. Thus oxidation in the presence of Ga_2O_3 and In_2O_3 [35] is characterised by virtually the same kinetic parameters as the processes on the reference silicon or slightly doped silicon ($n = 0.5-1$, similar effective activation energies and similar acceleration of the process compared with the reference standards). The composition of the layer approaches that of SiO_2 (IRS, XSA), but the inclusion of a certain amount of gallium (indium) in the films has a positive effect on their electrophysical characteristics.[36]

If the impurity oxide is miscible and is capable of forming vitreous layers, i. e.

$$mE_xO_y + nSiO_2 = mE_xO_y \cdot nSiO_2, \quad (3)$$

then the kinetics differ sharply from those for the reference standard and for the purely transition processes. Thus, when the oxides B_2O_3, PbO, Sb_2O_3, and Bi_2O_3 are introduced into the gas phase,[37–40] the acceleration is by a factor of 50–600. As a rule, the effective activation energies are high (reaching 950 kJ mol^{-1}) and the values of n can be both smaller than 0.5 (0.3) and greater than 1 (up to 2.16). The latter is due to reactions which lead to an increase in the thickness of the layer both on the inner and outer interfaces. The layers obtained are silicate glasses of different elements (IRS, XSA, LXSMA). In the vicinity of the inner interface, impurities (B, Pb, Sb, Bi) were detected, which confirms the occurrence of the transit reaction (2).

Thus two parallel processes—transit and vitrification—contribute to the accelerated increase in the thickness of the film. Whereas in the reference oxidation or oxidation of highly doped specimens, it was possible in the first instance to identify a sequence of stages and in the second to ignore the oxidation itself, considering only the accelerating factor (diffusion of the oxidant–transit–oxidation of the impurity element–renewal of transit), in the presence of two parallel accelerating processes, each of which proceeds via a series of consecutive stages, it is necessary to introduce the concept of the determining process.[41] This is the fastest of the parallel processes which makes the greatest contribution to the increment in the thickness of the layer. The latter addition is significant, since the fastest of the parallel processes may have no bearing on the increment in the thickness and as regards kinetics it will not be determining [for example, the diffusion of the element produced by reaction (2) into the support or the film]. Since the determining process is a multistage one, it is useful to identify the rate-limiting stage in it as the slowest in this sequence.

Clearly the determining process in oxidation with participation of impurities is either the transit reaction (oxidation of highly doped silicon; after the introduction of Ga_2O_3 and In_2O_3) or vitrification (in the presence of B_2O_3, PbO, Sb_2O_3, Bi_2O_3). The transit reaction is always limited by the diffusion of the oxidant [either O_2, or H_2O (vapour), or E_xO_y] to the inner interface via a film whose properties are similar to those of SiO_2. In the determining vitrification process, the rate-limiting stage is also the mass transfer of E_xO_y. However, here this proceeds not via SiO_2 but via a silicate glass of the given element having a less ordered and looser structure, which greatly accelerates the rate of transfer. Furthermore, in the experimental temperature range certain impurity oxides (PbO, Bi_2O_3) may be in the fused state, which also facilitates the mass transfer of E_xO_y.

The method used to introduce the oxide into the system without affecting significantly the process mechanism (the number of stages, their nature, and their sequence) greatly influences the rate of increase in the thickness of the layer (and hence also the kinetic characteristics). Evidently, in the oxidation of Si/E_xO_y structures with a layer of oxide deposited on the surface both the determining process and its rate-limiting stage are the same as in the previous case. The characteristic features of the procedure are as follows: (1) the transit interaction develops already in the initial instant at a high surface concentration of the impurity at the silicon/oxide interface generated; (2) the latter factor ensures an intense transit reaction with overlap of the local superheating fields;[42] (3) the mutual diffusion of the components in the vitrification process through the dense impurity oxide layer formed beforehand is hindered compared with mass transfer through the loose silicate film of the given element formed during the introduction of the impurity through the gas phase; (4) apart from the parallel consecutive process considered, which ultimately promotes an increase in the thickness of the resulting film, it is essential to take into account the competing process involving the evaporation of the deposited impurity film and leading to a decrease in its thickness. As a consequence of these causes, exponents $n < 0.5$ as well as somewhat reduced effective activation energies are characteristic of oxidation reactions of the Si/E_xO_y heterostructures.

Thus, when the reaction leading to the mutual dissolution of the oxides (vitrification) is possible, it in fact ensures the main increment in the mass of the film and is the determining process on which depends also the composition of the resulting layers. The possibility or impossibility of the transit reaction and of vitrification are determined primarily by the nature of the cation-forming element.

The method of introduction of the impurity into the system is as a rule dictated by the type of the anion-forming impurity element. The sulphides of Group IIIA–VA elements can be usefully deposited directly on the oxidisable silicon surface, because the evaporation of these compounds at the high temperatures (and in an oxygen medium) used in the growing of the films, is impossible without decomposition and chemical reaction. In other words, it is useful to create a limited source of the impurity.

The rate of increase in the thickness of the layers in the thermo-oxidation of Si/E_xS_y is the same as for Si/E_xO_y; the exponents n are less than 0.5 (0.12–0.40) and as a rule decrease in the course of time (to 0.05); the effective activation energies are 140–540

kJ mol^{-1} depending on the nature of the cation-forming impurity element and the process stage.[36] The Si/E_xS_y heterostructures are oxidised in two or three stages. In the first stage, the deposited sulphide layer is transformed in accordance with the sulphide–sulphate–oxide sulphate–oxide scheme (IRS, XSA, LXSMA). Bearing in mind the high temperatures of the thermo-oxidation of these heterostructures, it must be emphasised that, since this stage is limited by the diffusion of oxygen through a very loose sulphate–oxide–sulphate layer, it is completed very rapidly and it is as a rule possible to record the increment in the thickness of the layer starting from the second stage. By this instant, the front of the migration of the impurity oxide (as the final sulphide oxidation product) reaches the support and ensures the transit reaction.

We may note that oxides forming part of the composition of the oxide sulphate phases are also capable of entering into similar reactions. The transit reaction is the determining process in the oxidation of the Si/E_xS_y heterostructures for which the sulphide oxidation products do not form vitreous layers with SiO_2. The growth of the film is then limited by the given stage, for example, as in the Si/In_2O_3 heterostructures with $n_{av} = 0.13$.[43] Here the rate-limiting stage is the mass transfer of the impurity oxide, bound in the film (limited impurity source) to the internal interface; in the absence of vitrification, it is hindered and the process acceleration rapidly decays with time. The resulting layer consists of the impurity oxide and the concentration of SiO_2 increases only in the vicinity of the inner interface (XSA, IRS, MSMA). Some migration of SiO_2 from the inner interface to the outer one has apparently a favourable effect on the formation of bridge bonds and the "healing" of defects. The resulting layer therefore consists of a dielectric film, although In_2S_3 is in fact a semiconductor.

If vitrification is possible, then it is added to the above sequence, i.e. it follows the transit reaction. In this instance, the above process is in fact determining and leads to the formation of the silicate layer of the given element (IRS, XSA, MSMA, LXSMA). It is limited by the mass transfer of the impurity oxide, forming part of the composition of the deposited film, to the inner interface, which is faster than the analogous process in the absence of vitrification. This stage is in fact the first of those recorded (after the rapid oxidation of the deposited sulphide layer) for the Si/GeS_2, Si/PbS, Si/Sb_2S_3, and Si/Bi_2S_3 heterostructures.[44–47] Here the values of n are 0.22–0.40 and the effective activation energies are 180–240 kJ mol^{-1}.

The process does not terminate in the formation of a silicate framework of the given element because the impurity oxide incorporated in it is capable of mass transfer (rate-limiting stage) and a further transit reaction (determining process), which ultimately leads to the formation of a silicon oxide framework (IRS, XSA). The transfer of the impurity component, bound up in the network of the silicate glass of the given element, is more strongly inhibited than in the previous stage, although most of it is present in the form of the oxide. The formation of the silicate framework of the element is therefore rapid and that of the silicon oxide framework is much lower. Very low values of n (0.18–0.05) correspond to this stage and the effective activation energies are 240–540 kJ mol^{-1}.

The characteristic features of the processes considered depend also on the type of the cation-forming element. If the vitrification is limited, then the mass transfer of the impurity is strongly inhibited and the transition from the silicate framework of the element to the silicon oxide framework is difficult, so that the latter can hardly ever be detected in a pure form in the temperature and time range investigated. This is the situation in the oxidation of the Si/GeS_2 heterostructure, where the solubility is limited in the $SiO_2–GeO_2$ system.[44] On the other hand, antimony forms the most thermally unstable sulphide in the series considered and hence in the oxidation of the Si/Sb_2S_3 heterostructures the competing process involving the evaporation of the deposited sulphide is most marked, appreciably reducing the thickness of the deposited impurity layer in the initial instant of the oxidation.[46]

The stability of bismuth oxide sulphates gives rise to a definite arrest in the process in the sulphide layer oxidation stage.[47] On the other hand, the fastest conversion of the sulphide into the oxide takes place in the case of lead. This factor, together with the vigorous occurrence of reactions (2) and (3) as well as the facilitated mass transfer of the impurity oxide in the loose network of the lead silicate glass lead to the virtually instantaneous formation of the lead silicate framework and to the rapid replacement in the latter of the lead oxide component by the silicon oxide component.[45]

Thus the thermo-oxidation of the Si/E_xS_y structures makes it possible to obtain dielectric layers with a high rate of growth (acceleration by a factor from 5 to 60). The anion-forming agent (sulphur) ensures the gradual development of the process and the formation of the resulting layers under milder conditions than those established in the oxidation of Si/E_xS_y structures and also in the presence of oxides in the gas phase. On the other hand, sulphur is absent from the final product, evaporating predominantly in the form of SO_2 during the conversion of the sulphate into the oxide. On vitrification in the system, the oxide is fully consumed in the transit reaction; part of the impurity element produced in reaction (2) diffuses to the support, while another part diffuses into the film and then evaporates. In the impurity process considered, one can therefore obtain relatively pure silicon oxide layers with a satisfactory quality[36] and over a short period.

The idea of introducing anions into the film, where they are retained and ensure a change in its properties in the required direction, is undoubtedly fruitful. Here preference should be given to chlorine. A number of studies have been published[48–52] in which the influence of chlorine on the properties of silicon/oxide layers and heterostructures was demonstrated. It involves a decrease in the instability of the MOS† structures [metal oxide structures?], an increase in the lifetime of the minority carriers in the silicon support and in the electrical strength of the films, a decrease in the density of surface states at the Si/SiO_2 interface, and the suppression of the generation of packing defects and their "healing".

Taking into account the foregoing factors, it is useful to introduce chlorine together with the cation, i.e. to employ oxidation with participation of impurity chlorides. Here too the type of the anion-forming element determines the method used to introduce the impurity into the system—evaporation from the gas phase. The chlorides of the Group IIIA–VA elements employed are comparatively volatile and can be readily introduced into the gas phase, while it is almost impossible to use the method involving their deposition on a support because of their high chemical reactivity and tendency to hydrolyse.

Despite the fact that at high temperatures the impurity chlorides employed undergo pyrolysis and pyrohydrolysis to different extents in an oxidising medium (which contains in addition an undetermined amount of water vapour), the difference between the kinetics of the oxidation reactions of silicon on evaporation from the gas phase

† MOP in Russian (Ed. of Translation).

[sic!] [into the gas phase?] of impurities with the same cation-forming agent (oxides and chlorides) makes it possible to regard the involvement of the latter in "chloride" transit

$$2ECl_x + O_2 + Si = SiO_2 + 2E + xCl_2, \quad (4)$$

$$(4/x)ECl_x + 2H_2O + Si = SiO_2 + (4/x)E + 4HCl. \quad (5)$$

The thermodynamic feasibility of these reactions is one of the criteria governing the choice of the impurity chlorides and at the same time the choice of the oxidising medium. Thus reaction (4) is thermodynamically impossible for $GaCl_3$ and $InCl_3$ and the oxidation of silicon in the presence of these oxides therefore takes place in a H_2O (vapour) + O_2 mixture. On the other hand, if both reactions are impossible, then the chloride can be used in the form of an impurity merely for the introduction into the gas phase of a volatile compound of the given impurity (provided that the vapour pressure, for example, of the chloride, is much higher than that of the corresponding oxide), subject to the condition that the pyrolysis and pyrohydrolysis of the chloride take place preferentially in the system, while the oxide transit reaction (2) is thermodynamically feasible.

The thermo-oxidation of silicon in the presence of chlorides ($GaCl_3$, $InCl_3$, $SbCl_3$, $BiCl_3$, $PbCl_2$, $GeCl_4$, and PCl_3) [53-59] takes place in a linear-parabolic regime. For $GaCl_3$, $InCl_3$, $SbCl_3$, and $BiCl_3$, the determining process is reaction (4) or (5) whose rates are limited by the mass transfer of the chloride fragment across the growing layer. Under these conditions, there are countercurrents of chlorine or hydrogen chloride formed at the inner interface in the course of these reactions and responsible for the breaks observed in the growing films.[36] The latter facilitate to a certain extent the transfer of the impurity to the reaction surface. The grown films consist mainly of SiO_2 slightly doped with chlorine and (to different extents) with the impurity cation-forming agent (IRS, XSA, XES, EAS, LXSMA). The presence of chlorine in the vicinity of the inner interface (XES, SIMS, LXSMA) demonstrates the occurrence of the chloride transit reactions (4) and (5). If reaction (2) plays a decisive role in the growth of the films, then the film will probably have been partly etched by chlorine and hydrogen chloride—the reaction products derived from the chlorides—in the vicinity of the outer interface.

The degree of doping of the films by the cation-forming agent and the acceleration of their growth compared with the reference standard (process characteristics) are determined in this instance also by the nature of the cation-forming element. The acceleration is $\sim$1.5 for $GaCl_3$ and $InCl_3$ and $\sim$2 for $SbCl_3$ and $BiCl_3$. This is caused by the possibility of reaction (3) for $SbCl_3$ and $BiCl_3$. The tendency towards vitrification is most marked for bismuth and the level of doping of the films with bismuth is highest (XSA, LXSMA). However, the concentration in the given processes of impurity oxides as secondary oxidation products of the elements produced by reactions (4) and (5) is low. Thus the physicochemical characteristics of the cation-forming elements (Ga, In, Sb, Bi) are responsible for the nature of the determining process and hence of its controlling stage.

In the range of comparatively low oxidation temperature (750–950 °C), the principal accelerating agent in the growing of films in the presence of lead chloride[57] is the impurity introduced initially. It has been established that at these temperatures most of the $PbCl_2$ passes to the specimen being oxidised in a chemically unaltered state. For the given process, it is possible to identify the following sequence: (1) mass transfer of the impurity chloride to the inner interface; (2) transit interaction of type (4) with participation of $PbCl_2$; (3) oxidation of the lead generated in the transit reaction; (4) type (3) vitrification. Since the resulting film consists of a lead silicate glass (IRS, LXSMA), the determining process in this stage is the mutual dissolution of the oxides [reaction (3)], which, however, is limited by the mediating effect of the mass transfer of $PbCl_2$ from the outer to the inner interface. In the loose film of the lead silicate glass, this process is not greatly hindered, as is indicated by the value of the exponent n close to unity (n_{as} = 0.84).

The oxide forms of lead, which are the products of the interaction of $PbCl_2$ in the gas phase, exert the main influence on the kinetics and mechanism of the oxidation reaction in the range of high temperatures (1100–1200 °C). The nature of the determining process (vitrification) is retained in this stage and the rate-limiting stage is the mass transfer of PbO to the inner interface. At moderate temperatures (1000 and 1050 °C), the reactive reactants are simultaneously lead chloride and lead oxide.[57] $PbCl_2$ creates the most favourable conditions in the given process for the rapid formation of films. The acceleration of film growth is a maximum (by a factor of 22) in the range 750–950 °C and a minimum (by a factor of 3–5) in the range 1100–1200 °C, whilst in the range 1000–1050 °C the acceleration has intermediate values (by a factor of 6–12). Chlorine has been detected (LXSMA) in the films corresponding to the low-temperature stage, which, together with presence of lead in the support (XSA, LXSMA), constitutes proof of the occurrence of the chloride transit reaction (4).

The nature of the cation-forming elements determines the relative stabilities of the chlorides over the entire experimental temperature range ($GaCl_3$, $InCl_3$, $SbCl_3$, $BiCl_3$) or in a particular portion of it ($PbCl_2$) and hence are responsible for the definite influence of the impurity introduced initially on the characteristics of the growth of films and their properties.

On the other hand, $GeCl_4$ and PCl_3 [55,56,58] undergo virtually complete pyrohydrolysis already in the gas phase and are converted into the corresponding oxides. The latter give rise to a flux of the impurity in the film, the mass transfer of the $Ge(P)_xO_y$ fragments limiting its growth as a whole. At advanced stages of the process, vitrification is the determining reaction (IRS, XSA); on the other hand, at the beginning there is a possibility of an "induction" period where the film growth (process with $GeCl_4$) is determined by the finite rates of pyrohydrolysis of the chloride and of the deposition of the corresponding oxide on the support and also by the limited miscibility in the E_xO_y–SiO_2 system. These features of the processes arise from the properties of the cation-forming impurity elements, which exhibit the most marked non-metallic properties in the series of chlorides considered and hence form unstable chlorides.

The change in the mechanism of the thermo-oxidation of silicon after the introduction of impurity chlorides into the gas phase compared with the reference oxidation[3,18,36] and thermo-oxidation in the presence of the halogens and hydrogen halides,[48] on the one hand, and the growing of films in the presence of oxides, on the other, leads to an appreciable difference between the properties of the films. Thus, in the "chlorine" and "hydrogen chloride" oxidation, chlorine is known to be concentrated in the vicinity of the inner interface,[60] while in the cases examined above films comparatively uniformly doped with impurity cation and chlorine were obtained (XES). Under these conditions, there is a change in the kinetics of the etching. For example, the magnitude of the mobile charge changes by an order of magnitude (for $SbCl_3$ and $BiCl_3$; there is no charge on $GeCl_4$, $PbCl_2$, and PCl_3) and there is

also some decrease in the surface charge and in the density of the surface states. However, the last two characteristics are poorer for the chloride processes examined than for the "chlorine" and "hydrogen halide" processes, because the inner interfaces are disturbed and there is an increase in the degree of defectiveness of the films caused by the reactions (4) and (5), the evolution of gaseous products, and breaks in the direction of the outer interface.

III. Impurity thermo-oxidation of gallium arsenide

The foregoing ideas concerning the involvement of impurities in the formation of oxide layers on silicon can be largely extended to other semiconducting materials, in particular, to compounds of the type $A^{III}B^{V}$. The main principle of the selection of the impurity from the standpoint of its ability or the ability of its derivatives to participate in the transit transfer of oxygen is applicable also in this instance. On the other hand, determining processes of the second type (vitrification) do not play a significant role here, because such a process is retarded at the low oxidation temperatures characteristic of the compounds $A^{III}B^{V}$. Nevertheless, the mutual dissolution in the oxide systems $A_2^{III}O_3-B_m^{V}O_n$, $A_2^{III}O_3-E_xO_y$, and $B_m^{V}O_n-E_xO_y$, which is appreciable in many instances, can promote the improvement of the properties of dielectric layers, diminishing their defectiveness.

Compared with silicon, the oxidation of gallium arsenide, the most important of the compounds of the type $A^{III}B^{V}$, has a number of characteristic features which hinder the formation of high quality dielectric layers. Firstly, it is impossible to identify the sequence of processes, because the diffusion of oxygen to the support is always accompanied by the diffusion of gallium and arsenic into the film. Thus, there are always countercurrents of the components in the film. Under these conditions, the reactions ensuring the increment in the mass of the layer are possible not only on the inner interface but also on the outer one, as well as in the bulk of the film. Secondly, the evaporation of the volatile component of the support (arsenic) is responsible both for the imperfection of the semiconductor/dielectric interface and for the increased defectiveness of the growing film. The degradation of the support necessitates in its turn the application of comparatively low temperatures in the oxidation of GaAs at which the transport processes investigated are greatly retarded. Thirdly, thermodynamic calculation has shown,[64] that the thermo-oxidation of GaAs proper is itself a transit process because, on being oxidised, arsenic subsequently transfers oxygen to gallium:

$$As_2O_3+2GaAs=Ga_2O_3+4As, \quad (6)$$

$$3As_xO_y+2yGa=yGa_2O_3+3xAs. \quad (7)$$

Hence the thermodynamically stable pairs are Ga_2O_3-GaAs and Ga_2O_3-As.[62] The arsenic reduced in the course of the transit reactions (6) and (7) proper is concentrated on the inner interface and exerts a negative influence on the properties of the metal/dielectric surface structures (MDS structures) obtained subsequently.[63] The above features are responsible for the complexity of the composition of the layers obtained and also for its marked dependence on the process parameters. In the general case, the film grown on GaAs during its thermo-oxidation consists of Ga_2O_3, As, As_2O_3, and $GaAsO_4$,[62,64,65] the first of the above components predominating in layers obtained under not unduly severe conditions.

Thus impurity transit is essential for the acceleration of the oxidation of both the gallium and arsenic components of the support in order to increase the rate of formation of the layer consisting predominantly of Ga_2O_3 and to increase the efficiency of the oxidation of arsenic, promoting thereby its segregation in the film in an oxidised and not elemental state. The latter factor ensures the "healing" of defects and the improvement of the properties of the films and the MDS structures.[66]

The postulate of the transit interaction, put forward above, involving the oxide forms of the impurity as the main factor accelerating the oxidation of the supports in which impurity ions have been implanted was confirmed also for gallium arsenide. It was established that antimony implanted in GaAs accelerates the oxidation of the latter, that boron does not increase the rate of growth of films, and that phosphorus retards it.[67] These features are correlated with the results of thermodynamic calculations for the corresponding transit processes and the available information about the physicochemical properties of impurity oxides.[68] As for silicon, it has been found that the kinetics of the thermo-oxidation reactions of gallium arsenide doped with antimony ions and of the reference process are similar. However, for the Si/SiO_2 heterostructure the partition coefficient of antimony is such that it is mainly concentrated at the inner interface, while in the corresponding gallium arsenide/oxide heterostructures antimony is segregated in the film (EAS, SIMS, MSMA), which has a favourable influence on the electrical strength of the latter. This is apparently caused by the interaction of the oxide forms of antimony with Ga_2O_3 and As_2O_3 (IRS).

The thermo-oxidation of GaAs when the gas phase contains impurity oxides (GeO_2, SnO, PbO, Sb_2O_3, Bi_2O_3, V_2O_5) capable of the transit interaction

$$(3/y)E_xO_y+2GaAs=Ga_2O_3+(3x/y)E+2As, \quad (8)$$

$$(3/y)E_xO_y+2Ga=Ga_2O_3+(3x/y)E, \quad (9)$$

also ensures the acceleration of the formation of the films.[69-71] The acceleration is by a factor of between 2 and 26 depending on the type of the cation-forming impurity element. The resulting films contain mainly Ga_2O_3 and are weakly doped with arsenic and impurity oxides (XSA, MSMA, IRS, SIMS).

The influence of the oxides GeO_2 and SnO on the kinetics of the thermo-oxidation of GaAs is similar. This is caused by the characteristic features of the evaporation of the above impurity compounds. The rate of oxidation in the linear regime is smaller for both processes compared with the parabolic regime (n = 0.28 and 0.40). According to Tananaev and Shpirt,[72] the evaporation of GeO_2 entails the formation reactions of GeO, Ge_nO_n, and Ge (the products of the disproportionation of GeO), which reduce the surface concentration of the impurity in the initial instant of the oxidation reaction. In the process with participation of SnO, the main influence is apparently exerted by the polymeric Sn_2O_2, Sn_3O_3, and Sn_4O_4 molecules, which make an appreciable contribution to the overall pressure of the impurity vapour; however, they are formed as a result of a complex series of reactions,[73] which is in fact the reason for the induction period.

The films obtained are weakly doped with the impurity component, in contrast to the layers grown in the presence of PbO, Sb_2O_3, and Bi_2O_3 (XSA, EAS, IRS). Lead, antimony, and bismuth are incorporated to the greatest extent in the growing layer, but, compared with the element silicate glasses obtained in the

corresponding processes on silicon, their concentration is low (from 1 to 6 at.%; XSA, MSMA, EAS), which confirms the retardation of the mutual dissolution of the intrinsic and impurity oxides caused by the nature of GaAs and the corresponding oxides. The appreciable accelerations obtained (by a factor of up to 26) indicate the decisive role of the transit interactions (8) and (9) in the film formation processes involving all the oxides investigated. The transit reaction can proceed preferentially at the inner (Sb_2O_3, n = 0.77) and outer interfaces and also in the bulk of the films (PbO, n = 1.4; advanced stages of the processes with GeO_2, SnO, Bi_2O_3, n = 1.10–2.17). Since the main component of the layers obtained is Ga_2O_3, the rate-limiting stage is apparently in all cases the diffusion from the support into the gallium film, such a film being essential for the formation of films both by the impurity-transit mechanism and in the course of the parallel process of the oxidation of the support itself.

The creation of a restricted source of the impurity by depositing the corresponding oxides on the oxidisable GaAs surface leads, as for silicon, to values $n < 0.5$ (for the GaAs/PbO, GaAs/Sb_2O_4, GaAs/Bi_2O_3, and GaAs/V_2O_5 heterostructures, n = 0.01 to 0.42 [74,75]),which corresponds to the interactions in the solid phase. At the inner interface, the impurity oxide transfers oxygen to the gallium of the support already in the initial instant. The impurity element produced thereby diffuses both to the support and to the film and undergoes further oxidation. There is also simultaneous diffusion of gallium into the deposited E_xO_y layer, which is responsible for the transit reaction both at the outer interface and in the bulk of the layer. The rate-limiting stage is the diffusion of gallium. The resulting layers consist mainly of the impurity oxide containing Ga_2O_3, arsenic, and its oxides (IRS, EAS, XSA).

Thus, while the determining process and the rate-limiting stage are apparently identical for the unrestricted and restricted impurity sources, there is also a fundamental difference. In the former case, gallium diffuses in a layer whose composition is similar to that of its own oxide, while in the latter it diffuses into the pure impurity oxide. The formation of Ga_2O_3 in the oxidation of the GaAs/PbO heterostructures in argon,[74] the presence of the impurity element in the support, and the steady increase in the Ga_2O_3 content on moving from the outer to the inner interface (XSA, EAS) demonstrate the occurrence of the transit interactions. Again the retardation of the transport processes and the extremely low oxidation temperatures employed preclude, as in the case of silicon, the transition from the impurity oxide layer to a weakly doped intrinsic oxide.

It is quite important that an accelerated formation of films can be achieved on gallium arsenide in the presence of transition metal oxides, in particular V_2O_5. In the oxidation of the GaAs/V_2O_5 heterostructures, not only the acceleration of the increase in the thickness of the layers (by a factor of $\sim$6) but also an appreciable decrease in the effective activation energy compared with the value for the reference process has been observed, which makes it possible to interpret the process mechanism as catalytic. In this case, the method of introduction of the impurity into the system is evidently also extremely important. Thus, when V_2O_5 is introduced into the gas phase (an unrestricted source of impurity), there is no decrease in the effective activation energy and the determining process is the transit reaction, as for other impurity oxides. Only for a restricted impurity source are there possibilities for the development of the process via a heterogeneous-catalytic mechanism (contact between two solid phases along the entire surface, creating a high concentration of surface-active centres and possibly ensuring the coverage of the local superheating fields).

A similar retarded growth of films compared with the parabolic regime (n = 0.075–0.43) has been observed also for the thermo-oxidation reactions of the gallium arsenide/sulphide heterostructures.[76–80] Here the anion-forming impurity element determines, as already mentioned, the main features of the process and the method of introduction of the impurity into the system. Because of this, a similarity is manifested between the processes considered and the oxidation of the analogous silicon structures. The intensity of the chemical interactions in the heterostructure being oxidised depends on the nature of the semiconductor matrix. Thus the main bulk of the layer grown by the thermo-oxidation of the GaAs/In_2S_3 heterostructure consists of In_2O_3.[76] Here the transit reaction is fairly feeble because of the similarity of the chemical properties of Ga_2O_3 and In_2O_3 and also because of the low process temperatures. For the same reason, the content of antimony in the films grown by the thermo-oxidation of the GaAs/In_2S_3 heterostructures (as well as heterostructures with other deposited sulphides) is higher than in the analogous layers grown on silicon (XSA, SIMS, EAS, LXSMA). The increase in the gallium content in the vicinity of the inner interface (in the oxidised form) as the process develops (XSA, EAS) reflects the increase in the contribution of the transit interaction to the overall process. It is of interest to note that, compared with the relatively pure reference oxides, these films are enriched in silicon, which indicates a higher miscibility in the As_2O_3–In_2O_3 systems compared with As_2O_3–Ga_2O_3.[68]

In the layers obtained by the oxidation of the GaAs/E_xS_y heterostructures at comparatively low temperatures, it is possible to detect simultaneously all the products of the oxidation of the sulphide (XES). Here the determining process is the transit interaction of these products (the oxide and oxide sulphate forms) with the gallium of the support, which is limited as a rule by the diffusion of this component. Thus the films grown by oxidising the GaAs/GeS_2 heterostructures[77] contain GeO_2 and $Ge(SO_4)_2$ as well as Ga and As. As the process develops near the inner face, there is a steady increase in the Ga_2O_3 content and a decrease in that of GeO_2, which demonstrates the occurrence of the transit reaction. If the decrease in the concentration of the impurity oxide component were caused by the competing evaporation process, the ratio of its concentrations in the outer and inner layers would have been the reverse of that observed.

The layers obtained by the thermo-oxidation of the GaAs/PbS heterostrucures[78] contain lead in the form of $PbSO_3$ (XES). Apparently it is in this instance a secondary product of the interaction of PbO (formed on oxidation of the sulphide) with the SO_2 evolved. The presence of PbO in the system and the occurrence of the transit reaction are indicated by the presence of elemental lead in the support (XSA). The oxidation sequence of the deposited sulphide layer is clearly manifested for the GaAs/Sb_2S_3 heterostructure.[79] Antimony oxide as well as antimony sulphite are present at the outer interface; deeper layers contain the impurity sulphate and the incompletely oxidised impurity sulphide (XES). $Bi_2(SO_4)_3$, Bi_2O_3, and gallium and arsenic oxides have been detected in films grown by the thermo-oxidation of the GaAs/Bi_2S_3 structures (IRS, XSA).[80] In all the layers obtained in the presence of the sulphides of Group IV and V elements on the surface of gallium arsenide, the concentration of gallium is higher compared with the analogous films obtained by the oxidation of GaAs/In_2S_3, which indicates a greater contribution of the transit reaction and its decisive role.

Indeed, as already emphasised, the transit reaction in the $GaAs/In_2S_3$ heterostructure is relatively ineffective and hence the increment in the thickness of the layer (n = 0.075) is correspondingly very small; for $GaAs/GeS_2$, its probability is higher and n is now 0.21. The highest values of n occur for the GaAs/PbS (0.42), $GaAs/Sb_2S_3$ (0.43), and $GaAs/Bi_2S_3$ (0.35) heterostructures, in which there are conditions for an extremely vigorous transit reaction and in addition mutual dissolution is observed (IRS) in the $Ga_2O_3-E_xO_y$ systems. Together with the presence of large impurity ions (especially of lead and bismuth) in the bulk phase, this factor facilitates the mass transfer in the film. This feature and also the vigorous transit reaction actually explain the increased content of gallium in the given layers compared with the layers grown by the oxidation of the $GaAs/In_2S_3$ heterostructures.

The formation of arsenic sulphides at the inner interface, observed in the thermo-oxidation of the GaAs/PbS and $GaAs/Sb_2S_3$ heterostructures (XES), is especially important. This suggests that not only the oxygen transit reactions examined but also direct anionic transit takes place. Such transfer of sulphur from one component to another promotes the binding of arsenic and prevents the evaporation of arsenic, the degradation of the inner interface, and the penetration of arsenic into the resulting layer in a free state. For this reason, the electrical strength of the layers increases by a factor of 5–10 compared with the reference oxide, while the density of the surface states decreases severalfold.

Thus the same main kinetic features are manifested in the oxidation of the $GaAs/E_xS_y$ heterostructures as in the processes on the corresponding silicon structures: low values of n, the gradual occurrence of the interaction of oxygen with the sulphide film, and the occurrence of a competing evaporation process from the outer interface.

A common feature of the $GaAs/E_xS_y$ oxidation processes is the decisive role of the impurity oxide transit limited by the diffusion of gallium, which is indicated by the extremely high effective activation energies for the process, close in order of magnitude to the reference values. Naturally, the composition of the resulting layers is determined in many respects by the characteristics of the semiconductor matrix, which determines the oxidation regime. In the case of gallium arsenide, the successive conversion of the deposited sulphide into the oxide with subsequent transit interaction is retarded. This makes it possible to detect in the film various sulphide reaction stages but does not enable one to achieve a transition of the sulphide film–film oxidation products type and the interaction with the intrinsic oxide phases—the intrinsic oxide weakly doped with the impurity.

The features of each process examined above are determined by the nature of the cation-forming impurity. In particular, for the $GaAs/Sb_2S_3$ heterostructures the deposited layer, transformed during the oxidation process, hinders the diffusion of gallium to the least extent and the concentration of the latter near the outer interface is highest (XSA). Since the oxidation of the sulphide begins at precisely this boundary, the concentration of the oxide forms of the impurity is a maximum in this region and best conditions are created for the transit interaction. Furthermore, the similarity of the properties of the oxide in the $As_xO_y-Sb_xO_y$ system ensures to a certain extent their miscibility, while gallium antimonates are apparently formed in the $Ga_2O_3-Sb_xO_y$ system (by analogy with arsenates). This is in fact the reason why the acceleration of the oxidation of these heterostructures is greatest (by a factor of $\sim$20).

The influence of the cation-forming impurity element is revealed most strikingly in the thermo-oxidation of gallium arsenide in the presence of chlorides, whose introduction into the gas phase is actually determined by the nature of the anion-forming element. It was already emphasised above that $PbCl_2$, $SbCl_3$, and $BiCl_3$ are stable in an oxidising medium even at the high temperatures used to grow the films on silicon.[81,82] These compounds actually ensure a flux of the impurity to the support in the oxidation of gallium arsenide when they participate and enter into the chloride transit reaction:

$$2ECl_n + 4Ga + 3O_2 = 2Ga_2O_3 + 2E + nCl_2. \quad (10)$$

As in all the previous cases, there is simultaneous oxidation proper of the support by oxygen. The chloride transit reaction is determining, because, on the one hand, the process is accelerated relative to the reference process (by a factor up to 230) and, on the other, the process kinetics differ appreciably from those of the process in the presence of the oxides of the same elements where the oxide transit reaction is determining. The determining process is in the general case limited by the diffusion of gallium atoms bound initially in the support. The process thus controls the reaction on the outer interface to an even greater extent, because of the source of the impurity is unrestricted and the mass transfer of ECl_n in the gas phase takes place at a high rate.

The characteristics of the processes depend on the nature of the cation-forming agents. Thus the oxidation in the presence of $PbCl_2$ and $BiCl_3$ proceeds in the linear regime owing to the loosening of the resulting layer and the facilitation of the mass transfer in the latter.[81,82] This fact is not only responsible for the acceleration of the diffusion of gallium and of the impurity chloride fragments but also promotes the rapid outflow of arsenic from the inner interface, which also limits the hindrance to the transfer of gallium. Antimony, on the other hand, enters the layer in such small amounts apparently owing to the rapid diffusion in the film and evaporation in the form of the oxide produced in the transit of the element from the outer interface. On the other hand, the inclusion of a certain amount of antimony in the film does not promote its loosening and does not create conditions which prevent the accumulation of arsenic at the inner interface. These factors retard the diffusion of gallium and the film grows the linear-parabolic regime.[82]

Depending on the process characteristics, the composition of the layers also varies (IRS, XSA). The films grown in the presence of $PbCl_2$ are doped with the impurity to the greatest extent; they constitute complex formations which are the products of the interaction of Ga_2O_3, PbO, and As_2O_3 and contain also oxide chloride fragments. The layers grown in a medium with $BiCl_3$ are fairly weakly doped with bismuth, but their arsenic content is increased apparently as a result of the miscibility in the $As_2O_3-Bi_2O_3$ system. Oxidation in the presence of $SbCl_3$ results in the formation of Ga_2O_3 films weakly doped with antimony and chlorine.

The characteristics of the cation-forming elements are responsible for the instability of the chlorides $GaCl_3$ and $InCl_3$. After the introduction of $GaCl_3$, n = 1.63 and the effective activation energy is only 6 kJ mol^{-1} for the oxidation process.[83] This is a virtually non-activated process and such parameters indicate the occurrence of physical adsorption.[84] Thus in the given instance the determining process is the deposition on the support of a layer of Ga_2O_3 formed during the reactions

$$ECl_3 + H_2O = EOCl + 2HCl, \quad (11)$$

$$EOCl + 2H_2O = E(OH)_3 + HCl, \quad (12)$$

$$2E(OH)_3 = E_2O_3 + 3H_2O. \quad (13)$$

In this instance the growth of the oxide film is virtually unlimited, since the mass transfer in the gas phase is rapid. Naturally the resulting layer consists of Ga_2O_3, which, however, is strongly doped with arsenic (IRS, XSA). The competing arsenic evaporation process is suppressed, because the rate of growth of the layer is so high that it inhibits kinetically the diffusion of arsenic to the outer interface and hence its evaporation in the form of oxides.

On introduction of $InCl_3$, the deposited In_2O_3 layer, formed by reactions (11)–(13), is capable of entering into a transit interaction with the gallium of the support. This process is determining,[85] since, for the high value of the exponent n at an advanced stage of the process (n = 1.57), the effective activation energy is likewise high (110 kJ mol^{-1}) and is close to the corresponding reference value. This means that the rate-limiting stage is the diffusion of gallium. Here film growth takes place on two interfaces ($n > 1$) and on the outer one the pyrohydrolysis of the chloride makes an appreciable contribution to the increment in film thickness. The resulting layer consists mainly of In_2O_3 containing chlorine and also of gallium and arsenic oxides (XSA, MSMA, SIMS). The vigorous interaction in the $In_2O_3-As_2O_3$ oxide system ensures the "healing" of the defects in the In_2O_3 semiconductor and sharply increases the electrical strength of the layers (by more than two orders of magnitude) compared with the films grown on GaAs under relatively clean conditions.

Thus, taking into account the characteristic features of the cation-forming elements under the conditions employed, the chlorides examined can be divided into two groups—stable and unstable. Within the framework of each group, the similarity of the cation-forming elements leads to the similarity in the behaviour of their chlorides in the oxidising medium. However, the fact that gallium is one of the components of the support whilst the derivatives of indium interact both with the components of the support and with their oxide forms is responsible for the difference between the mechanisms of the formation of the layers and hence of their properties.

IV. Characteristic features of the effect of impurity compounds on the thermo-oxidation of indium phosphide

The following conditions must be maintained for the formation of impurity oxide layers with a satisfactory quality on semiconductors: (1) the impurity introduced initially or its oxidation products must ensure the acceleration of the formation of layers via the transit or catalytic mechanism; (2) the mutual dissolution of the intrinsic and impurity oxides, possibly with formation of compounds (silicates, arsenates, etc.) is desirable; (3) in the presence of the quantities of the cation-forming agent listed above, the anion-forming agent should improve the properties of the layers ("healing" the defects, neutralising the charge in the film, etc.); (4) in the oxidation of semiconducting compounds with a volatile component, it is desirable to create a restricted source of impurity in the form of a deposited film; (5) the optimum chemical binding of the volatile component of the support by the anion-forming impurity element (and not the cation-forming element, since in this case the "metallic" nature of the inner interface is more marked).

These general conditions are applicable also to semiconducting compounds such as InP. Its main feature is that, among all the compounds of the type $A^{III}B^{V}$, the enthalpy of formation of $B^{V}_{m}O_{n}$ (P_2O_5) is greater than that of $A^{III}_{2}O_3$ (In_2O_3) only for InP. Therefore, according to the results of thermodynamic analysis,[86] phosphorus should remove oxygen from indium, i.e. its transit reactions

$$0.3P_4O_{10}+2InP \rightleftharpoons In_2O_3+3.2P, \quad (14)$$

$$0.3P_4O_{10}+2In \rightleftharpoons In_2O_3+1.2P \quad (15)$$

will occur in the reverse direction—"reverse" transit.

However, it is believed[87] that the $InPO_4-P$, $In(PO_3)_3P$ pairs should be thermodynamically stable under equilibrium conditions in the In–P–O system. Thus in the above system the growing of regular films is possible only over an extremely long period as a result of the secondary interaction of the indium and phosphorus oxides with formation of $InPO_4$. Indeed, according to the literature data,[88,89] the composition of the intrinsic oxide layers on InP approaches that of $InPO_4$. Furthermore, in contrast to, for example, GaAs, non-oxidised indium has been detected in the intrinsic oxide films grown on InP.[90]

The thermo-oxidation of InP itself in the temperature range 575–675 °C is a two-stage process. The first stage ($n \simeq 0.5$) corresponds to diffusional control and the rate-limiting stage is apparently the diffusion of indium from the support. The second stage with n = 0.13 corresponds to the type of process in which the interaction in the solid phase, namely the formation of $InPO_4$, is determining. The process is limited by the mutual diffusion of the oxides. There is a high content of indium in the resulting layers (EAS, IRS), which indicates its presence in a free state. This may be a consequence of the degradation of the support[88] or, what is more likely, may be a result of reactions (14) and (15), which are apparently determining in the first stage. The $INPO_4$ content in the layers on the whole increases with increase in the process parameters, but the concentration of free indium also increases in the same direction (XSA, EAS). The latter is responsible for the very low resistivity of the films ($< 10^6$ Ω cm).

Thus the very mechanism of the formation of intrinsic dielectric layers on InP is responsible for their unsatisfactory properties and it is essential to introduce an impurity, in the first place with the aim of increasing the efficiency of the oxidation of indium both directly (with indium as the transit impurity) and indirectly by enhancing the oxidation of phosphorus (with phosphorus as the transit impurity) and of weakening its effects on In_2O_3 via reactions (14) and (15). Furthermore, in contrast to $Ga_2O_3-As_2O_5$ system, in the analogous $In_2O_3-P_2O_5$ system better possibilities arise for interactions, since indium possesses metallic properties to a greater extent than gallium, while phosphorus possesses non-metallic properties to a greater extent than arsenic. The correct choice of the impurity can therefore intensify the process, for example, by increasing the mutual diffusion on loosening.

The introduction of impurity compounds into the gas phase, capable of undergoing both the transit reactions indicated above and reactions responsible for the increase in the rate of diffusion ($PbCl_2$) or a possible catalytic effect (V_2O_5), does indeed increase the rate of formation of oxide layers on indium phosphide. Acceleration by a factor of 2–3 has been achieved as regards thickness and by a factor of 8–11 as regards time using $PbCl_2$; for V_2O_5, the above factors are 8–9 and 40–60 respectively. In both cases, the kinetics change compared with the impurity-free reference process. The introduction of $PbCl_2$ ensures a more favourable kinetic regime for film growth by increasing the amount of oxygen capable of being

"retained" in indium (EAS) and also by loosening the resulting layer by incorporating lead atoms in it. The films consist mainly of $InPO_4$; their composition also includes impurity components: lead and chlorine (XSA, EAS, IRS). Vanadium oxide is believed tentatively to accelerate the formation of films via a catalytic mechanism, but it is incorporated in the growing layer (IRS, XSA, EAS). The fraction of oxidised indium in these impurity layers is greater than in the reference layers, but the content of unoxidised indium is still appreciable and the dielectric characteristics are therefore unsatisfactory.

Good results are obtained by the preliminary deposition of a PbS layer on the InP surface to be oxidised. As in the oxidation of similar heterostructures based on silicon and gallium arsenide, in this case the process begins with the formation of a sulphate framework. Indium phosphate is then formed and adds to the framework. It may be that $PbSO_4$ phases interact with one another (IRS). In the vicinity of the outer interface of the heterostructure, mainly $PbSO_4$ is concentrated, the $InPO_4$ content increasing on moving towards the inner interface (IRS, EAS, XSA). Indium sulphides are formed at the inner interface (EAS), which diminishes sharply the concentration of indium in the films and frees them from the unoxidised indium. Therefore, in the oxidation of the InP/PbS structures, not only is the formation of the layers accelerated (by a factor of 4–6) but an appreciable increase in their electrical strength (approximately by an order of magnitude) compared with the reference standard is ensured.

Thus analysis of the surveyed data concerning the thermo-oxidation reactions of silicon and gallium arsenide in the presence of impurities shows that on silicon the greatest acceleration of the process is attained after the introduction of lead compounds, i.e. this element is optimal as a cation-forming agent. As mentioned above, among the anion-forming agents chlorine exerts the most favourable modifying effect on the properties of the layers, whilst oxygen compounds as a rule react too vigorously with the oxidisable surface.

The best cation-forming agent for gallium arsenide is antimony, which has the same valence as arsenic. Its compounds ensure an appreciable acceleration of the process. In addition, as already emphasised, here there is the greatest probability of the mutual dissolution of the intrinsic and impurity oxides, which promotes the healing of defects and the improvement of the properties of the resulting layers. Among anion-forming agents, sulphur is best. It binds the volatile components of the support and diminishes thereby the degradation of the inner interface, improving its properties. For compounds of the type $A^{III}B^{V}$ with a volatile component (B^{V}), the method of introduction of the impurity into the system which depends on the nature of the anion-forming element, i.e. the creation of a restricted impurity source, is convenient. Under these conditions, the deposited impurity layer not only interacts chemically with the support but also serves as a mechanical barrier to the evaporation of the volatile component.

In the thermo-oxidation of InP/PbS structures, the component A^{III} is bound chemically by sulphur on the inner interface which, together with the greater effectiveness of its oxidation as a result of the transit reaction, minimises the probability of the appearance of free indium in the resulting layers. In contrast to the corresponding structures based on gallium arsenide, the deposited impurity layer fulfills various functions in relation to the components of the support (A^{III} and B^{V}): it binds chemically the former, preventing its rapid diffusion into the film, and prevents the evaporation of the latter. The general criteria governing the selection of the impurity formulated above retain their validity also for a material such as indium phosphide which is not simple as regards the growing of dielectric layers.

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Translated from *Uspekhi Khimii* 60 1920–1945 (1991) U.D.C. 541.63:541.44:546.654:543.422

Asymmetric hydrogenation on metals

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ABSTRACT. The most recent findings in the field of asymmetric hydrogenation of prochiral compounds with C=C and C=O bonds on dissymmetric catalysts—bimetals and hydrides of intermetallic compounds modified with (*RR*)-(+)-tartaric acid and (*S*)-α-amino acids—are reviewed.

The bibliography includes 121 references.

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I. Introduction

Despite the well recorded progress made in recent years in carrying out asymmetric reactions with the use of chiral metal-complex catalysts, and primarily in the asymmetric hydrogenation of dehydroamino acids on rhodium phosphine complexes, there is continued interest in studies on dissymmetric metal hydrogenation catalysts modified with chiral ligands. This is mainly due to the ease in preparing them and the technological effectiveness of their application. Amongst the disadvantages of dissymmetric heterogeneous catalysts should be included the relatively narrow spectrum of their action; effective systems have so far only been found for the hydrogenation of the carbonyl bond in ketoesters and diketones. Attempts to extend the range of such reactions and substrates have so far not produced the required results, although there are individual reports of the successful asymmetric hydrogenation of prochiral compounds with C=C and C=N bonds.

A significant proportion of current research has been directed at improving dissymmetric metallic catalysts and the preparation of novel, including polymetallic, catalysts that are active in the asymmetric hydrogenation of the C=O bond, an elucidation of their structure, action mechanism, and the general characteristics that make it possible to predict their catalytic and enantioselective properties. In this review† the results of studies carried out over the last years are examined. Previous studies have been reviewed by Klabunovskii and Vedenyapin.[1]

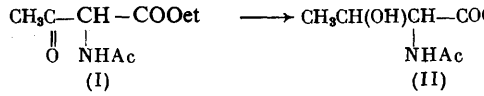
†In this review the following notation is used: Ni–TA is a catalyst modified with (*RR*)-(+)-tartaric acid; Ni-AA is a catalyst modified with an amino acid (Ala—alanine, Val—valine, Glu—glutamic acid, Phe—phenylalanine, Pro—proline, Ile—isoleucine); MAA is methyl acetoacetate; EAA is ethyl acetoacetate; MHB is methyl β-hydroxybutyrate, EHB is ethyl β-hydroxybutyrate, PEA is (*S*)-phenylethylamine.

II. Skeletal nickel catalysts

The skeletal catalysts also known as Raney catalysts have been extensively used in organic synthesis in the hydrogenation of unsaturated organic compounds because of the ease in preparing them and their high activity. Skeletal Ni catalysts exhibit high enantioselectivity in the hydrogenation of prochiral carbonyl compounds.

Skeletal Ni catalysts are obtained by leaching a Ni–Al alloy usually containing up to 50% Ni with a solution of NaOH on heating to 80–100 °C and washing the resulting Ni powder with water. The catalyst is then modified with optically active compounds. The modification process involves bringing into contact a previously reduced catalyst at a given temperature and pH with a solution of the modifying agent—an optically active hydroxyacid or amino acid.

In general, modification of catalysts with chiral compounds can help to increase the selectivity of hydrogenation. Thus ketoacid (I)—a precursor of threonine—can be hydrogenated on Ni–TA with 100% selectivity and with an overall yield of 82% on the *allo*-threonine derivative (II),[2] while hydrogenation of (I) on a skeletal Pd–Cu–TA catalyst containing 15.1% Pd at 75 °C and 50–100 atm results in the yield of *allo*-threonine increasing to 90% while the *threo* isomer is completely absent[3,4]



In the diastereoselective hydrogenation of *D*-fructose to a mixture of sorbitol and mannitol, a catalyst such as the hydride of the intermetallic compound $LaNi_3Co_2$ proved effective only after it was modified with (*RR*)-(+)-tartaric acid.[5]

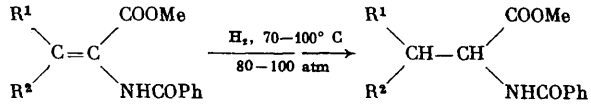
Attempts have been made to use modified Ni catalysts for the synthesis of optically active compounds of practical importance. Thus, for example, optically pure (3*S*,5*S*)-2,6-dimethylheptane-3,5-diol[6] and (*R*)-(−)-3-hydroxytetradecanoic acid (an endotoxin component) were obtained on Ni modified with (*RR*)-(+)-tartaric acid.[7] Modified catalysts were also studied in the synthesis of α-amino acids of practical importance. One of the methods used to synthesise them is hydrogenation of C=C or C=N bonds to the corresponding precursor compounds. However, enantioselective hydrogenation of the C=N bond was ineffective. For example the optical yield‡ of the product derived from hydrogenation of

‡The optical yield (*p*, %) that characterises the enantioselectivity of the reaction is determined from the following equations:

$$p = \frac{([R] - [S])}{([R] + [S])} \times 100 = \frac{[\alpha]^t_{exp}}{[\alpha]^t_{lit}} \times 100\%.$$

acetophenoxime to PEA is only 3.5%,[8] whereas diastereoselective hydrogenation of azomethines is very successful.[9]

A more promising method is the enantioselective hydrogenation of the C=C bond in the (*E*) and (*Z*)-methyl esters of *N*-benzoylaminoacrylic acids in methanol of Ni–(*S*)-AA.[10,11]



(III, a): R^1 = Me, R^2 = Et; (III, b): R^1 = Et, R^2 = Me.

On a Ni–(*S*)-Phe catalyst, Ile containing 70% as the *erythro* form and 30% as the *threo* form is obtained from (*Z*)-(III, a), while Ile containing 60% as the *erythro* isomer and 40% as the *threo* isomer is obtained from (*E*)-(III, b). In the latter case p = 15%.[12] Replacement of Ni–(*S*)-Phe by a Ni–(*S*)-Pro catalyst resulted in an optical purity of p = 8%, while when a Ni–(*R*)-Pro catalyst was used the value of p was only 1.5%. Other amino acids such as Ala, Val, GluOme proved ineffective as modifying agents.

It was recently reported[13] that enantioselective hydrogenation of the C=C bond in (*E*)-PhCH=C(Ph)COONa (30 °C, 1 atm., absolute ethanol) can be carried out on Ni–TA with p = 17.03%. Hydrogenation of the (*Z*)-isomer is less effective.

The poor efficiency of modified Ni–Ta catalysts in a number of cases has been attributed by Harada et al.[14] to the residual content of Al in the skeletal catalysts impairing their enantioselective properties as a result of the formation of considerable quantities of Al_2O_3 or bayerite after leaching of the metal–aluminium alloy. Thus, metals deposited on Al_2O_3, such as Ru/Al_2O_3 modified with (+)-TA did not exhibit enantioselectivity in the hydrogenation of EAA[15] most likely because the formation of highly dispersed X-ray-amorphous metal on the surface of the catalyst.

Studies by Nitta et al.[16] carried out recently showed that only when there is a sufficiently high nickel content (50% or more) deposited on Al_2O_3 can the catalyst be effective in enantioselective hydrogenation.

It was shown by Zubareva et al.[17] that in a 2% Ni/Al_2O_3 catalyst the metal phase cannot be detected by X-ray phase analysis (XPA) because of the formation of an X-ray-amorphous phase. An increase in the content of metal deposited on the surface helps to increase the size of crystallites, and starting with 8% Ni on Al_2O_3 the catalyst modified with TA by now has the ability to cause asymmetric hydrogenation of ethyl acetoacetate (EAA) to ethyl β-hydroxybutyrate (EHB) with p = 3%.

$$\underset{\text{(EAA)}}{CH_3COCH_2COOEt} \xrightarrow{\text{Ni.(+)-TA}} \underset{\text{(}R\text{(−)-EHB)}}{CH_3CH(OH)CH_2COOEt}$$

On increasing the percentage of Ni on Al_2O_3 to 50% (reduction temperature 500 °C, current of $H_2:N_2$ = 1:1, modified with tartaric acid at pH 4.7) the optical yield of (*R*)-(−)-EHB increased to 19.5%.[17] On changing the conditions for preparing the Ni/Al_2O_3 catalyst (reduction temperature 400 °C, current of H_2, modification with TA at 83 °C, pH 4.2) and the hydrogenation (135 °C, 100 atm., ethyl acetate as solvent, EAA:catalyst = 8:1) the composition of the catalyst was found to be 20% Ni/Al_2O_3, and by using it the value of p could be increased to 66–76% with, however, a low degree of conversion (~10%). On increasing the degree of conversion (y) of EAA to 98%, the value of p decreased to 50%.[17]

It was to be expected that the powdered catalysts that are obtained by decomposition of metal salts by the Sabatier method would prove effective in asymmetric hydrogenation processes. Thus, highly effective Ni–TA is obtained by decomposition of Ni nitrate in a current of He with subsequent decomposition of the resulting Ni oxides in a current of H_2 + He (1:10) at 280 °C and modification at 50 °C in a 0.5 solution of TA at pH 5.1.[18] It was not necessary in this case to introduce also into solution NaBr, which is known[19] to increase the enantioselectivity of hydrogenation. Hydrogenation of EAA at 100 °C and 100 atm takes place at a high rate on this catalyst, the rate of formation of excess (*R*)-(−)-EHB (w) being 20.5 mmol (g Ni)$^{-1}$ h^{-1} ($w = pv$). It should be noted that, according to Smith and Misoiu,[20] the optical yield in the hydrogenation of EAA is usually lower than in the hydrogenation of methyl acetoacetate (MAA) under the same conditions, so the optical yield of p = 63–71% obtained on this catalyst may be regarded as quite high.

It was found by XPA of samples of skeletal Ni–(+)-TA catalysts which actively hydrogenate EAA,[21,22] obtained from Ni–Al alloys containing 50.0, 45.2, and 38.3% Ni, that with an increase in the fraction of Ni in the alloy the content of the $NiAl_3$ phase increases, assisting a more effective removal in the leaching of Ni–Al alloys and an increase in the optical purity of EHB. During the reaction the value of p passes through a maximum, which occurs at a degree of conversion of the initial EAA of y = 30–60%. In a number of cases of asymmetric hydrogenation, in particular on Ni catalysts, an antibatic variation of p and y occurred, i.e., the enantioselectivity of reaction decreased as the overall rate of hydrogenation increased.[1] Often during the reaction the initially constant value of p starts to decrease after significant degrees of conversion are reached.[23] This is possibly due to the adsorption inhibition of reaction by both the initial substrate (a fall in p in the hydrogenation of EAA on Ni–TA when the initial concentrations of EAA are increased has been recorded by Lipgart et al.[24]) and the reaction product. In the latter case it is to be expected that this inhibition will differ according to whether a racemic or optically active reaction product interacts with the chiral centre of the catalyst.

For a quantitative determination of this interaction, Chernysheva et al.[25] studied the degree of inhibition of the asymmetric hydrogenation of EAA by the reaction product EHB on a Ni–TA catalyst, and the relative adsorption coefficients were determined by the method of Balandin,[26] according to the equation

$$\frac{1}{v} = \frac{b_2/b_1}{k}\frac{C_2}{C_1} + \frac{1}{k},$$

where k is the rate constant of the reaction, b_1 and b_2 are the adsorption coefficients of the initial EAA and reaction product EHB (or inhibitor) C_1 and C_2 are their concentrations.

It was found that the hydrogenation of EAA is markedly inhibited when even small quantities of EHB are added to the initial EAA. Moreover, some variation in the rates of hydrogenation also occurs when the (−)-enantiometer of EHB instead of racemic EHB is added to the initial mixture. Inhibition by the raction product does not have a significant effect on the ratio of the adsorption coefficients—b_{EHB}/b_{EAA} is usually 0.2–0.3. However, when other compounds, such as thiophene or pyridine, which strongly inhibit the catalyst are added to the initial EAA, b_{EHB}/b_{EAA} varies considerably—from 15 to 25. This ratio increases even more (up to 1400) if the catalyst is first treated with thiophene and then modified with TA. At the initial stages of the reaction when the degrees of

conversion of EAA are no greater than 10%, the introduction of pyridine has a favourable effect on the optical yield of yield—the value of p increases from 2.35 to 13.5%. This suggests that introduction of strongly absorbing compounds which poison the most active unmodified catalyst sites (at small degrees of conversion) increases the proportion of modified sites and thus increases the optical yield.

Similar results were obtained by Yasumori[27] in the hydrogenation of MAA on Ni–TA in the presence of pyridine and also NH_3, Et_3N, $BuNH_2$, whereby with an increase in the amounts of poison the rate of hydrogenation decreased by a factor of 2–3 while the optical yield increased from 11% (without introduction of poison) to 17, 33, 39, and 50% respectively.

According to the results given by Klabunovskii and Vedenyapin,[1] an optically active site must contain an array consisting of regularly ordered metal atoms and molecules of modifying agent and substrate. Hence an enantioselective reaction, according to Budar, is classed as a structurally sensitive reaction and the enantioselectivity should vary in relation to the surface structure. In fact, as was first found for Ru–TA–SiO_2 catalysts,[1] the value of p in the hydrogenation of EAA increased to a given limit with the increase in size of crystallites of Ru (up to 4.5 μm). This observation was subsequently confirmed for Ni–TA/SiO_2 and Pt–quinine/Al_2O_3 catalysts.[28]

The idea[1] that two types of site—optically selective and non-selective—exist on the surface of dissymmetric catalysts was applied in an electrochemical study of the mechanism of the modification of skeletal Ni catalysts with (+)-tartaric acid.[29] The assumption that a selective site is a ternary heteroligand complex of the type metal–modifying agent–substrate, which was first stated by Petrov et al.[30] was subsequently supported in two studies.[29,31]

It was found[32] that modification of Ni catalysts with solutions of chelates such as Ni[(*S*)-Ala]$_2$ and Ni[(*S*)-Glu]$_2$ in the hydrogenation of MAA gives the product MHB with p = 3.7 and 17.4% respectively [these values of p are similar to those obtained on Ni–Ala and Ni–Glu catalysts (p = 4.7 and 15.1%)].

Correlation of the rates of hydrogenation of acetylacetone (AA) and EAA with the hydrogenation of their chelates with Cu, Ni, Co, and Zn on skeletal Ni and Ni–TA showed[33] that both at atmospheric pressure and at 100 atm the rate of hydrogenation of the chelates is lower than the rate of hydrogenation of pure AA and EAA, but the composition of the products is the same, with the rate of hydrogenation decreasing in the series of chelates Cu–Ni–Zn–Co in accordance with the values of the stability constants of the acetylacetonate complexes of these metals. Hydrogenation of Co, Zn, Cu, and Ni acetylacetonates on a Ni–TA catalyst gives an optically active pentanediol with similar values of p, equal to 9.6, 11.1, 10.6, and 12.4% respectively. The difference between the rates of hydrogenation of EAA and Ni(EAA)$_2$ is not so large as for AA and Ni(AA)$_2$, which is due to the lower stability of the Ni(EAA)$_2$ complex compared to Ni(AA)$_2$.

The formation of a ternary complex on the surface of the catalyst was studied by means of IR spectroscopy of the adsorbed molecules.[34–36] It was found that (+)-TA, AA, and Ni^{2+} in solution form a ternary complex in which, according to the IR spectra, the AA molecule experiences an effect from (+)-TA. Comparison of the absorption bands for AA in this complex with the absorption bands for AA adsorbed on the surface of Ni–TA/SiO_2 showed that an AA molecule forming part of an adsorbed complex assumes a shape which is different to that of the pure heteroligand complex in solution. There is an increase in the asymmetry of the substrate molecule as a result of a surface effect, i.e., in this case an achiral factor assists a chiral process.

The steric model of the surface complex proposed previously[1] is supported by IR spectroscopic data on the adsorption of CO on a Ni–TA/SiO_2 catalyst, which show that TA adsorbed on the faces of a Ni crystal inhibits the adsorption of CO. This conclusion is based on the absence of an absorption band at 1940 cm^{-1} that characterises the bridged form of CO adsorption and on the decrease in intensity of the absorption band in the region of 2050 cm^{-1}.[36]

The high enantioselectivity of powdered Ni–TA catalysts in the hydrogenation of EAA is not corroborated during electrocatalysis.[37] Electroreduction of EAA in a monolayer, carried out on Ni–TA deposited on a Pt electrode, took place with 100% conversion but with a low optical yield (p = 8–12%). According to the charge curves, modification of the Ni catalyst reduces the surface area by a factor of 10 (from 4 to 0.4 m^2). In the region of the hydrogen overvoltage the conversion of EAA was 10–25% and p = 8–10%. During electrocatalysis, those sections of the surface (edges and apexes of the crystals) where the intensity of the electrical field is highest would appear to be the most active; however, these sections are least suitable for enantioselective hydrogenation because of the steric hindrance towards orientation of chiral clusters, which require quite an extensive area.[1]

At the same time, in the electroreduction of phenylglyoxylic acid in the presence of strychnine,[38] for example, it would appear that in a double electrical layer asymmetric synthesis occurs with considerable efficiency ($p \sim 20\%$).

III. Dissymmetric bimetallic catalysts

Dissymmetric bimetallic catalysts are of considerable interest both from the practical viewpoint (the possibility of synergism occurring for catalytic and enantioselective properties) and from the theoretical point of view, since the possibility arises for studying the influence of their phase state, cluster, and ligand effects on the catalytic and dissymmetric properties of these catalysts.

Bimetallic and modified dissymmetric catalysts were first studied in the case of Cu–Ru catalysts.[1] Systems based on Ni were subsequently developed.[39]

Dissymmetric Ni–Cu powdered catalysts without a support, modified with TA, displayed high enantioselectivity in the asymmetric hydrogenation of EAA. Their efficiency depends to a significant extent on their genesis and the reaction conditions.

Zubareva et al.[39–42] studied the hydrogenation of EAA in the presence of powdered Ni–Cu–TA catalysts which were prepared by reduction of mixtures of Ni and Cu oxides (nickel–copper catalyst, NCC-1), hydroxides (NCC-2), or carbonates (NCC-3) in hydrogen or a mixture of H_2 + N_2. It was established that varying the nature of the initial salts leads to a change in the phase and surface composition of the catalysts obtained, and the ratio of reduced to non-reduced forms of the phases of Ni compounds in an NCC is a factor that affects the magnitude of the optical yield. As is shown in Table 1, the NCC-1 catalyst consists of phases of solid Ni–Cu solutions enriched with Ni or Cu and a small quantity of NiO (~5%). In precipitated NCC-2 and NCC-3 catalysts, Cu and Ni form separate phases, as a result of which there is a sharp increase in the total hydrogenating activity of these catalysts. For catalyst samples that were reduced in a current of pure H_2, in which Ni, according to the XPA data, occurred in a reduced state, the value of p did not exceed 20–24% and did not depend on the

nature of the initial compounds used to prepare the catalysts. With reduction in a current of $H_2 + N_2$ the optical yield for NCC-1, NCC-2, and NCC-3 was 50.0, 14.4 and 8.4% respectively. The fact that a small quantity of NiO is contained on the surface of NCC-1 [up to 10% according to the results of X-ray photoelectron spectroscopy (XPES)] evidently assists complexation with TA. However, the presence of fairly large quantities of NiO in NCC-2 and NCC-3 leads to a reduction in p.

Table 1. Effect of conditions of formation on the catalytic and enantioselective properties and phase composition of nickel–copper catalysts (NCC) modified with (*RR*)-(+)-tartaric acid in the hydrogenation of EAA.[41]

Catalyst*	H_2/N_2**	S_{sp}, $m^2 g^{-1}$	$A \times 10^2$, (mmol m^{-2} min^{-1})	p, %	Composition of NCC from X-ray phase analysis, wt. %							
					Phase 1		Phase 2		Cu	Ni	NiO	CuO + Cu_2O
					Cu	Ni	Cu	Ni	the rest consists of phases 1 and 2			
NCC-1	0.1	9.3	0.6	50.0	23.3	76.7	79.4	20.6			5.1	–
NCC-2	1	1.3	10.6	24.2					48.2	48.2	–	3.6
	0.1	1.5	8.5	14.4					49.8	26.0	22.4	1.8
NCC-3	1	1.3	11.8	21.3	23.3	76.7	85.4	14.6	23	35.2	–	1.6
	0.1	0.7	24.3	8.4	–	–	86.0	14.0	39	20	27.5	–

* Catalysts NCC-1, NCC-2, and NCC-3 were obtained by reduction of Ni and Cu oxides, hydroxides, and carbonates respectively.

** Composition of gas flow during reduction of catalysts.

According to the XPES data[41] (in the region of Ni3*p* and Cu3*p*) the ratio of surface concentrations of Ni/Cu is close to 1.5 in the initial NCC-1 (Fig. 1*a*, curve *2*). In NCC-2 the surface layer is enriched with copper in the form of Cu^0 (curve *2*). After modification of both catalysts their surface is enriched with nickel—for NCC-1 the ratio of Ni/Cu is 1.3 while for NCC-2 the ratio of Ni/Cu is equal to 2. From the spectra in the region of Ni2*p* and Cu2*p* (Fig. 1*b* and 1*c*) it follows that the Cu and Ni atoms in NCC-1 are in a reduced state (with a small quantity of NiO). Moreover, it follows from the shift in Ni2*p* lines (Fig. 1*b*, curve *3*) that a certain proportion of Ni in modified NCC-2 changes to the Ni^{2+} oxidation state, which is consistent, according to the results of Balandin,[26] with the spectrum of nickel oxide NiO modified with TA. Thus, on the surface of NCC-1, which displays the highest enantioselectivity, Ni^0, Cu^0, and Ni^{2+} sites occur.[42] This conclusion is consistent with the results obtained by Zubareva et al.[42] for Ni–TA/SiO_2 catalysts, for which the presence of Ni^0 and Ni^{2+} sites on the surface of the catalyst has been demonstrated.[43]

The effect of the conditions for reducing Cu and Ni oxides obtained by decomposition of the nitrates on the enantioselectivity of these mixed catalysts modified with (+)-TA in the hydrogenation of EAA (100 °C, 100 atm) was studied by Klabunovskii et al.[44] According to differential thermal analysis data, the reduction of NiO and CuO occurs at the same time in the mixture, despite the difference in reduction temperatures of the individual oxides (320 and 270 °C respectively). It was established that the value of p does not depend on the time of reduction of the catalyst if modification is carried out at 50 °C and pH 5.0 but it increases slightly with an increase in time of reduction from 51 to 65% when modification is conducted at pH 10.0. Reduction at higher temperatures results in more complete alloying and homogenisation of the alloy.[45] However, the maximum value of p is reached when the oxides are reduced at 220 °C. It was established[46] that Ni–Cu catalysts contain two phases—a Cu phase and a Ni–Cu alloy phase. With an increase in the Cu content in the catalyst, the Ni–Cu alloy phase is enriched with nickel in bulk and with copper on the surface. According to the results of Klabunovskii et al.,[47] the hydrogenating activity of (70% Ni–30% Cu) catalysts is 5 times higher than that of a pure nickel catalyst, while the activity of the latter is 5 times higher than the activity of a Cu catalyst. However, the enantioselectivity of a (70% Ni–30% Cu) catalyst proved to be lower than that of Cu–TA (p = 50%) and Ni–TA (p = 33%) catalysts. Thus, in bimetallic Ni–Cu catalysts synergism occurs in the total catalytic activity but not in the enantioselectivity.

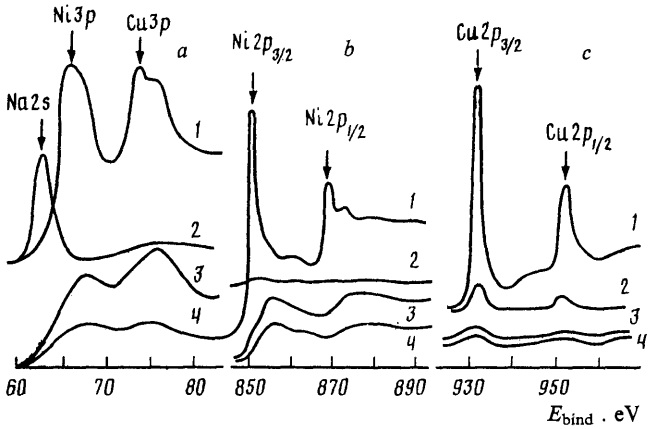


Figure 1. X-Ray photoelectron spectra of nickel–copper catalysts[41] in the region of Ni3*p* and Cu3*p* (*a*), Ni2*p* (*b*), and Cu2*p* (*c*). *1*, Initial NCC-1; *2*, initial NCC-2; *3*, NCC-1 modified with (*RR*)-(+)-tartaric acid; *4*, NCC-2 modified with (*RR*)-(+)-tartaric acid.

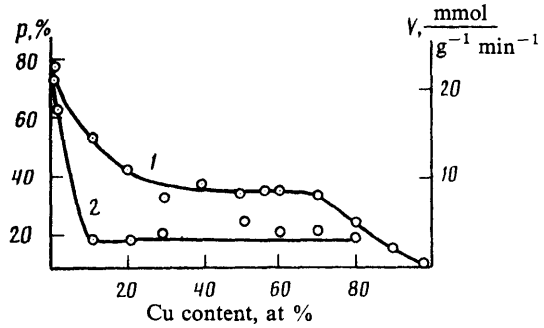


Figure 2. Dependence of the rate of hydrogenation of EAA (curve *1*) and optical yield (curve *2*) on the composition of dissymmetric Ni–Cu catalysts modified with (*RR*)-(+)-tartaric acid.[44]

Increasing the Cu content in a mixed Ni–Cu catalyst deactivates the catalyst, since Cu as an inactive component dilutes the Ni sites[44] that are responsible for the enantioselectivity of reaction. If the specific activity is attributed solely to the Cu–Ni alloy phase over the range 20–80% Cu (Fig. 2), the value of p and the specific rate remain constant, which is an indication of the constant magnitude of the surface concentration of the active component in a Ni–Cu catalyst. The value of p is little affected by both the phase state and the total hydrogenating capacity of Ni–Cu catalysts, in contrast to pure Ni catalysts, in which the enantioselectivity is strongly dependent on these factors.

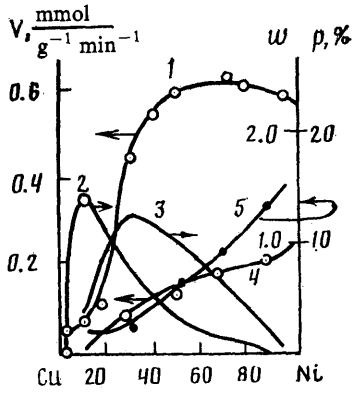


Figure 3. Dependence of the rate of hydrogenation v (curves *1* and *4*), the optical yield p (curves *2* and *5*), and rate of formation w of excess (–)-enantiomer (curve *3*) on the composition of Ni–Cu catalysts modified with (*S*)-phenylalanine (curves *1*, *2*, and *3*) and (*RR*)-(+)-tartaric acid (curves *4* and *5*) in the hydrogenation of EAA.[48]

The fact that on increasing the proportion of Ni in a Ni–Cu catalyst the latter segregates on the surface is apparently supported by data[48] on the hydrogenation of EAA on a Ni–Cu catalyst modified with (*S*)-phenylalanine (Fig. 3, curves *1–3*). In fact, whereas (*S*)-(+)-EHB is formed on Cu–(*S*)-Phe, the other enantiomer, (*R*)-(–)-EHB, is formed on Ni–Cu–(*S*)-Phe even with a Ni content of 10–15%, as on a Ni–(*S*)-Phe catalyst. The conclusion that Ni segregates on the surface of a Ni–Cu catalyst is also supported by the correspondence of the maxima on the curves plotting the change in w and the content of surface H_2 in Cu–Ni catalysts, which according to Takai[49] have a Ni content in the Ni–Cu catalysts ranging from 20 to 40%. The effect of the pH of the modifying solution of TA on the value of p for Ni and Ni–Cu catalysts for all compositions[44,50] is evident in the appearance of two maxima for p at pH 6 and 10.5.[50] For a pure Ni–TA catalyst p is equal to 57% (pH 5) and 71% (pH 10), while for a Ni–Cu–TA catalyst p = 20% (pH 5) and p = 22% (pH 10) (Fig. 4). This type of dependence of p on the pH of the modifying solution is substantially different from that reported previously for Ni,[1,48] when only a single maximum for p was found.

The introduction of just 10–15% Cu into Ni–TA sharply reduces the values of y and p. This demonstrates that Cu cannot be regarded as simply an inert component of the catalyst. It would appear that when there is a large content of Cu, it breaks up the dissymetric clusters[50,51] that are responsible for asymmetric hydrogenation and which consist of several surface atoms of Ni in a different valence state.

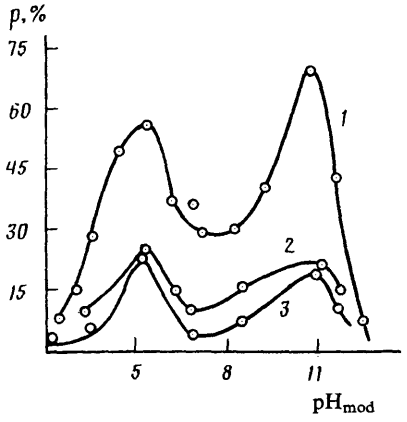


Figure 4. Dependence of the optical yield of (–)-EHB on the pH of the modifying solution of (*RR*)-(+)-tartaric acid.[44] Catalysts: *1*, Ni; *2*, Cu(50%)–Ni(50%); *3*, Cu(20%)–Ni(80%).

It was shown by Vedenyapin et al.[36] that tartaric acid forms complexes on the surface of Ni/SiO_2 and Cu/SiO_2 catalysts, and the value of ν_{COO^-} in the region of ν_{as} at 1600 cm^{-1} and ν_s at 1400 cm^{-1} for Ni/SiO_2 and Cu/SiO_2 catalysts modified with TA at pH 5 and 10 does not differ by more than 10 cm^{-1}, which suggests that there is a similar type of coordination of the COO^- group in TA. This is supported by the fact that for Ni/SiO_2 catalysts modification at pH 5 and 10 leads to the highest and approximately equal values of p. It should be noted that a change in the temperature of modification and concentration of TA solution has no effect on the type of adsorption of TA on Ni and Cu.[36] The same type of effect of the pH of the modifying solution of TA on p for Ni and Cu–Ni catalysts supports the assumption that the structure of the dissymmetric sites remains unchanged on introduction of different quantities of Cu to the composition of the catalyst. When both acidic and alkaline modifying solutions are used, two types of dissymmetric clusters having similar enantioselective properties are formed on the surface of the catalyst. It can be assumed from this that copper does not exhibit a ligand effect in Cu–Ni catalysts and the properties of the dissymmetric clusters do not change; its introduction only changes the number of such clusters.

According to Klabunovskii and Vedenyapin,[1] a dissymmetric cluster is located on specific sites of the surface, which makes it possible for contacts to occur between the metal, modifying agent, and substrate with the minimum steric hindrance. These sites can be steps on the crystallographic faces of the metal, which accounts for the high sensitivity of asymmetric hydrogenation to the structure of the active surface of the catalyst and in particular the size of the metal crystallites. This is supported by the dependence of p on

reaction temperature and on the concentration of hydrogen in the reducing atmosphere in the reduction of oxides (a decrease in the ratio of H_2:He increases p from 11 to 19%), since these factors affect the rate of formation of a Ni–Cu metal catalyst, its phase composition, the structure of the surface, the size of the metal particles, and hence the steric hindrance and magnitude of the optical yield.

It follows from the dependence of p, v, and w on the composition of Ni–Cu catalysts that the sites of enantioselective hydrogenation contain 4 times more active formations (atoms, clusters) than sites of non-selective hydrogenation.[52] It is assumed in this case that only one enantiomer is formed on the enantioselective sites.

Dissymmetric Ni–Co catalysts have been investigated in a number of studies.[53,54] On a skeletal Co catalyst modified with TA, the optical yield in the hydrogenation of EAA did not exceed 5–8%.[1] At the same time, it was found that intermetallic compounds (IMC) (for example, $LnNi_5$) modified with TA display considerable enantioselectivity in this reaction only after the introduction of cobalt into their composition (in this case the value of p reaches 52% or more).[55] It was to be expected that the introduction of Co would assist the segregation of Ni on the surface of the IMC, thus increasing the enantioselectivity of the catalyst. Therefore it was of interest to study the effect of genesis of Ni–Co–TA catalysts of different compositions on their enantioselective properties in the hydrogenation of EAA. In order to do this, a study was made of powdered Ni–Co catalysts obtained by decomposition of Ni and Co acetates or nitrates at 450 °C and by reduction of the resulting mixed oxides at 350 °C in a current of H_2 or H_2 + He for 1.5 h. Modification was carried out with a 5% solution of TA at pH 4.5–5.0.[56,57] Hydrogenation of EAA was carried out at 20–80 °C and 25–100 atm in a solution of ethyl acetate with added acetic acid.[56] Under these conditions a Co–TA catalyst did not exhibit enantioselectivity, but when 20% Ni was introduced into the catalyst the optical yield reached 3.6%, introduction of 50% Ni gave p = 6.3%,[53] and introduction of 80% Ni gave p = 9–15%.[57] A variation in the conditions for preparing the catalysts did not result in any improvement in their enantioselective properties whereas a change in the pH of modification and the nature of the solvent used in hydrogenation had a considerable effect on the values of p and y.

The conditions were found (120 °C, 110 atm) at which an increase in the content of Ni in Ni–Co catalysts to 50% increased the optical yield to 46–50% [58] (for Ni–TA catalysts under these conditions p = 65%, with a conversion of EAA close to 100%). This shows that, as in the case of Ni–Cu catalysts, the Ni component of the catalyst is mainly responsible for asymmetric hydrogenation, so that even a small increase in its content in Ni–Co catalysts markedly increases their enantioselectivity.

Thus, a Ni–Co system is considerably different in terms of its enantioselective action to the corresponding IMCs based on La, Ni, and Co, in which, on the other hand, an increase in the content of Co rather than Ni [for example, in the series $LaNi_3Co_2$–$LaNi_2Co_3$, which correspond to the systems 67% (60% Ni–40% Co)/La and 67% (40% Ni–60% Co)/La]§ results in an increase in optical yield in the hydrogenation of EAA.

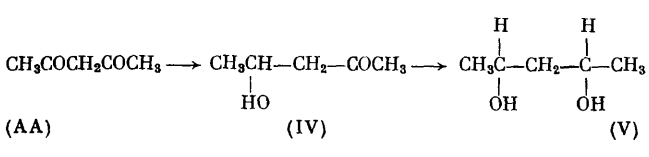
Ni–Co catalysts were tested in the practically significant reaction involving hydrogenation of an equilibrium mixture of menthone–isomenthone (70:30) to isomeric menthols. On unmodified Ni, Co, and Ni–Co catalysts the reactions occur most effectively in an aqueous medium, the conversion reaching 99%.[59] The maximum yield of racemic menthol (40–44%) was obtained on Ni and Ni–Co catalysts in an alkaline medium. Modification of these catalysts with a solution of TA reduced the rate and selectivity of the reaction, although in the hydrogenation of EAA the samples of modified catalysts exhibited high enantioselectivity—p = 65% on Ni–TA and p = 54% on (90% Ni–10% Co)–TA.[60]

In the hydrogenation of the same mixture on a Co–TA catalyst it was possible to obtain up to 80% of neoisomenthol,[61] which is difficult to prepare, whereas on Ni, Pd, Rh, and copper chromite catalysts, neoisomenthol was not formed during hydrogenation in the gaseous and liquid phases.[62]

Supported dissymmetric catalysts based on Ni are of definite interest since they make it possible to study the asymmetric adsorption of the modifying agent and substrate on the surface of the catalyst by means of IR spectroscopy of the adsorbed molecules and to elucidate a number of questions concerning the theory of a strong interaction between metal and support. As has been demonstrated above, supported dissymmetric catalysts are less effective than skeletal ones,[1] especially when Al_2O_3 is the support, and only by increasing the content of metal on the support (up to 50% for Ni)[16,63] or by selecting special conditions of preparation (see below) is it possible to obtain an enantioselective catalyst.[17]

This may be due, as in the case of bulk catalysts, to the effect of an increase in the size of the crystallites[63] or to the diffusion of TA into the pores during modification of the catalyst.[64] For a clear demonstration of the effect of crystallite size on the enantioselectivity it is necessary to vary the size of the crystallites when there is a constant degree of covering the surface of the support with metal. In addition, it is known that, apart from the average dimensions of the crystallites, their distribution in size plays an important part, since crystallites of a smaller size are responsible for a greater activity but a lower enantioselectivity.

A bimetallic Ni–Cu–TA catalyst deposited on an Aerosil support that was active in the asymmetric hydrogenation of acetylacetone (AA) was first reported by Klabunovskii.[65] The conditions were found at which hydrogenation occurred selectively with the formation of only the (*R*)-(−)-ketol (IV) with p = 9.1% without the presence of diol (V).[65]



(AA) (IV) (V)

(Ni–Cu–TA)/Aerosil and Ni–TA/Aerosil catalysts were also studied in the hydrogenation of EAA.[65] It was found that with an increase in Ni content on the support the optical yield and rate of formation (w) of excess (−)-EHB increased, while the rate of formation of EHB racemate v_r ($v_r = v - w$) passed through a maximum (Fig. 5). This occurs because the increase in Ni content on the support is accompanied by an increase in the total surface of the unmodified part of the metal phase. On increasing the Ni content, the surface area starts to diminish as a result of the enlargement of Ni particles from small crystallites of Ni that are inactive in asymmetric hydrogenation. This was demonstrated for both Ni[66] and Ru–TA catalysts.[1] Thus, the optical yield (small in the case of dilute catalysts) increases with an increase in metal content on the surface of the support.[43] This may account for the

§ This representation of the catalyst composition denotes a 67% metal content (60% Ni and 40% Co) on the surface of La.

high efficiency of catalysts with a large content of metal on the support.[16] The nature of the support also has a considerable effect on the enantioselective action of the catalyst. Thus, it was found for Ni/support (1 : 1) catalysts that were active in the enantioselective hydrogenation of MAA that there was a decrease in optical yield in the following series of supports (p in brackets, %): no support (57) > SiO_2 (56.2) > zeolite Y (45.6) > Al_2O_3 (43.7) > kieselguhr (29.1) > MgO (6.1) > TiO_2 (3.1). In the same series the degree of interaction between Ni and the support increases, which during reduction of the catalyst inhibits the growth of the large crystallites which increase the enantioselectivity of the process.[43]

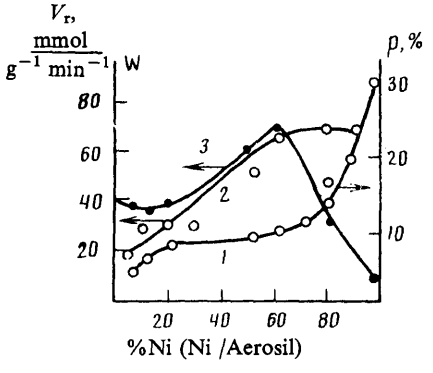


Figure 5. Dependence of the optical yield p (*1*), the rate of formation w of excess (−)-EHB (*2*), and the rate of formation v_r of the racemate of EHB (*3*) on the content of Ni in Ni−TA/Aerosil catalysts during the hydrogenation of EAA.[65]

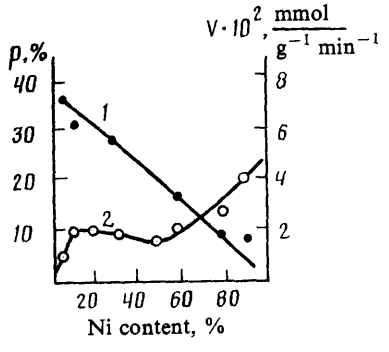


Figure 6. Dependence of the rate of hydrogenation (curve *1*) and optical yield (curve *2*) on content of Ni on the support in the hydrogenation of EAA on a Ni−TA/Aerosil catalyst.[67]

Vedenyapin et al.[67] studied catalysts obtained by impregnating supports [silica gel, Aerosil (120 m^2 g^{-1}), and kieselguhr (7.8 m^2 g^{-1})] with a solution of salts and then reduced in a current of H_2 at 380 °C. It was established that the enantioselectivity of these catalysts depend on the nature of the support, decreasing from 9% to zero in the following series: Aerosil > kieselguhr > silica gel. The average diameter of the particles ($\overline{D}$) decreases in the same series: 22, 17, and 12 nm respectively. Introduction of only 5% Cu into a 5% Ni/Aerosil catalyst leads to a decrease in $\overline{D}$ to 2−3 nm, which causes a reduction in p from 4.1 to 3.3%.

On increasing the Ni content on the support from 10 to 60% the value of $\overline{D}$ increases from 8−11 to 120 nm. This increase in $\overline{D}$ has hardly any effect on p, but with a further increase in Ni content, p increases while the rate of hydrogenation falls (Fig. 6). The fact that powdered Ni metal catalysts under these conditions give EHB with p = 50−60% demonstrates the complex nature of the dependence of p, whose increase cannot be solely related to the growth of the Ni crystallites. The depositing of Ni on a support results in an increase in the degree of dispersion of the metal phase and a reduction in p. This "inhibiting" effect of the support (Aerosil) occurs with a Ni content of up to 80%.

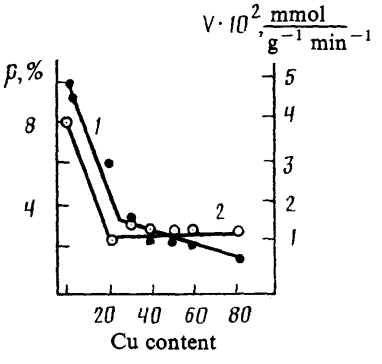


Figure 7. Dependence of the total rate of hydrogenation (curve *1*) and the optical yield (curve *2*) in the hydrogenation of EAA on Ni−Cu−TA/Aerosil catalysts on their Cu content.[67]

For Ni−Cu/Aerosil catalysts (Fig. 7) the values of p and v fall sharply when even small quantities of Cu are introduced. This effect had been observed previously[68] for bulk (powdered Ni−Cu−TA catalysts. This may occur because Cu under these conditions is inactive in the hydrogenation of EAA, but assists an increase in the degree of dispersion of the metal phase. From IR spectroscopic studies of supported Ni−Cu−TA catalysts it was possible to obtain information about the coordinate interaction between the metal phase and the molecule of modifying agent. IR spectra of adsorbed TA and AA on 20% (Ni−Cu)/Aerosil catalysts with a varying composition of Ni−Cu showed that in the interaction between TA and the Ni−Cu phase adsorption of both COOH groups of tartaric acid occurs, but to an unequal degree. This follows from the dependence of the spectroscopic characteristics of the Ni−Cu catalysts on their composition, and the bond between TA and metal which has the least covalent character occurs for Ni−Cu catalysts of composition 1 : 1.[36,69,70] The proximity of the COO^- vibration frequencies in the regions of 1600 and 1400 cm^{-1} for catalysts that are modified at pH 5 and 10 indicates the similar nature of the coordination of COO^- with the metal phase in both cases, which also results in similar values of p (in the hydrogenation of EAA, for example).[68] Substantial differences in the spectra of TA adsorbed on

Ni (1751 and 1275 cm^{-1}) occur if the surface of Ni is treated with TA in the presence of NaBr, in the latter case TA is adsorbed in the form of carboxylate ions (1416 and 1257 cm^{-1}).[71]

Supported dissymmetric bimetallic catalysts based on ruthenium have been the subject of a number of studies.[72-77] It was in the case of skeletal Cu–Ru catalysts modified with TA that the possibility of using bimetallic dissymmetric catalysts in enantioselective hydrogenation was first demonstrated.[72]

Since Cu does not adsorb hydrogen, the magnitude of the surface area of Ru in these catalysts could be determined electrochemically from the charge curves for H_2 adsorption by galvanostatic and potentiodynamic methods in KOH and H_2SO_4.[73]

Hydrogenation of EAA in the liquid phase on Cu–Ru–TA occurs enantioselectively, but p falls from 17–20% for pure Cu to 0.6% when even 0.5% Ru is introduced into the catalyst and then increases to 2.5% on a Ru–TA catalyst (with an increase in H_2 pressure the value of p increases slightly).[74] As the Ru content increases, the size of the crystallites first increases then diminishes, the specific surface increasing at the same time.[75] The effect of the size of crystallites of a metal catalyst on enantioselectivity was first demonstrated by these experiments,[1] and this was confirmed subsequently in a number of studies.[28,66]

A study of supported 10% (Cu–Ru)/Aerosil catalysts with a variable ratio of Cu:Ru in the liquid-phase hydrogenation of EAA (90 °C, 100 atm) showed that an antibatic relationship occurs between v and p, whereby when Ru:Cu = 4:6 falls from 4% to almost zero, while at the same time v increases linearly.[76,77] Under these conditions a Cu–TA/Aerosil catalyst does not hydrogenate EAA asymmetrically [whereas a skeletal Cu–TA catalyst gives (–)-EHB with p = 17%] [78] and only Cu–Ru–TA catalysts with Ru:Cu = 4:6 exhibit enantioselectivity, which suggests that there is synergism in the enantioselective action of Ru–Cu catalysts as a result of the activation of Cu in a mixed catalyst over a given Cu–Ru composition range.

This assumption about the enantioselective activity of just the Cu atoms in Cu–Ru/Aerosil catalysts is consistent with a dependence of p on pH of the modifying solution that is typical for a skeletal Cu–TA catalyst. Optically active (*R*)-(–)-EHB with p = 12% is obtained in the modification of a Cu catalyst only in the region of pH 3–7 with a maximum value of p at pH 5.[68]

A characteristic feature of Cu–Ru catalysts is that the value of p, as in the case of Ni–TA catalysts, depends on the total metal content on the support (with a constant Ru:Cu ratio, equal to 2:8). An increase in metal content from 5% (Cu+Ru) to 15% reduces p from 25 to 4%, and with a further increase in metal content p falls to zero, while retaining, however, quite a high overall rate of hydrogenation. The results obtained can be regarded as an indication that there are two types of sites on the surface of a bimetallic catalyst—inactive but stereospecific Cu sites and highly active but non-stereospecific Ru sites. Despite the lack of mutual solubility between these two metals, Cu and Ru are in close contact in supported catalysts, according to Sachtler,[79] possibly in the form of bimetallic clusters.

In skeletal Cu–Ru–TA catalysts Cu has an effect on Ru but the reverse action of Ru on Cu does not occur, which is attributed to the difference in the structures of supported and skeletal catalysts. In the latter a structure is formed that assumes the covering of the Cu phase by the Ru phase. Correlation of data obtained for Ru/SiO_2 and Ru/Al_2O_3 catalysts indicates the effect of supports on the activity of catalysts and their adsorbing capacity relative to hydrogen.

In a study of skeletal Ru that contained a small quantity of bayerite [$Al(OH)_3$] after leaching of a Ru–Al alloy, it was established that metallic Ru interacts with hydrated Al_2O_3, the Ru atoms being located close to the OH groups of bayerite, thus achieving a high degree of dispersion of Ru and the possibility of chiral modification of the catalyst when it is treated with TA,[80] whereas Ru/Al_2O_3 undergoes virtually no chiral modification.[1] These conclusions were based on a study of the spill-over of hydrogen on these catalysts. In skeletal ruthenium catalysts a more uniform distribution of metal particles and OH groups is achieved, and their interaction is more intimate than with supported catalysts. The possibility of chiral modification of the former has been attributed to this.[80]

Because of the small asymmetrising activity detected in bimetallic catalysts based on ruthenium, it was of interest to study other bimetallic systems containing Group VIII metals, in particular, palladium.

Skeletal Cu–Pd catalysts of different compositions were obtained and studied in the hydrogenation of EAA. The catalysts were obtained by leaching of a Cu–Pd–Al alloy (70% Al), and they contained Cu and Pd phases, their solid solution, and bayerite (about 40–58%). An increase in Pd content from 5 to 100% additively increase the rate of hydrogenation of EAA (100 °C, 100 atm).[81] A more complex relationship between activity and enantioselectivity occurs when there are small quantities of Pd present (up to 5% Pd). In the region of 1–5% Pd the values of w and p pass through a maximum.[82] From an electrochemical study of the catalysts using charge curves and $i\varphi$ curves it was possible to determine the quantity of hydrogen adsorbed on the catalyst. The curve showing the dependence of the ratio of H:(Pd + Cu) on the content of Pd (%) for catalysts with a Pd content of less than 10% deviates from linearity, displaying a decrease in adsorption of hydrogen on catalysts with this composition. This is attributed[81] to a screening of the Pd phase (or Cu–Pd alloy) by the Cu phase, which is supported by the results of enantioselective hydrogenation. Only catalysts containing less than 5% Pd exhibit enantioselectivity in the hydrogenation of EAA, and when the content of Pd is increased from 1 to 5 at.%, p decreases from 9 to 1%.

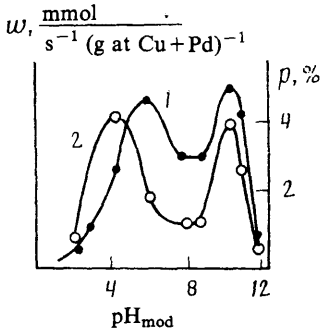


Figure 8. Dependence of the rate of formation of excess (*R*)-(–)-EHB (curve *1*) and optical yield (curve *2*) on the pH of a solution of (+)-tartaric acid during modification of a Pd(2.7%)–Cu(97.3%).

Two optimum regions of pH of the modifying solution were established by Vedenyapin et al.[82] At pH 5 and 10 the values of p were 4.1 and 4.6 % respectively in the hydrogenation of EAA on a Cu–Pd–TA catalyst containing 2.7% Pd (Fig. 8).

By carrying out the hydrogenation of EAA in ethanol solution it is possible to increase p slightly, as occurred for Co–TA catalysts.[83] However, this solvent effect proved insignificant for Cu–Pd–TA catalysts—p remained at a level of 2–3% and only the total rate of hydrogenation increased. It should be noted that, despite the results of Sachtler,[64] the rates of hydrogenation of pure EAA on modified and unmodified Cu–Pd catalysts proved to be similar, whereas the rate of hydrogenation of EAA in ethanol on a modified catalyst is higher than its rate of hydrogenation on an unmodified catalyst.

On changing the Pd content in Cu–Pd–TA catalysts, the values of p and w pass through a maximum at a level of 2% Pd (Fig. 9), while on changing from skeletal Cu–TA to Cu–Pd–TA p falls from 15 to 4–5%.

Thus, as in the case of Cu–Ru catalysts, a deviation from additivity occurs when small quantities of Pd are introduced into a Cu catalyst. With a Pd content of about 5% the specific rate, relative to 1 m^2 of surface of the Pd phase, increases by a factor of about 150 compared to the rate of hydrogenation on pure Pd. This may be regarded as evidence that in a bimetallic catalyst the properties of copper vary markedly when it is promoted by palladium, and it acquires a capacity to hydrogenate EAA and make a contribution to both the total rate and the rate of enantioselective hydrogenation.

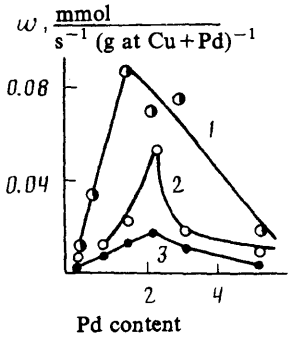


Figure 9. Dependence of the rate of formation of excess (*R*)-(−)-EHB on the composition of Pd–Cu catalysts in ethanol (curve *1*) and without a solvent (curves *2* and *3*) at pH_{mod} 4.5 (curves *1* and *2*) and pH_{mod} 10.5 (curve *3*) during hydrogenation of EAA.[82]

A comparison of different dissymmetric catalysts containing copper, such as Cu–Pd and Cu–Ru, reveals considerable differences between them. While the presence of only 0.1–0.5% Ru in the case of Cu–Tu–TA causes almost complete suppression of enantioselectivity, this suppression in Cu–Pd–TA catalysts only occurs when more than 5 at.% Pd is added. The total activity of Cu–Ru catalysts increases with an increase in Ru content, whereas on Cu–Pd synergism of catalytic action occurs, which may be due to a difference in structure of the active phase and dependent on a ligand effect.[81,82] A similar effect was detected for skeletal Cu–Ru–TA catalysts. Comparison of Cu–Pd and Cu–Ru catalysts by an electrochemical study of the adsorption of H_2 on them showed that with an increase in Cu content in the catalysts the strength of the Ru–H and Pd–H bonds decreases. The maximum on the $i\varphi$ curves is shifted to lower potential when copper is introduced into a Ru or Pd catalyst, which suggests that they interact electronically, i.e., there is a ligand effect.[84]

In contrast to the phase composition of Cu–Ru catalysts, for which a sandwich structure has been accepted (the surface is mainly covered with Ru atoms), the surface of Cu–Pd, according to electrochemical data,[82] is enriched with copper when Pd < 5%, which assists the formation of Cu–Pd clusters that provide synergism of catalytic action of such a catalyst through the ligand effect. This leads to a change in state of the Cu atoms, resulting in not only their high catalytic activity but also the distinctive dependence of p on the pH of modification.

Kuznetsova et al.[85] studied copper–palladium (CPC) and nickel– palladium (NPC) catalysts deposited on A-300 Aerosil and on γ-Al_2O_3. The catalysts were obtained by impregnation of the support with solutions of Cu^{2+} and Pd^{2+} or Ni^{2+} and Pd^{2+} salts, reduction in a current of H_2/He (1 : 10) at 360 °C, followed by modification at pH 5 and 50 °C with a solution of TA (method A) or by modification of reduced Cu/SiO_2 and Ni/SiO_2 catalysts with a solution of $PdCl_2$ + TA (method B).

Table 2. Activity and enantioselectivity of supported catalysts modified with TA in the hydrogenation of EAA.[85]

Catalyst	Optical Yield, p, %	Activity $A \times 10^2$ mmol (g cat)$^{-1}$ min^{-1}
10% Pd/SiO_2	0	18
10% Ni/SiO_2	7.1	9
(2% Pd–8% Cu)/SiO_2	0	5
(1% Pd–10% Cu)/SiO_2	1.6	5
(1% Pd–9% Ni)/SiO_2	7.0	8
(1% Pd–10% Ni)/SiO_2	4.6	11

It was established that asymmetric hydrogenation with p = 1.6% only occurred on the CPC obtained by method B and not by method A, which is apparently due to the presence of Pd^{2+} ions on the surface of the catalyst that can form a complex with TA. In the case of the NPC, regardless of the method of preparation (A or B), an enantioselective reaction occurred with p = 7 and 4.6% respectively. It should be noted that under these conditions a nickel catalyst—(10% Ni–TA)/SiO_2—also exhibited low enantioselectivity (Table 2), while in all cases replacement of SiO_2 by Al_2O_3 led to complete inhibition of the asymmetric activity of the catalyst.

IV. Dissymmetric intermetallic catalysts

Multicomponent hydrogenating metal catalysts—intermetallic compounds (IMCs) of rare earth elements (REEs) with Ni, Co, Cu, and other *d*-metals and their hydrides—are of interest for

asymmetric catalysis as cluster models, in a similar manner to bimetallic systems.

A study was made of two structural types of IMC enriched with nickel—LnM_3 and LnM_5.[65] Comparison of $LnNi_5$ catalysts (Ln = La, Sm, Gd, Ce, Pr, Nd) with Ni catalysts deposited on the oxides of the same REE demonstrated the high activity of IMCs and their hydrides in the hydrogenation of propylene, the greatest activity (1 atm, 100 °C) being exhibited by $LaNi_5$ [86] and the least activity by $CeNi_5$.[87] The specific activity of the hydrides of IMCs such as $LaNi_5$ and $LaCo_5$ is ten times higher than that of a supported 5% Ni/CeO_2 catalyst.[88] In this case the catalytic activity is higher the lower the equilibrium pressure of hydrogen in the system $IMC-H_2$, i.e., the more stable the hydride,[89] which was demonstrated for a $LnNi_5$ series of IMCs (Ln = La, Ce, Pr, Nd, Sm) and for $La_{1-x}Pr_xNi_5$.[89–91]

According to XPES data and magnetic measurements, segregation of Ni and its enrichment of the surface occurs on the IMC hydrides during the reaction, with the Ni:La ratio increasing from 5 to 6. However, conventional metal catalysts such as Ni/CeO_2, Ni metal, and skeletal Ni—have low activity under these conditions. This suggests that IMC hydrides may be regarded as a new class of hydrogenation catalysts with high activity, despite their small specific area.[87,92,93] The high activity of intermetallic REE compounds may be related to their ability to form hydrides with a high IMC—carbon bond energy that significantly exceeds the metal—C bond energy for Ni, Pt, and Pd catalysts. Calculated values of the bond energies of $(LnH_3)-C$ (for Ln = La, Pr, Gd, and Lu) according to the multiplet theory of catalysis[26] were 56.7, 34.3, 34.8, and 50.3 kcal mol^{-1} respectively.[94]

Replacement of a proportion of the Ni atoms by Co gives more stable hydrides with higher IMC—H bond energies, and the highest activity in the hydrogenation of propylene is exhibited by $LaNi_{5-x}Co_x$—hydride when $x = 2$. For this system the greatest density of hydrogen occurs in the $LaNi_3Co_2-H_4$ lattice. A similar pattern occurs for $LaNi_{5-x}Cu_x-H_4$, for which, according to the multiplet theory of catalysis,[26] the highest catalytic activity corresponds to the maximum hydride stability. The strength of the $IMC-H_x$ bond increases with an increase in x, and the free energy of the system ΔG decreases from 1.46 ($x = 1$) to −0.63 ($x = 3$); a further reduction in ΔG leads to a decrease in catalytic activity.[96] Other systems of $LaNi_{5-x}M_x$ and their hydrides, where Ln = La, Sm, Gd, and M = Al, Ti, V, Cr, Mn, are also active in the hydrogenation of propylene.[57]

It was found for the first time by Konenko et al.[97] that IMC hydrides such as $LaNi_5-H_6$ and $La_{1/2}$, $Pr_{1/2}Ni_5-H_5$ treated with a solution of (+)-tartaric acid at pH 4.8 exhibit enantioselectivity in the hydrogenation of EAA at 80 °C and 100 atm to (*R*)-(−)-EHB, with $p = 9.8$ and 5.7% respectively. However, a similar asymmetric effect ($p = 5.7\%$) was found for a 5% Ni/CeO_2 catalyst that was modified under the same conditions. This could suggest that the Ni which enriches the surface of the IMC as a result of segregation and forms dissymmetric clusters during modification with tartaric acid is responsible for the enantioselective properties of the catalyst. However, the fact that enrichment of an IMC with lanthanum, as in the case of La_3Ni, will hinder the segregation of Ni and affect the catalytic properties does not support this theory (partial replacement of La by Pr generally results in catalyst deactivation).[98] It is found that the initial La_3Ni, being modified with TA, achieves the asymmetric hydrogenation of EAA with $p = 11.9\%$, whereas a ferromagnetic sample with a specific magnetisation of saturation $\delta = 0.6-0.75$, in which considerable segregation of Ni has occurred as a result of the initial treatment of the sample, is inactive in enantioselective hydrogenation.[99]

Replacement of a proportion of the Ni atoms in $LaNi_5$ by other metals results in the formation of paramagnetic IMCs and their stabilisation. Thus, $LaNi_5$ forms the least stable hydride while an IMC of the type $LaNi_{5-x}Cu_x$ forms the most stable hydride.[99,100] According to the multiplet theory of heterogeneous catalysis, the catalytic system with the optimum energy values of the bonds between the catalyst and the atoms of the substrate molecule will have the highest catalytic activity. In fact, the highest catalytic and enantioselective activity in a series of $LaNi_{5-x}Cu_x$ IMCs was exhibited by $LaNi_3Cu_2-H_{3.7}$ ($p = 15.6\%$), which in terms of stability occupies a position between $LaNi_5$ and $LaNiCu_4$.[100] Thus, the isostructural replacement of one or two Ni atoms by Cu in $LaNi_5$ leads to more efficient dissymmetric catalysts. Similarly, in Ni—Cu catalysts modified with TA,[102] an increase in Cu content to 30 at.% gives a maximum value of p (in $LaNi_3Cu_2$ the Cu content is 28.7% and p reaches 17%).[100] This shows that it is the IMC hydrides as a whole, rather than the individual phase of Ni that separates out during segregation, which exhibit catalytic and enantioselective activity.[101]

The effect of pH of the modifying solution of TA on the value of p also confirms the participation of the whole IMC cluster, i.e., all of its components, in the formation of a complex with TA. Thus, for IMCs of the type $LaNi_4Cu$ the optimum value of pH is 5, whereas for $SmNi_4Cu$ and $GdNi_4Cu$ the optimum is pH 9. Modification of an IMC of composition $LnNi_3Cu_2$, where Ln = La, $La_{0.5}Sm_{0.5}$, and $Sm_{0.5}Gd_{0.5}$, at pH 9 leads, in line with the stability constants of Ln—TA complexes, to an increase in optical yield p from 4.4 to 6.1 and 9.9% respectively. The hydrogen pressure and reaction temperature also affect p. On the most active IMC of composition $LaNi_4Cu-H_{6.3}$, values of $p = 11.5\%$ at 80 °C and 40 atm, $p = 17\%$ at 80 °C and 80 atm, and $p = 9.7\%$ at 40 °C and 80 atm were obtained.[101]

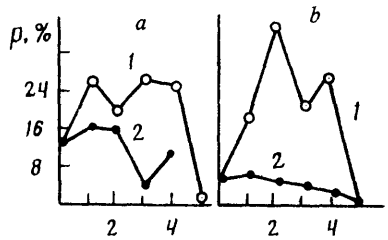


Figure 10. Dependence of the optical yield (*a*) and degree of conversion (*b*) in the hydrogenation of EAA on the number of atoms of M in the lattice of intermetallide $LaNi_{5-x}M_x$ [M = Co (*1*) and Cu (*2*), $pH_{mod} = 4.5$, hydrogenation conditions: 80 °C, 80 atm, 7 h].[103]

Thus, the dissymmetric properties of intermetallic catalysts are governed by both the ratio of Ni/Cu in the crystal lattice and the nature of the cluster that incorporates REE atoms of different types. The most effective catalysts were obtained[95,103] when cobalt was

introduced into the matrix of $LaNi_5$ hydride. These catalysts exhibit higher enantioselectivity and catalytic activity than that of $LaNi_{5-x}Cu_x$ catalysts. For the hydride $LaNi_4Co-H_{3.3}$ the value of p (26.6%) is more than twice that of $LaNi_5$ (p = 12%) and that of IMCs containing Cu.

The dependence of p on the number of Co atoms in an IMC of the type $LaNi_{5-x}Co_x$ is shown in Fig. 10. The corresponding $LaNi_{5-x}Cu_x$ are given for comparison. It is clear that for both types of catalysts there is an extremal dependence of the optical yield and degree of conversion of EAA on the number of Co or Cu atoms replacing Ni in $LaNi_5$.[103] While the optical yield did not exceed 17% when Cu was introduced into $LaNi_5$, when Co was introduced it increased to 30%, and with modification of $LaNi_3Co_2$ with a solution of TA at pH 4.5 with added trimethylacetic acid it rose to 45%.[104,105] It should be noted that the introduction into the modifying solution of NaBr, which is very effective for skeletal Ni,[18] has almost no effect in the case of IMCs, which is an indication once again of the special properties of IMC catalysts.[104]

When instead of Co other metals such as Mn, Cr, Ti, V, or Al are introduced into $LaNi_5$, the stability of the corresponding hydrides increases but their enantioselectivity is reduced. Only when Mn and Cr are introduced ($LaNi_4Mn-H_3$ and $LaNi_4Cr-H_{2.5}$) is there any appreciable activity (p = 20 and 16%).[104]

Interesting results were obtained in the partial replacement of Co by Cu in $LaNi_{5-x}Co_x-H_n$.[106] In this case both the total catalytic activity and enantioselectivity of the catalyst were reduced, the latter being greatest in $LaNi_3Co_2-H$ (p = 52%).[55]

Hydride of intermetallide	y, %	p, %
$LaNi_3Co_2-H_{3.5}$	100	52
$LaNi_3CoCu-H_{5.7}$	96	9
$LaNi_3Co_2Cu-H$	20	27
$LaNi_2CoCu-H_{3.8}$	30	17
$LaNiCo_2Cu_2-H_{3.6}$	12	13

Intermetallic catalysts that do not contain Ni have low activity. The successive and complete replacement of Ni by Co leads to a sharp decrease in catalytic and asymmetric activity. The partial introduction of Cu atoms into $LaCo_5$ does not lead to an increase in activity.[106]

The highest value of p (about 60%) was found for a $LaNi_{5-x}M_xM_y$ system containing Co and Cu. This asymmetrising effect is attributed to the formation of heterometallic complexes $[LaM_xM_y-TA]$.[107]

This behavioural feature essentially distinguishes intermetallic catalysts from bimetallic Ni–Co catalysts that are modified under the same conditions as IMCs and for which the value of p steadily increases with an increase in Ni content.

According to Klabunovskii et al.,[108] asymmetric activity in the hydrogenation of EAA and AA decreases in the following series of metal catalysts modified by TA and amino acids: Ni > Cu > Co, the value of p not exceeding 5–8% for Co. It was therefore to be expected that IMCs containing Ni and Cu would be more enantioselective than those containing Ni and Co. However, the results obtained indicate that, on the contrary, Ni–Co IMCs are more active than Ni–Cu IMCs. This may occur because Ni and Co are not segregated to any significant degree on the surface of an IMC, otherwise the enantioselectivity of the catalyst would be governed by the nature of the metal segregated on the surface of the catalyst. The catalytic and enantioselective activity of IMCs are determined rather by the nature of the cluster which contains the atoms of three different metals—La, Ni, and Co (or Cu).

Intermetallic catalysts that are modified in the optimum pH region decompose to a lesser degree during catalysis, which is supported by a test for their ferromagnetic properties) (test carried out by the Faraday method). Hence, a higher value of p is characteristic of those hydrides that decompose to a lesser degree during modification and hydrogenation. Moreover, the catalytic properties also depend on the strength of the IMC–H bond. Introduction of Co into an IMC increases the strength of the IMC–H bond and improves the stability of the hydride. This relates in particular to $LaNi_3Co_2$, for which maximum values of the magnetic moment, a maximum density of the hydrogen atoms in the hydride lattice, and optimum values of the IMC–H bond energy have been found.[95]

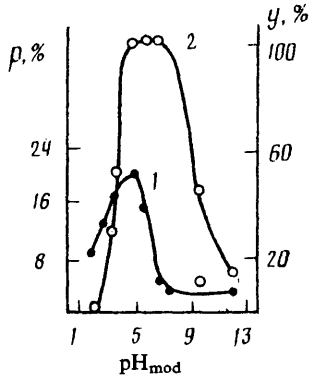


Figure 11. Dependence of the optical yield (*1*) and degree of conversion (*2*) on $LaNi_3Co_2-H_{3.5}$ on the pH of the modifying solution of (+)-tartaric acid.[103]

The dependence of p on the pH of the modifying solution of TA has the same extremal nature as the dependence for modified Cu and Co metal catalysts.[102,109] The dependence of p and y on the initial pH of the modifying solution of TA for $LnNi_3Co_2$ and $LaNi_4Cu$ catalysts is shown in Fig. 11.[103] This suggests the identity of the tartrate complexes of the metals contained in the dissymmetric site that are formed on the surface of the catalysts.[1]

The increase in pH of the solution of TA in the course of modification and the evolution of hydrogen during modification of the hydride also point to complexation on the surface of the IMCs during their modification, in addition to the asymmetric effect in hydrogenation. At the same time a proportion of components of a $LaNi_3CoCr-H_{4.2}$ catalyst passes into solution (especially La) and the surface of the IMC is enriched with Ni. Data on the

composition of the surface layer, obtained by using XPES,[13] are given below.

Hydride of intermetallide	La	Ni	Co	Cr
IMC (initial)	14.7	60.0	15.8	9.5
IMC hydride	17.5	64.6	7.9	10.0
IMC–$H_{4.2}$ after modification at pH 4.5	8.3	65.2	7.8	18.7
The same after modification at pH 7.0	22.3	44.5	12.2	21.2
Bulk composition of the initial hydride $LaNi_3CoCr-H_{4.2}$	32.3	40.9	13.7	12.1

Replacement of La in $LaNi_3CoCr-H_{4.2}$ by Sm or Gd results in a sharp fall in catalytic and enantioselective activity of the catalyst, which is an indication of the inclusion of REE atoms in addition to *d*-metals in the dissymmetric cluster.

The decrease in *p* may be related to the increase in strength of the tartrate complexes of IMCs containing Sm and Gd in comparison to IMCs based on La.[101] Replacement of La in $LaNi_5-H_4$ by other rare earth elements (Pr, Sm, Gd)[60] leads to a reduction in stability of the corresponding hydride, and this gives rise to the need for a considerable increase in the hydrogen pressure that is necessary for hydride formation in the preparation of an IMC hydride. On the other hand, replacement of Ni in $LaNi_5-H_4$ by atoms of other transition metals strengthens the IMC–H bond. Therefore, catalysts based on more stable hydrides, such as $LaNi_4M$ with M = Al, Ti, V, with a high overall catalytic activity exhibited low enantioselectivity.[110] Data on a number of polymetallic hydrides that have been studied are summarised in Table 3.[57,96,103,110–112]

Table 3. Dependence of the degree of conversion (*y*, %) and optical yield (*p*, %) in the hydrogenation of EAA on IMC catalysts (80 °C, 80 atm, 7 h) on the composition of IMC hydrides modified with (+)-tartaric acid (pH 4.5).[57,96,103,110–112]

Catalyst	*y*, %	*p*, %	Catalyst	*y*, %	*p*, %
$LaNi_5$-$H_{6.0}$	14.9	12.7	$LaNi_4Cu$-$H_{5.8}$	17.5	17.0
$LaNi_4Co$-$H_{4.8}$	48.8	26.6	$LaNi_3Cu_2$-$H_{3.7}$	13.0	15.6
$LaNi_3Co_2$-$H_{3.7}$	100	20.0	$LaNi_2Cu_3$-$H_{3.5}$	9.5	4.3
$LaNi_2Co_3$-$H_{3.9}$	52.9	28.0	$LaNi_3CoCr$-$H_{4.2}$	58.2	13.5
$LaNi_2Co_2Cu$-$H_{3.9}$	10.0	21.0	$LaNi_3CuCr$-$H_{3.9}$	64.7	16.0
$LaNiCo_4$	0	0	$LaNi_4Co_{0.5}Cu_{0.5}$-$H_{4.2}$	10.3	0
$LaCo_4Cu$	19.3	3.5	$LaNi_3CrMn$-$H_{3.9}$	48.2	3.8
$LaCo_3Cu_2$	14.4	0	$LaNi_3Co_{0.5}Cu_{0.5}Cr_{0.5}Mn_{0.5}$-$H_{4.2}$	36.6	6.8
$LaCo_2Cu_3$-$H_{3.0}$	0	0	$LaNi_2Co_{2.5}Mn_{0.5}$-$H_{5.3}$	65.4	20.9
$La_{0.5}Sm_{0.5}Ni_4Co$	27.7	19.7	$LaNi_2Co_2Mn$-$H_{3.5}$	77.8	7.2
$Sm_{0.5}Gd_{0.5}Ni_4Co$	0	0			
$CeCo_3$	5.6	0			
20% Ni – 80% Co	22.0	11.0			
$LaNi_4Al$-$H_{4.0}$	60.9	6.3			
$LaNi_4Ti$-$H_{3.5}$	93.4	1.1			
$LaNi_4V$-$H_{3.5}$	95.4	5.2			
$LaNi_4Cr$-$H_{4.0}$	96.0	16.3			
$LaNi_4Mn$-$H_{5.0}$	40.7	23.4			

It is evident from Table 3 that the use of catalysts based on polymetallic IMCs, especially 5- and 6-component systems, in asymmetric hydrogenation does not have any advantages over IMCs of a simpler composition. In certain cases the polymetallic systems generally proved inactive. However, for an understanding of the mechanism of action of these catalysts, the important conclusion that a change in the nature of all the components of the IMC, including the REEs, has a considerable effect on the catalytic and enantioselective properties of the catalysts follows from the data given.

This again provides confirmation that during the modification of IMC hydrides, heterometallic tartrate complexes contained in a catalytic cluster of asymmetric hydrogenation are formed on the surface. This cluster is similar to that which has been proposed for dissymmetric monometallic hydrogenation catalysts.[1]

Dissymmetric intermetallic catalysts were studied in the practically significant diastereoselective hydrogenation of fructose to mannitol and sorbitol.[113,114] Previously[112] the hydrogenation of *D*-fructose to sorbitol and mannitol had been optimised with respect to sorbitol by means of mathematical planning of the experiment. Skeletal Ni modified with (+)-tartaric acid proved to be the best catalyst. Hydrogenation of an aqueous solution of *D*-fructose at 80 °C and a hydrogen pressure of 90 atm gave sorbitol in 65.7% yield (sorbitol : mannitol = 1.9 : 1).

A number of isostructural IMC hydrides — $LaNi_3Co_2$ and $LaNi_3Cu_2$ and also $LaNi_3M'M''$, where M'M'' = CuCo, CoCr, MnCr, $Co_{0.5}Cu_{0.5}Cr$, modified with (+)-tartaric acid — were studied[113,114] for the diastereomeric hydrogenation of *D*-fructose. The task involved finding catalysts and optimising the hydrogenation of fructose to mannitol — a product of practical importance. It was found that the pH of the modifying solution of TA is of crucial importance for preparing the optimum catalyst. The maximum values of the degree of conversion of fructose were achieved by pH 7–8 for $LaNi_5$, $LaNi_3Co_2$, and $LaNi_3Cu_2$ and at pH 4.5–5.5 for $LaNi_3CoCr$. By varying the reaction conditions it was found that the highest yield and maximum diastereoselectivity could be attained when $LaNi_3Cu_2$ was used. The optimum conditions were: 1.5 g of catalyst, a 15% solution of fructose, 80–90 °C, a hydrogen pressure of 50 atm. It should be noted that by introducing up to 50% sorbital into the reaction mixture it was possible to increase substantially the diastereoselectivity of the reaction with respect to the formation of mannitol. The excess of mannitol was 46% and the total yield was 73%. The $LaNi_3Co_2$ catalyst was more selective towards formation of sorbital (39% excess of diastereoisomer and 70% yield).

Comparison of the selectivity of action of the catalyst with the content of the stereoisomeric forms of *D*-fructose in the reaction system showed that the stereoisomers of α-*D*-fructopyranose and α-*D*-fructofuranose are mainly responsible for the formation of *D*-mannitol.[113]

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The studies described above have not covered all aspects of research into asymmetric hydrogenation on metals. Questions relating to the reaction mechanism, which has recently been the subject of considerable attention in a number of studies, have remained untouched. Ideas have been developed concerning the decisive role in asymmetric hydrogenation of the coordination of metal ions on the surface of the catalyst with molecules of modifying agent — these are usually hydroxyacids or amino acids — and with

substrate ions—mainly readily complexing diketones and ketoesters. The previously advanced theories[1] about asymmetric hydrogenation occurring via the formation of an intermediate ternary complex of metal–modifying agent–substrate have received support in a number of studies.[26,31,64] The nature of the chirodiastaltic interaction between molecules of modifying agent and substrate (or semihydrogenated compound) in such complexes is evident in correlation[108] between the stability constants of complexes that simulate an intermediate complex on the surface of the catalyst and the enantioselectivity of the catalyst containing this complex.[65] By finding these correlations it is possible to predict the composition of effective dissymmetric catalysts and the nature of the modifying agent—in the metal series Ni–Cu–Co with (*S*)-α-amino acids as modifying agents. Additional correlations between the conformation of a ternary complex determined from circular dichroism spectra and the configuration of the hydrogenation product make it possible to establish the configuration of the product with sufficient reliability.[69,115]

The second aspect of asymmetric hydrogenation (which was only mentioned in two studies)[6,7] is the problem of the industrial development of asymmetric catalysis for the preparation of optically active compounds of practical importance. Considerable progress in the field of asymmetric metal-complex catalysis is known to have been achieved in this area. Chiral rhodium phosphine complexes proved very effective in the synthesis of a number of important optically active products, and only the complex nature of synthesising the ligands and the high cost of the processes have placed a restraint on their widespread application.[116,117] In certain cases these processes have had a practical application in the synthesis of high-cost products [for example, 3,4-dihydroxylphenylalanine (DOPA) for the treatment of Parkinson's disease, phenylalanine[117] for the production of the sweetener Aspartame, menthol[118] for the food and perfumery industries and medicine] on a large scale.

Modified heterogenous metal catalysts, because of the limited range of their action (on the whole it is only the C=O bond that is effectively hydrogenated), have so far found less applications, despite their evident technological advantages over metal-complex catalysts. However, there is an indication[119] that a Ni–TA catalyst has been used to obtain (2*R*,4*R*)- and (2*S*,4*S*)-pentanediol by hydrogenation of acetylacetone. (*S*)-Alkyl-β-hydroxybutyrates—important optically active synthons[120] that have already come on the market—have also been obtained in this manner. Thus, it is possible to look forward to a wider practical realisation of asymmetric hydrogenation on heterogeneous metal catalysts modified with optically active compounds.

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Translated from *Uspekhi Khimii* **60** 1946–1968 (1991) U.D.C. 546.443;547.979

Reactivity of transition metal solvates

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ABSTRACT. Reactivity data are generalised for one of the most important classes of complexes, solvates, which are quantitatively nearly unstudied. Various approaches to studying and describing the reactivity are compared with respect to solvation of the reagents and the transition state. The specifics and mechanism of ligand substitution in pure and mixed organic solvents are found. The reactivity of simple (homoleptic) and mixed solvates toward macrocycles is examined in detail using porphyrins as an example. The kinetic method of indicator reactions is applied to porphyrins in order to study the state of transition metal salts in organic solvents and the stability of the coordination spheres of acidosalts (MX_n^{n-2}), acidosolvates (MX_2S_{n-2}) and their transition states. The concentration dependence of the rate constant of an indicator reaction is demonstrated to be due to a change in the inner coordination sphere and a shift of equilibria between the various coordination complexes.

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I. General concepts of the reactivity of complexes

The reactivity of a compound refers to the rate at which the given compound reacts with others. The rate constant at 298 K, k_v^{298}, is used as a measure of the reactivity of a compound in a series of similar reactions.[1] The number of chemical reactions in which one compound or another participate can be practically infinite. However, the rates differ dramatically from reaction to reaction. Therefore, the reactivity of any compound refers to a specific reaction or at least a specific type of reaction (acid–base, complexation, redox, etc.). The rate constant is related to the free energy of activation

$$\Delta G^{\neq} = -RT \ln k_v - RT \ln \frac{kT}{h}, \quad (1)$$

which is determined by the energy and structural changes occurring during activation in the transition state (Fig. 1). Hence, the numerical values of k_v^{298} and ΔG^{298} are controlled by the mechanistic subtleties of the fundamental reaction step.

The free energy of activation contains two components. These involve energy (energy E or enthalpy of activation $\Delta H^{\neq}$) and structure (entropy of activation $\Delta S^{\neq}$)

$$\Delta G^{\neq} = \Delta H^{\neq} - T\Delta S^{\neq}. \quad (2)$$

According to the basic equation of the theory of absolute reaction rates[2]

$$k_v^{298} = \varkappa \frac{\kappa T}{h} \exp(S_0/R) \exp(-\Delta H_0^{\neq}/RT). \quad (3)$$

For complicated reactions, which include ligand substitution in solvates, the coefficient representing surmounting of the potential barrier by the reagents, $\varkappa$ (transmisison coefficient), cannot be found. It is usually taken equal to unity. The enthalpy of activation is less frequently used in kinetic calculations than the activation energy, which is usually found graphically using the Arrhenius equation. The quantities $\Delta H^{\neq}$ and E are interrlated

$$\Delta H^{\neq} = E - RT. \quad (4)$$

At 298 K, the difference between $\Delta H^{\neq}$ and E is 2.5 kJ mol^{-1}. The enthalpy of activation for a complicated chemical reaction in solution is determined by the energy change resulting from the cleavage of some and the formation of other chemical bonds, the energy difference of electrostatic repulsion and attraction, and the energy changes due to loss or addition of solvent molecules in the transition state. The entropy of activation is related to the probability of forming the transition state, i.e. to the steric relationship of the reaction centres in the reacting reagents. If the solvent actively participates in the reaction (as a reagent and as a strongly solvating species), this is reflected in $\Delta S^{\neq}$. As a rule, desolvation favours conversion from the transition state to the final one and increases $\Delta S^{\neq}$. Conversely, additional solvation reduces the probability of generating the transition state and reduces $\Delta S^{\neq}$. Especially complicated situations are encountered in complexation involving macrocycles where the macrocyclic effect appears.[3] The quantities $\Delta H^{\neq}$ and $\Delta S^{\neq}$ are interrelated for formation of complexes with porphyrins. Desolvation of the reagents in the transition state increases the energy requirements for their activation, i.e. the increase of $\Delta S^{\neq}$ causes $\Delta H^{\neq}$ to increase. Solvation in the transition state is energetically favourable but structurally unfavourable. Therefore, a decrease of $\Delta S^{\neq}$ decreases $\Delta H^{\neq}$. This is known as the kinetic compensation effect,[1] which is mathematically described by

$$\Delta H^{\neq} = a + b\Delta S^{\neq}, \quad (5)$$

where a and b are coefficients. The transition state serves as a manifestation of the chemical form of the mass action.[4] The complexity of this action is reflected in the activation mechanism of the fundamental chemical reaction.

The reactivity of complexes has been well studied and is well documented in a monograph.[5] This refers not to ligand substitution processes in complexes but to a change of the chemical nature of coordinated ligands under the influence of outer-sphere species. There are no broad systematic data for the reactivity of coordination (complex) compounds in substitution reactions of some ligands by

others, except for the case water ⇆ ligand. Existing books[6–8] contain only anecdotal kinetic data for these reactions. Ligand substitution in solvates apparently obeys the same rules as substitution of water molecules in aqua complexes. Their stoichiometric mechanisms[8] are apparently also similar.

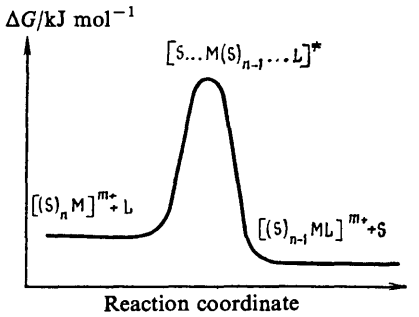


Figure 1. Coordinate and transition state of an $S_N2(I)$ solvate coordination reaction.

Let us examine in general the mechanisms of complexation in solution. The limiting steps of ligand substitution reactions are usually classified by their molecularity. Unimolecular, bimolecular and termolecular reactions differ in the number of species used in forming the transition state (and in activating the reagents). The duration of the fundamental step is $\sim 10^{-13}$ sec. The theory of termolecular reactions in solutions is complicated and not fully solved.[2] Bimolecular reactions are more numerous. Representing as a reagent the ligand (L or X^-) entering the coordination sphere of the complex, these reactions are denoted by the symbol S_N2 (according to Ingold–Hughes). This stands for substitution of a ligand by another nucleophilic ligand in the complex

$$[M\ (S)_n]^{m+} + L \rightleftharpoons [M(S)_{n-1}L] + S \ldots \quad . \tag{6}$$

In this instance, L should be an electron donor, i.e. have an O, N, S, Hal, etc. atom with a negative charge or an electron pair or both. Therefore, H_2O, NH_3, solvents derived from them, H_2S, all solvents with $-S-R$ bonds, $R-S-R$, $R_2S=O$, R_2SO_2, and certain others are nucleophiles. According to the Langford and Gray classification,[8] three types of bimolcular reaction mechanisms can be distinguished: *D*, dissociative; *A*, associative; and *I*, interchange. The *D*-mechanism of substitution includes two steps and presumes two possible routes for its occurrence. If the solvent loss step is fast and the second step of ligand L or X^- addition is slow

$$[M(S)_n]^{m+} \overset{-S}{\rightleftharpoons} [M(S)_{n-1}] \overset{+L}{\rightleftharpoons} [M(S)_{n-1}L], \tag{7}$$

then the $S_N2(D)$ mechanism is observed. If the first step is slow and the second fast, then the reaction wil be monomolecular (its rate does not depend on [L]). Such a mechanism is denoted $S_N1(D)$. Both *D* mechanisms are equally probable. Realisation of one or the other depends on the nature of the metal and solvent. In both instances, the intermediate formed is $M(S)_{n-1}$, a solvate with coordination number smaller than maximal by one unit.

The associative mechanism (*A*) is less probable for solvates since it is caused by deformation of the initial coordination sphere of $[M(S)_n]^{m+}$ by the substituting ligand L

$$M(S)_n]^{m+} + L \rightleftharpoons [M(S)_nL]^{m+} \rightleftharpoons S + [M(S)_{n-1}L]^{m+}. \tag{8}$$

If the coordination number *n* does not reach the maximal value in a given solution, then one stable form of the coordination sphere simply rearranges into another. The species $[M(S)_{n-1}L]$ becomes an intermediate and a stable solvate. On the other hand, the intermediate $[M(S)_nL]^{m+}$ with a strained coordination sphere converts to the stable solvate $[M(S)_{n-1}L]$. This is an example of the $S_N2(A)$ mechanism. Hence, intermediates of different stability with a coordination number greater than *n* of the initial solvate can form in the $S_N2(A)$ mechanism.

The interchange mechanism (*I*) is very common. In this mechanism, movement along the reaction coordinate causes the M–S bond to stretch and then cleave whereas the M–L bond forms and strengthens. Both processes occur simultaneously (Fig. 1). this is the $S_N2(I)$ mechanism

$$[M(S)_n]^{m+}L \rightleftharpoons [L \ldots M(S)_{n-1} \ldots S]^{*} \rightleftharpoons S + [M(S)_{n-1}L]^{m+}. \tag{9}$$

Reactions of this type are often encountered, even in organic chemistry. Their occurrence is due to the large deformation of the coordination sphere or organic radical at which substitution is occurring. Langford and Gray[8] assume incorrectly that an outer-sphere intermediate (for example, $[M(S)_n \ldots L]^{m+}$) is formed in $S_N2(I)$ reactions. An outer-sphere complex forces the reaction to take path *D* or *A* and not the interchange route.

The activation mechanisms of the reacting species or their separate fragments are very important. Langford and Gray[8] prefer to differentiate two activation mechanisms: associative activation (denoted '*a*') and dissociative activation ('*d*'). The symbols '*a*' and '*d*' coincide with (*A*) and (*D*). Obviously the entering group L contributes greatly to activation in stoichiometric *A* processes; the leaving group S, in *D*. Also, interchange mechanisms with associative I_a and dissociative activation I_d, where the principal contribution to the activation comes from the leaving group S, should be differentiated in $S_N2(I)$ processes.

We discovered and studied[9] a large group of $I_{a,d}$ reactions with associative–dissociative activation where the entering and leaving groups contribute equally to the activation. In order to find the stoichiometric mechanism of the reaction (S_N1, S_N2, S_E1, S_E2, *A*, *D*, *I*) It is necessary to study the substitution kinetics, find the kinetic equations and investigate the influence of the nature and concentration of entering and leaving groups on the type of kinetic equation. Fulfilment of a first-order kinetic equation

$$-\frac{dC_{solvate}}{dt} = k_v C_{solvate}, \tag{10}$$

suggests that the substitution reaction is unimolecular, dissociative, and $S_N1(D)$. If a second-order kinetic equation is obeyed

$$-\frac{dC_{solvate}}{dt} = k_v C_{solvate} C_L, \tag{11}$$

a bimolecular associative $S_N2(A)$ or interchange $S_N2(I)$ mechanism is expected.

The mechanistic subtleties, also called the intimate[8] or activational mechanism (this last term is more definitive) must be found by studying the temperature dependence in a series of substitution reactions involving various entering and leaving ligands. The presence or absence of a dependence of the enthalpy of activation

$(\Delta H)^{\neq}$ on the nature of L and S enables the activational mechanism (I_a, I_d or $I_{a,d}$) of the reactions to be defined as interchange substitution of ligands. Due to a lack of experimental data, the mechanism was not examined where activation involves accompanying ligands (X^-) in mixed and similar complexes $[MX_m(S)_{n-m}]$ in addition to inner-complex and macrocyclic compounds.[8] Complicated mechanisms with multi-centered interactions in the transition state are possible here.

Determination of the stoichiometric and activational contributions to the reaction mechanism still does not provide a comprehensive understanding. A model of the transition state must be constructed. The type of reaction centres and orbitals used in the chemical interaction in addition to the role of the solvent in forming the transition state (solvation of the transition state) can be determined by changing the structure of its component parts and the nature of the medium. Quantum-chemical calculations of the potential energy surface must be performed.

Therefore, the term 'reaction mechanism' represents a complicated and gradual transition of the starting reagents into the final products that is examined on a molecular and electronic level.

A large volume of experimental data exists on formation in aqueous solutions of complexes involving metal salts and ligands. Almost all monographs on coordination chemistry in aqueous solutions treat this topic.[6-8,10-15]

The stability of complexes is controlled by the dynamic equilibrium of two opposing processes: substitution of H_2O by ligands (direct process) and substitution of ligands by H_2O (reverse process). The stability constant of a complex K_s reveals which process predominates. If $K_s > 1$, the formtiton reaction predominates; if $K_s < 1$, dissociation prevails. If $K_s = 1$, $k_v^f = k_v^d$.[16] It is very important to obtain data on the mechanism and transition state of both complexation steps. Since complexation (if it is true complexation) is reversible, the reaction passes through the same transition state on moving forward or backward along the reaction coordinate.

Complexation in mixed solvents is more complicated. This can give rise to mixed solvate and ligand coordination spheres $[MX_mS_1S_2]$, $[MX_{m-p}L_pS_1S_2]^{m-p}$, $[ML_mS_1S_2]^{m+}$, $[MS_{1m}S_{2n-m}]$, $[M(S_1)_n]^{m+}$, $[M(S_2)_m]^{m+}$ and all intermediate forms. The quantity K_s in binary solvents (even more complicated in ternary systems) is determined by the simultaneous occurrence of very many reactions in equilibrium with each other. More often than not the dependence of K_s on solvent composition in these complicated systems provides no definitive information on the reaction. For this, the kinetics of all competing reactions must be studied. Such a fruitful approach has previously been used.[17]

Let us examine substitution of water in aqua complexes by other ligands. Analysis of the data in Table 1,[8] which contains experimental values of the rate constants (k_H^{298}, sec^{-1}) for substitution of H_2O in $[Pt(dien)OH]^{2+}$, indicates that the substitution accelerates where the chemical affinity of the ligand for Pt^{2+} increases.

The high rate of 'substitution' by OH^- is not due to the chemical affinity of hydroxide for Pt (it is not large compared with other ligands[11]) but to the extensive inner-sphere ionisation of H_2O. This is supported by the fact that the rate of exchange of Cl^-, Br^- and I^- by X^- is completely independent of the presence of OH^- in solution.[8]

Data for the influence of the nature of the solvent on the rate of substitution of $^{35}Cl^-$ by $^{36}Cl^-$ in *trans*-$[Pt(py)_2Cl_2]$ are presented in Table 2. The substitution includes a formation step of two solvates *trans*-$[Pt(py)_2S(Cl)_2] \rightleftharpoons [Pt(py)_2SCl]^+$ and conversion of the latter into $[Pt(py)_2Cl^{36}Cl]$. It is clear from Table 2 that formation of $[Pt(py)_2Cl_2S]$ or $[Pt(py)_2Cl_2S_2]$ and their conversion into $[Pt(py)_2SCl]^+$ strongly affects the reaction rate and changes its mechanism. The ligand exchange rate is especially high if such solvates are not formed (in C_6H_6 and CCl_4) or if the solvent can solvate the leaving ligand (DMSO, H_2O, CH_3NO_2, ROH). If the solvent can solvate Pt^{II} but not the leaving ligand [DMF, $(CH_3)_2CO$, $CH_3CO_2C_2H_5$], the ligand substitution rates are minimal.

Table 1. Rate of H_2O substitution by a ligand in $[Pt(dien)OH_2]^{2+}$ in aqueous solution at 298 K*.[8]
$[Pt(dien)OH_2]^{2+} + X^- \rightleftharpoons [Pt(dien)X]^+ + H_2O$.

Ligand	$10^2 k_H^{298}$, s^{-1}	Ligand	$10^2 k_H^{298}$, s^{-1}	Ligand	$10^2 k_H^{298}$, s^{-1}
Cl^-	0.52	NO_2^-	0.090	OH^-	very fast
I^-	3.9	SCN^-	1.45	Py	0.19

*The uncertainty in the rate constants given here and below is from 5 to 20%.

Table 2. Solvent influence on exchange rate of Cl^- in *trans*-$[Pt(py)_2Cl_2]$ at 298 K.[8]

Solvent	$10^5 k_H$, s^{-1}	Solvent	$10^5 k_H$, s^{-1}
H_2O	3.5	DMF	10^{-3}
DMSO	380	$(CH_3)_2CO$	10^{-2}
CH_3NO_2	3.2	$CH_3COOC_2H_5$	10^{-2}
C_2H_5OH	1.3	*m*-$C_6H_4(CH_3)OH$	10^{-1}
n-C_3H_7OH	0.42	C_6H_6	10^2
trans-C_4H_9OH	0.10	CCl_4	10^4

The ligand substitution rate depends mainly on solvation of the leaving ligand X^- in complexes where the central atom is coordinatively saturated and is incapable of further solvation, for example, $[Co(en)_2X_2]^+$ (Table 3).

Before commenting on Table 3, attention should again be drawn to the very unfortunate terminology that for some unknown reason complicates the coordination chemistry of ligand substitution reactions.[6-8] This concerns solvolytic dissociation of acidocomplexes, for example:

$$[CoL_mX_{n-m}]^{z+} + S \rightleftharpoons [CoL_mX_{n-m-1}(S)]^{z+1} + X^-, \qquad (12)$$

in which the Co–X bond is completely broken by the solvent. If H_2O acts as S, then reaction (12) represents hydrolytic dissociation. Reactions of type (12) have incorrectly been called 'solvolysis' or 'hydrolysis'[6-8] since in general chemistry hydrolysis (solvolysis) means splitting of water (solvent) into ions with subsequent bonding

by a cation, anion or neutral molecule. Therefore, the term 'acid hydrolysis' in the sense used before[6,8] does not correspond to the actual process. The term 'base hydrolysis' is just as incorrect.[6,8]

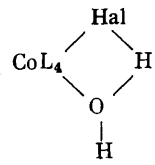
Table 3. Rate of hydrolytic dissociation of the Co–X bond at 298 K in Co^{III} complexes.[8]
$[CoL_mX_{n-m}]^{z+} + H_2O \rightleftharpoons CoL_mX_{n-m-1}(H_2O)]^{z+1} + X^-$.

Complex type	Ancillary ligand (L)	Leaving ligand (X^-)	Rate constant, $10^4 k_v$, sec^{-1}
$[Co(L)_2Cl_2]^+$	en	Cl^-	0.32
$[Co(L)_2Cl_2]^+$	1.2-pn	Cl^-	0.62
$[Co(L)_2Cl_2]^+$	2.3-bn (*d, l*)	Cl^-	1.5
$[Co(L)_2Cl_2]^+$	2.3-bn (*meso*)	Cl^-	4.2
$[Co(L)_2Cl_2]^+$	$H_2N-[C(CH_3)_2]_2-NH_2$	Cl^-	330
$[CoL_4L'X]^{2+}$	NH_3, H_2O	Cl^-	$2.2 \cdot 10^{-2}$ *
trans-$[CoL_4X_2]^+$	NH_3	Cl^-	18
cis-$[CoL_4X_2]^+$	NH_3	Cl^-	very fast
$[CoL_5X]^{2+}$	NH_3	Br^-	$6.3 \cdot 10^{-2}$
trans-$[CoL_2L'X_2]^+$	en, NH_3	Br^-	$1.2 \cdot 10^{-2}$
trans-$[CoL_2X_2]^+$	en	Br^-	1.4
trans-$[CoL_2XX']^+$	en	Br^-, NO_2^-	40
cis-$[CoL_2X_2]^+$	en	Cl^-	2.5
cis-$[CoL_2L'X]^{2+}$	en, NH_3	Cl^-	$1.4 \cdot 10^{-2}$ **
trans-$[CoL_2L'X]^{2+}$	en, NH_3	Cl^-	$4.0 \cdot 10^{-3}$
cis-$[CoL_2XX']^+$	en	Cl^-, NO_2^-	1.1
trans-$[CoL_2XX']^+$	en	Cl^-, N_3^-	2.5
$[CoL_5X]^{2+}$	NH_3	NO_3^-	0.27
$[CoL_5X]^{2+}$	NH_3	I^-	0.083
$[CoL_5X]^{2+}$	NH_3	Br^-	0.063
$[CoL_5X]^{2+}$	NH_3	Cl^-	0.017
$[CoL_5H_2O]^{3+}$	NH_3, H_2O	NH_3	0.058
$[CoL_5X]^{2+}$	NH_3	SO_4^{2-}	0.012
$[CoL_5X]^{2+}$	NH_3	$H_2PO_4^-$	$2.6 \cdot 10^{-3}$
$[CoL_5X]^{2+}$	NH_3	CH_3COO^-	$1.2 \cdot 10^{-3}$
$[CoL_6]^{3+}$	NH_3	NH_3	10^{-6}
$[CoL_5X]^{2+}$	NH_3	F^-	$8.6 \cdot 10^{-4}$
$[CoL_5X]^{2+}$	NH_3	SCN^-	$5.0 \cdot 10^{-6}$
$[CoL_5X]^{2+}$	NH_3	N_3^-	$2.1 \cdot 10^{-5}$
$[CoL_5X]^{2+}$	NH_3	NO_2^-	very slow
$[CoL_5X]^{2+}$	NH_3, OH^-	NH_3	very slow
$[CoL_5X]^{2+}$	NH_3	PO_4^{3-}	very slow
$[CoL_4L'X]^{2+}$	NH_3, H_2O	Cl^-	0.035
$[CoX_5X']^{3-}$	X=CN⁻	X=N_3^-	$5.8 \cdot 10^{-4}$
$[CoX_5X']^{3-}$	X=CN⁻	X⁻=SCN⁻	$2.7 \cdot 10^{-4}$

* T=293 K; ** T=308 K.

Investigation of ligand (Cl^-, Br^-) substitution in Co^{III} complexes with a mixed coordination sphere containing covalently bound and difficultly exchangeable molecular ligands [NH_3, en = $NH_2(CH_2)_2NH_2$; 1,2-pn = $CH_3CH(NH_2)CH_2NH_2$; 2,3-bn = $CH_3CH(NH_2)CH(NH_2)CH_3$] and relatively readily substituted acidoligands enables some useful conclusions to be drawn (Table 3). Chelating ligands (diamines) hinder dissociation of the $Co^{III}-Hal$ bond (where Hal is a halogen) more than NH_3. However, adding methyls to the diamine increases the rate of dissociation by weakening the Co–Hal bond and creating steric hindrances that stabilise the $[CoL_2Hal]^{z+}$ species with coordination number 5. Therefore, the rate constant for removal of Cl^- from the tetramethylethylenediamine complex is three orders of magnitude greater than that for the ethylenediamine complex. Obviously the dissociation takes the same path, *D*, with preliminary loss of Cl (Br^-) due to solvation and substitution by H_2O. The *trans*- and *cis*-effects are evident in $[CoL_2X_2]^+$ and $[CoL_4X_2]^+$ in which L is a diamine or NH_3, respectively. The presence of NO_2^- or N_3^- *trans* to Cl^- accelerates dissociation of the Co–Cl bond by 4–8 times. An analogous effect of Br^- on a bond *trans* to Co–Br is seen. Susbtitution of NH_3 by Br^- in the position *trans* to Br^- in *trans*-$[Co(en)_2LX]^{2+}$ accelerate the reaction by almost two orders of magnitude.

In an analogous situation, Cl^- weakens the Co–Cl bond by almost 200 times. The *cis*-effect was unexpectedly large in Co^{III} complexes. The *cis*-effect in these Co^{III} complexes is apparently even stronger than the *trans*-effect. All of the changes in the dissociation rate are probably not assignable to only the electronic influence of the atom *trans* or *cis* to the Co–Hal bond. An analysis of Table 3 leaves no doubt that other factors, especially solvation, play a large role. For example, the *cis*-effect in Co^{III} complexes on dissociation in H_2O can be visualised as stabilisation of species



due to an intramolecular H-bond.

Data on the structural and energy activation parameters and systematic investigations of the kinetics in nonaqueous and mixed solvents are not available. Therefore, the role of solvation in solvolytic dissociation of Co^{III} complexes cannot be found.

The mechanism of substitution of an anion X^- by water or a molecule of another solvent is apparently very complicated.[6] The role of the H-bond $X^-...H_2O$, which should be large, is not overlooked. The rate of cleavage of Co–X in $[CoL_5X]^{2+}$ increases in the halide series from F^- to I^- (for F, Cl, Br and I, k_v is 8.6×10^{-4}, 1.7×10^{-2}, 6.3×10^{-2} and 8.3×10^{-2} sec^{-1}, respectively). The reduction of the Co–X bond strength in this order affects the dissociation kinetics. Other anions in aqueous solution fall into the following order of dissociation rate: NO_3^- (0.27) > SO_4^{2-} (0.012) > $H_2PO_4^-$ (2.6×10^{-3}) > $CH_3CO_2^-$ (1.2×10^{-3}) > N_3^- (2.1×10^{-5}) > SCN^- (5×10^{-6}). This also clearly demonstrates the role of strengthening the Co–X bond in the dissociative mechanism *D*. Apparently a drop in the rate generally corresponds to an increase in K_s of $[Co(NH_3)_5X]^{2+}$.[6]

The K_s of these complexes borrowed from previous work[6] are presented in Table 4. Comparison of k_v and K_s indicates that a known correlation exists between the ease of breaking the Co–X bond and the stability of $[Co(NH_3)_5X]^{2+}$.

However, the relative dissociation rates and K_s do not agree. It should be remembered that K_s is not a measure of the M–X bond strength since formation of the complex in solution is related to desolvation of the reagents. The results presented in Table 3 leave open the possibility that Co^{III} complexes and those of other M^{III} dissociate by an interchange mechanism $S_N2(I_{a,d})$. The dissociation rate constants of $[CoL_4Cl_2]^{2+}$ can be several hundreds of times greater than k_v^{298} of $[CoL_5Cl]^{2+}$ whereas the corresponding ones for Rh^{III} complexes are the same. This suggests a possible bimolecular *cis* attack of the reagent (including solvent molecules) on the central atom near the Co–X bond.[6] For strongly covalent Rh^{III} chloride complexes, the attacking molecules contribute insufficiently to activation of a system reacting by the S_N2 mechanism to cause it to occur.

Kinetic data for substitution reactions of water in octahedral Co^{III} complexes and in other M^{III} and M^{II} complexes are very interesting to the chemistry of solvates.

Table 4. Rate constants of $[Co(NH_3)_5X]^{2+}$ at 298 K in aqueous solution.[6]
$[Co(NH_3)_5H_2O]^{3+} + X^- \leftrightharpoons [Co(NH_3)_5X]^{2+} + H_2O$.

Anion	K_s^{298}	Anion	K_s^{298}	Anion	K_s^{298}
NO_3^-	0.018	SO_4^{2-}	12.4	NO_2^-	10^{10}
Br^-	0.37	F^-	25	H_2O	0.018
Cl^-	1.25	CNS^-	470	NH_3	$2.5 \cdot 10^4$
$H_2PO_4^-$	7.4	OH^-	$2 \cdot 10^8$	–	–

Table 5. Kinetic parameters of H_2O substitution in the coordination sphere of $[CoL_5H_2O]^{3+}$, where L = NH_3, at 298 K in aqueous solutions.[6]
$[Co(NH_3)_5(H_2O)]^{3+} + X^- \leftrightharpoons [Co(NH_3)_5X]^{2+} + H_2O$.

X⁻	k_v, $dm^3\ mol^{-1}\ sec^{-1}$	Outer-sphere association constant*, sec^{-1}	Outer-sphere–inner-sphere conversion constant**, sec^{-1}
Cl^-	$2.1 \cdot 10^{-6}$	–	–
Br^-	$2.5 \cdot 10^{-6}$	–	–
NO_3^-	$2.3 \cdot 10^{-6}$	–	–
CNS^-	$1.3 \cdot 10^{-6}$	4.5	$2.9 \cdot 10^{-7}$
$H_2PO_4^-$	$2.0 \cdot 10^{-6}$	2.75	$7.3 \cdot 10^{-7}$
SO_4^-	$1.5 \cdot 10^{-5}$	11.2	$1.3 \cdot 10^{-6}$
NH_3	$2 \cdot 10^{-6}$	–	–
H_2O	$6.6 \cdot 10^{-6}$	–	$6.6 \cdot 10^{-6}$

*Formation constant of the associate of the complex with X^-.
**Conversion with loss of H_2O.

Rate constants for H_2O substitution in $[Co(NH_3)_5H_2O]^{3+}$ are given in Table 5. The substitution rate of H_2O by the acidoligand in octahedral monosolvates within experimental and calculational uncertainty is independent of the nature of X^- and averages $k_v \approx 2 \times 10^{-6}$ $dm^3\ mol^{-1}\ sec^{-1}$. Such a small rate constant is indicative of a rather covalent $Co^{III}-H_2O$ bond. Even for NH_3 the rate constant of H_2O substitution has such a value. The rate of exchange of H_2O by SO_4^{2-} is slightly greater. There is no doubt that the substitution reaction of H_2O in octahedral Co^{III} complexes follows the dissociative mechanism S_n1 (or D)

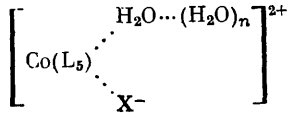
$$[CoL_5H_2O]^{3+} \underset{fast}{\overset{slow}{\rightleftharpoons}} [CoL_5]^{3+} + H_2O, \quad (13)$$

$$[CoL_5]^{3+} + X^- \underset{slow}{\overset{fast}{\rightleftharpoons}} [CoL_5X]^{2+}. \quad (14)$$

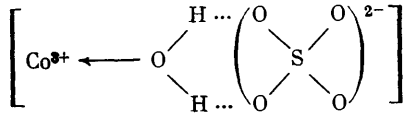
Therefore, the mechanism here is different from that of $[ML_3H_2O]^{2+}$, where M = Pt^{II} and others.

It has been proposed[6] that reaction (13) passes through formation of an outer-sphere encounter complex and that anion X^- enters the inner sphere from the outer. However, this does not provide a very detailed mechanism since outer-sphere associates (complexes) occur in practically all solutions of complexes and participate in practically all reactions. The intermediate $[CoL_5]^{3+}$ apparently does not accumulate (the probability of its formation is very small) during reaction of $[CoL_5H_2O]^{3+} + X^-$. It is a highly reactive species and reacts immediately. The high charge of the central atom facilitates this. The water exchange rate, i.e. dissociation of the $M-OH_2$ bond, in $[M(H_2O)_6]^{2+}$ is very fast[17] (k, sec^{-1}: Cr^{2+}, 7×10^9; Mn^{2+}, 3×10^7; Fe^{2+}, 3×10^6; Co^{2+}, 10^6; Ni^{2+}, 3×10^4; Cu^{2+}, 8×10^9).

Owing to the low covalency of the $M^{II}-H_2O$ bond in octahedral complexes, the probability of removing a water molecule from the coordination sphere of $[M(H_2O)_6]^{2+}$ is very large. Therefore, intermediates $[M(H_2O)_5]^{2+}$ are formed in one concentration or another on coordination of aquasolvates with various ligands. A different situation ensues for M^{3+} solvates. The transition state arising through exchange of a solvent molecule for X^- in octahedral complexes sterically shielded by ligands can be represented as the system



with a Co...OH_2 bond. From this H_2O migrates into the bulk solvent (into a vacancy in the second corodination sphere). As a result, a very weak bond to X^- forms. The reaction occurring by this path is second-order. The constant k_v in this instance does not depend on the nature of X^- since the energy demands for activation with any X^- are determined by the same process, cleavage of the $Co^{III}-OH_2$ bond and removal of H_2O. Entry of SO_4^{2-} (Table 5) into the Co^{III} aquasolvate introduces substantial corrections into the process since removal of H_2O is enhanced by SO_4^{2-}. There is a probability of forming the associate



II. Kinetics of complexation in organic solvents

We will now examine the reactivity of complexes in nonaqueous solvents, without touching upon the broad range of aqueous–organic solutions where the composition of the solvates is, as a rule, unknown. It has been correctly noted[6] that ability to investigate the kinetics and mechanisms of a reaction involving complexes in nonaqueous media is limited by the very low solubility of many complexes.

A very important feature of complexation in organic solvents[16] is the weaker solvation of simple acidoligands and the strong solvation of complicated organic acidoligands, especially inner-sphere types. Water readily forms solvates of simple inorganic acidoligands (F^-, Cl^-, Br^-, I^-, NO_3^-, ClO_4^-, SO_4^{2-}, etc.) and enhances solvolytic dissociation of complexes with these ligands and formation of simple solvates. If the acidoligand contains a hydrocarbon residue, water does not solvate it. Such an anion is unstable in aqueous solution

and remains within the complex or in the solid as a salt. The opposite picture is seen in many organic solvents.

Transition metal cations can be solvated more strongly in nonaqueous solvents than in water [for example, DMSO, DMF, NH_3, amines, simple chain polyethers (glymes), crown ethers, their N and S derivatives, etc.[18]] and more weakly (alcohols, simple monoethers, ketones, carboxylic esters, alkylsuphides, alkylphosphines, etc.). Solvation can be practically absent (alkanes, cycloalkanes) or very weak (alkenes, arenes).

Hence, the contribution of partial or complete loss of the solvation sphere on complexation in organic media to the energy and entropy of activation can be greater or less than in aqueous medium.

It is usually weaker than in H_2O. The structuring of the organic solvents can have a substantial effect on the reactivity of solvates. The possibilities of outer-sphere complexation and substitution of X^- in octahedral complexes (Table 6) with release of them into the outer sphere drop sharply.

Table 6. Rate constants of Co—X bond dissociation in organic solvents (k_v, sec^{-1}) at 303 K.[6]

Solvent	Complex		
	trans-$[Co(En)_2Cl_2]^+$	*trans*-$[Co(En)_2NO_2(Cl)]^+$	*trans*-$[Co(En)_2NO_2(Br)]^+$
H_2O	$1.2\cdot10^{-4}$	$2.8\cdot10^{-3}$	$4.2\cdot10^{-3}$
DMSO	$3.7\cdot10^{-5}$	$1.4\cdot10^{-4}$	$8.0\cdot10^{-4}$
DMF	$5.8\cdot10^{-6}$	$5.4\cdot10^{-5}$	$6.9\cdot10^{-4}$
Methanol	$2.0\cdot10^{-5}$	$2.0\cdot10^{-4}$	–

The rate of solvolytic dissociation of the Co^{III}—Hal bond decreases in the order H_2O > DMSO, CH_3OH > DMF. This is probably a result of the decreased total chemical affinity of the solvent for Hal and Co^{III}.

The ability of Co^{III} cationic complexes to form outer-sphere associates with X^- depends on the *cis*- or *trans*-configuration of $[CoL_4XY]^+$ and is determined by the size of the dipole moment of the complexes, the relative permittivity of the solvent and the degree of solvation of X^-.[6] Outer-sphere complexes (ion pairs) are formed more readily for *cis*-complexes than for *trans*-complexes.

A large amount of experimental data has been accumulated on reactions of *d*-metal solvates with porphyrins.[9,19] Porphyrins are far from the only ligands that can be used effectively to study the complex-forming reactivity of *d*-metal solvates.

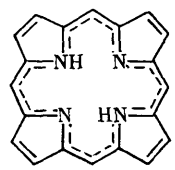
The method developed has been called the kinetic method of porphyrin indicator reactions.

III. Indicator reactions and the stability of *d*-metal coordination spheres

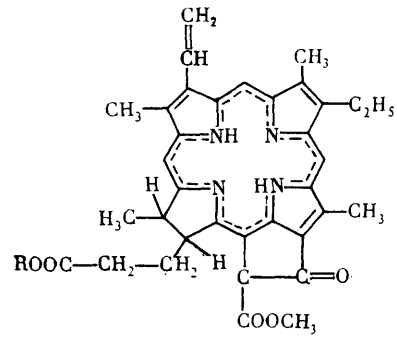
An indicator reaction between a solvate and a porphyrin (H_2P) (I) to form a porphyrin complex (MP)

$$[MX_mS_{n-m}] + H_2P \rightarrow MP + 2HX + (m-2)X^- + (n-m)S, \quad (15)$$

is a unique instrument for studying various solvate coordination spheres. Their composition in various salts, the relative stability of the M—S bond, and the variability as a function of solvent can all be found.[9,19,20]



(I)
Porphyrin nucleus



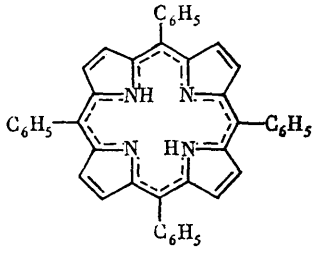
(II)
Chlorophyll ligand ($R = C_{20}H_{39}$)

A series of studies[21–28] has been carried out on the influence of the organic solvent and the structure of the transition-metal coordination sphere on the kinetics of complex formation with the most important natural porphyrin, the chlorophyll ligand (II). It was discovered that the inner coordination sphere of the metal determines the rate in addition to the energy and entropy of activation of the coordination. Therfore, coordination of H_2P by metal salts was called[20] the kinetic indicator reaction of porphyrins. The kinetic parameters of these reactions are very sensitive to the composition of the metal solvate coordination sphere, i.e. to the number and nature of ligands S and X^-.

Indicator reactions of porphyrins lie at the base of the kinetic method for studying the structure and properties of solvates. There apparently are few ligands that can be used successfully to study the change of composition, structure and properties of metal solvates as a function of concentration, solvent, temperature, the presence of force fields, etc., owing to the stringent requirements placed on kinetic indicator reactions.[20] The kinetic indicator reaction (15) should have a simple stoichiometry, i.e. its product should be the 1:1 complex (one metal per one ligand). Complexes with the indicator ligand should be kinetically and thermodynamically stable.[9] They should retain their composition and geometric configuration over the whole range of concentration changes of the coordinating solvent S and the acidoligands X^-. The reaction should proceed slowly enough to be easily controlled by ordinary chemical kinetics. One of the reagents should have a specific, accurately determined property, for example, a distinctive electronic absorption spectrum (EAS) with strong absorption bands. Porphyrins satisfy all these requirements. They form highly stable complexes MP of 1:1 composition. Their rate of formation is easily measured. Metalloporphyrins have distinctive EAS with very large molar absorption coefficients (ε) that reach 200 000. Therefore, formation of metal complexes with porphyrins is an ideal indicator reaction enabling a retention or change of the $[MX_m(S)_{n-m}]$ coordination sphere to be easily and quickly detected.

Ethanol homosolvates of MCl_2 (M = Fe, Co, Cd, Hg and Pd), $M(NO_3)_2$ (M = Co, Ni, Cu, Zn, Cd and Ag), $M(CH_3CO_2)_2$ (M = Co, Ni, Cu and Zn), MI_2 (M = Cd and Hg),[21–26] homosolvates of $Cu(CH_3CO_2)_2$ with monohydric alcohols, acetone, ethylacetate, dioxane, CH_3CO_2H, DMF, py and XL,[27–29] binary heterosolvates of $Cu(CH_2CO_2)_2$ and $Zn(CH_3CO_2)_2$ in CH_3CO_2H—ROH (R = CH_3,

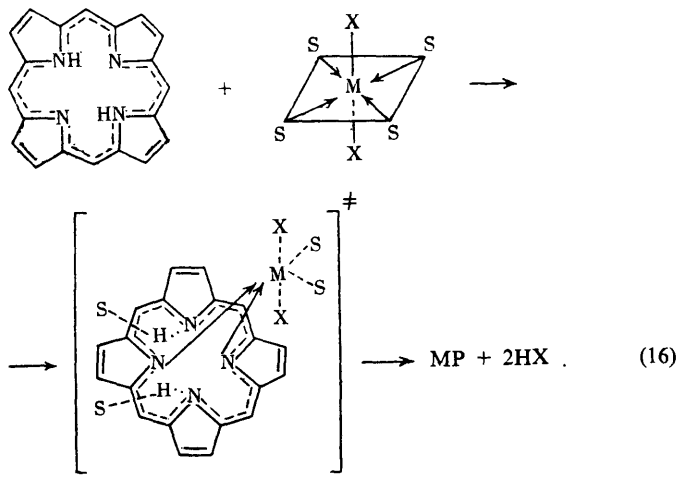
C_2H_5, C_5H_{11}), CH_3CO_2H–py, CH_3CO_2H–dioxane, CH_3CO_2H–acetone,[20,30] binary heterosolvates of Co^{II} and Zn^{II} acetates in CH_3CO_2H–ethylacetate, CH_3CO_2H–ethyleneglycol, CH_3CO_2H–monoethanolamine, CH_3CO_2H–CH_3OH, CH_3CO_2H–DMF, CH_3CO_2H–DMSO, CH_3CO_2H–py, CH_3CO_2H–H_2O, CH_3CO_2H–n-C_4H_9OH [31] and other solvates have been studied using indicator reaction (15) and II and tetraphenylporphine (III) as ligands. Systematic investigations carried out in our laboratory and those of others[9,20,31,32] demonstrated that the reaction of solvates of divalent 3*d*-metals with porphyrins in organic solvents follows very complicated kinetic laws.



(III)

The formation rate of MX_2 complexes with II, III and other porphyrins in addition to the energy and entropy of activation of reaction (15) are determined primarily by the steric relationship of both reagents, i.e. the macrocyclic effect;[3] the electronic structure of the porphyrin reaction centre (H_2N_4); the nature of the chemical bond M^{2+}←S, i.e. the nature of M and S; the presence of acidoligands X^- in the inner sphere and their number and nature; the compatibility of the various solvents S_1, S_2, etc., in the inner sphere of heterosolvates; the polarity and donor–acceptor nature of solvents S_1, S_2, etc. as media in which the reagents are activated, the solvation or desolvation of the transition state $[MX_2.H_2P]^{\neq}$; the removal of H^+ and X^- after overcoming the potential barrier; and the formation of metalloporphyrins MP or their solvates $(S)_iMP$.[33]

Compared with all other known complexation reactions, indicator reaction (15) proceeds extraordinarily slowly. Its rate typically is 10^6 times less than that of the other reactions. The bimolecular multicentered mechanism, denoted $S_{EN}2$ by the Ingold–Hughes classification or $I_{a,d}$ by Langford–Gray, is responsible for this. The transition state is formed by loss of two solvent molecules (S) from the inner sphere of the solvate, the weak coordinative interaction M←P, and lengthening of the two N–H...S bonds in the porphyrin:



$\longrightarrow$ MP + 2HX . (16)

The reaction with porphyrins of coordinatively saturated complexes, for example $HgCl_4^{2-}$ or HgI_4^{2-}, that do not contain solvent molecules also follows a bimolecular mechanism.[9] In this instance atoms are not lost from the coordination sphere as the transition state is approached. The coordination sphere of MX_4^{2-} in the transition state is probably only deformed. This produces instead of the tetrahedral configuration a distorted octahedron with two vacant coordination sites that are necessary for bonding to two tertiary N atoms of the porphyrin. The reaction mechanism is also denoted $S_{EN}2$. The octahedral acidocomplexes $[Fe(CN)_6]^{3-}$ and $[Fe(CN)_5H_2O]^{2-}$ or the covalent molecular-ligand complexes $[Co(NH_3)_6]^{3+}$ and $[Co(NH_3)_5H_2O]^{3+}$ do not have the required number (two or more) of solvent molecules to experience compression of the coordination sphere. Therefore, the above salts cannot react with porphyrin even under forcing conditions.

Porphyrins are molecular ligands that lose two H^+ during complex formation. Therefore, complexation reaction (15) follows a $S_{EN}2$ mechanism. Hence, H_2P is simultaneously electrophilic and nucleophilic.

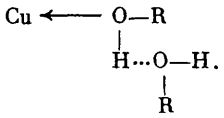
Table 7. Kinetics of formation of Cu(Chl) from $[CuAc_2(S)_4]$ and the chlorophyll ligand in organic solvents (S).[9]

S	k_7^{298}, $dm^3\ mol^{-1}\ sec^{-1}$	E, $kJ\ mol^{-1}$	$\Delta S^{\neq}$, $J\ mol^{-1}K^{-1}$	*DN* *
CH_3OH	4.45	58	−17	(30)
C_2H_5OH	1.65	44	−96	(32)
n-$C_5H_{11}OH$	0.555	113	126	(25)
CH_3COCH_3	0.905	46	−67	17
$O(CH_2CH_2)_2O$	0.046	72	−25	14.8
CH_3COOH	5.30	44	−79	20
$(CH_3)_2NCHO$	0.036	79	−8	26.6
C_5H_5N	0.0092	96	37	33.1
C_9H_7N	0.028	100	+63	32
$CH_3COOC_2H_5$	0.515	61	−63	17.1

*Estimated *DN* are given in parentheses.

An examination of the indicator reaction mechanism would seem to indicate that its rate and activation parameters should depend on the structure and stability of the inner coordination sphere in general and on the structure and stability of the solvation sphere in particular. The rates of formation of complexes from homosolvates of $[CuAc_2(S)_4]$ in various solvents are listed in Table 7. The stability constants of the homosolvate salts have not been determined. The relative stability of the copper acetate solvation sphere can be judged from the donor numbers (*DN*). It is clear from Table 7 that the reaction rate tends to decrease at the same time as the activation energy increases and *DN* increases, i.e. as the strength of the Cu–S bond increases and the solvation sphere becomes stronger. However, there are several exceptions to this rule. Methanol forms a stronger solvate and reacts faster than ethanol and especially propanol. Attention should be drawn to the donor numbers in parentheses in Table 7. In alcoholic solutions $SbCl_5$ is extensively solvolysed. Therefore, it is difficult to determine the electron-donating ability of alcohols relative to $SbCl_5$.

In estimating the change of electron-donor properties of various alcohols relative to metal salts, their structure and known properties should be considered. Methanol should form stronger solvates than ethanol firstly because conditions are favourable for formation of a second solvation sphere in its solvates. This second sphere stabilises the first by forming H-bonds to coordinated CH_3OH. As the alkyl chain lengthens, steric hindrances to the interaction are created



This interaction facilitates formation of the second and successive alcohol solvate spheres. Secondly, the electron-donor ability of the electron pair of the alcohols depends little on the size of the alkyl group, i.e. on its inductive effect. Therefore, the electron- and proton-donor properties of uncoordinated CH_3OH and C_2H_5OH are almost identical. The higher $\Delta S^{\neq}$ and E for methanol are due to the presence of a second solvation sphere.

The rate of coordination of solvates by porphyrins is affected by the exchange conditions of coordinated solvent molecules with the medium. The rate of exchange substantially decreases and the conditions for it worsen for alcohols as the length of the alkyl chain and other large molecules increases. This feature of solvates formed by large molecules has been called steric hindrances of the solvation sphere.[9] They are created during attack of the solvation sphere of such a hugh reagent as a porphyrin. We are inclined to assign the increase in energy and entropy of activation and the decrease of reaction rate of $CuAs_2$ solvates with pentanol, dioxane, DMF, py and quinoline to steric hindrances of the solvation sphere. As we suppose, such hindrances lead not only to loss of two solvent molecules but also to deformation of the remaining sphere of ancillary ligands.[34] There is no doubt that steric hindrances created by a huge coordination sphere will affect the kinetics of reactions between many large ligands with a shielded reaction centre.

An important property of the indicator reaction (15) is the dependence of its rate on the concentration of a 3*d*-metal salt (the so-called 'concentration' dependence of the rate constant) and of a coordinating or uncoordinating salt background,[25,26,35] where the porphyrin does not change but the structure of the coordination sphere of the 3*d*-metal salt does. Results characterising the influence of concentration of 3*d*-metal salt on the formation rate of chlorophyll (Chl) analogues with Cu^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+} and Cd^{2+} are presented in Table 8.

Evidently the coordination spheres of $[CuAc_2(C_2H_5OH)_4]$ are rather stable as the salt concentration changes from 2.5×10^{-4} to 25×10^{-4} mol dm^{-3} since the concentration dependence of k_v is very weak. The dependence of k_v on salt concentration increases in the order $CdAc_2 < Co(NO_3)_2 < Ni(NO_3)_2$. This order apparently corresponds to the ease with which the composition and structure of the coordination sphere changes and the number of solvate forms increases, i.e. the stability of the coordination sphere of $[MX_2(S)_4$ decreases.

Therefore, the kinetic method of porphyrin indicator reactions enables the uniqueness or variety of solvate coordination spheres to be judged. It follows from Table 8 that ethanol solvates of Ni^{2+} and especially Co^{2+}, compared with those of Cu^{2+} and Cd^{2+}, have a much lower ability to complex porphyrins. However, the reactivity of solvates can depend strongly on the nature of the porphyrin and solvent. It is important that not only k_v but also more frequently E and $\Delta S^{\neq}$ change on changing the composition of the solvate.[9,19,26,35]

The methanol solvate of $CoCl_2$ (Table 9) has many forms in solution. Therefore, the concentration dependence of k_v is very strong. Increasing the concentration of $CoCl_2$ in methanol shifts the equilibrium toward the stable forms of low reactivity. The situation is the same for $CoAc_2$ in methanol.

Table 8. Coordination-sphere stability of solvates and concentration dependence of formation rate constants (k_v) of metalloporphyrins, chlorophyll (MChl) analogues, in ethanol at 298 K.[9]
$MX_2 + H_2Chl \rightarrow MChl + 2\,HX$.

MX_2	$10^4\,C_{MX_2}$, M	True k_v, dm^3 mol^{-1} sec^{-1}	E, kJ mol^{-1}	$\Delta S^{\neq}$, J mol^{-1} K^{-1}
$CdAc_2$	1.25	1.55	13	−62
	3.75	1.55	–	–
	25	0.75	–	–
$Zn(NO_3)_2$	2.5	0.415	59	−67
	25	0.0720	59	−52
$Co(NO_3)_2$	25	0.00295	100	44
	250	0.00189	75	−44
$Ni(NO_3)_2$	2.5	0.0394	99	60
	25	0.0095	65	−64
$CuAc_2$	2.5	1.64	44	−109
	25	1.60	44	−109

Table 9. Influence of a salt background on coordination-sphere stability of methanol solvates in Co(Chl) formation reactions.[20]
$H_2Chl + [CoX_m(S)_{n-m}] \rightarrow Co(Chl) + 2\,HX + (m-2)\,X^-$.

Reagent salt MX_2	Background salt MX	Concentration of reagent salt, $c\,10^3$ M	k_v^{298}, dm^3 mol^{-1} sec^{-1}	E, kJ mol^{-1}	$\Delta S^{\neq}$, J mol^{-1} K^{-1}
$Co(NO_3)_2$	–	2.5	$2.56 \cdot 10^{-3}$	43	−161
$Co(NO_3)_2$	3M $LiNO_3$	2.5	$2.40 \cdot 10^{-2}$	56	−87
$CoCl_2$	–	2.5	$1.78 \cdot 10^{-3}$	65	−93
$CoCl_2$	–	25	$3.10 \cdot 10^{-4}$	67	−87
$CoCl_2$	2M LiCl	2.5	$4.90 \cdot 10^{-3}$	52	−114
$CoCl_2$	2M LiCl	25	$1.89 \cdot 10^{-3}$	50	−128
$CoAc_2$	–	2.5	$1.32 \cdot 10^{-2}$	99	+52
$CoAc_2$	–	25	$3.40 \cdot 10^{-3}$	83	−15
$CoAc_2$	2M LiAc	2.5	$1.11 \cdot 10^{-3}$	–	–
$CoAc_2$	2M LiAc	25	$1.13 \cdot 10^{-3}$	86	−12

Addition of LiAc stabilises the form $[CoAc_4]^{2-}$. This causes the dependence of k_v on $CoAc_2$ concentration to vanish.

A detailed analysis of the kinetic data demonstrated that the dependence of k_v (and also E and $\Delta S^{\neq}$) on 3*d*-metal salt concentration is mainly determined by the change of properties of $MX_2(S)_{n-2}$. Similar changes of k_v in aqueous solutions have usually

been ascribed to a change of the salts activity coefficient. For the example involving 3*d*-metal salts in organic solvents that are incapable of solvolytic dissociation

$$MX_2(S)_{n-2} \overset{+S}{\rightleftharpoons} [MX(S)_{n-1}]^+ + X^- \quad (17)$$

$$[MX(S)_{n-1}]^+ \overset{+S}{\rightleftharpoons} [M(S)_n]^{2+} + X^- \quad (18)$$

the reaction proceeds without involving the ions, i.e. with a small change of salt activity coefficient as classically interpreted.

As the salt concentration increases, the geometry of the solvate can change owing to a shift of autocomplexation equilibria, the isomerisation *cis*-octahedron $\rightleftharpoons$ *trans*-octahedron, changes in the degree of solvation

$$MX_2(S)_4 \rightleftharpoons MX_2(S)_2 + 2S,$$

loss of the second solvation sphere, a reduction of the solvating ability of the solvent, salt dimerisation, etc.

In this instance, the lack of a concentration dependence of k_v (and also $\Delta S^{\neq}$ and E) is consistent with a stable salt coordination sphere within the given concentration range. On the other hand, the presence of such a dependence means that the initial coordination sphere is unstable and changes.

Kinetic data for the indicator reaction (15) occurring in the presence of a salt background (Table 9) suggest whether the complex coordination sphere is stable and if stabilising conditions can be found.

It follows from Table 9 that the inert (noncoordinating) background salt $LiNO_3$ has a different effect from that of a coordinating salt (LiCl, LiAc) which can provide inorganic ligands (Cl^-, Ac^-) for the Co^{II} solvate.

Lithium nitrate does not change the EAS of $Co(NO_3)_2$. It can be concluded on the basis of the EAS[35] that $Co(NO_3)_2$ in methanol exists as the octahedral complex $[Co(CH_3OH)_6]^{2+}$. In the presence of $LiNO_3$, ion pairs of the type shown below can form

$$Co^{2+} \longleftarrow \overset{CH_3}{\underset{|}{O}}—H\cdots NO_3^-$$

and partially $Co^{2+} \leftarrow NO_3^-$.

Therefore, NO_3^- ions reduce the stability of the solvate. The formation rate of Co(Chl) increases almost 10 times on adding $LiNO_3$. The energy and entropy also considerably increase. Free methanol molecules are practically nonexistent in 3 M $LiNO_3$. Therefore, the acceleration of the indicator reaction can be attributed to weakening of the bonds in the fragments

$$Co^{2+} \longleftarrow \overset{CH_3}{\underset{|}{O}}—H,$$

associated with NO_3^- in addition to a decrease of solvation in the transition state ($\Delta S^{\neq}$ increases by 74 J mol^{-1} K^{-1}; the activation energy, by 13 kJ mol^{-1}). The increased solvation in the transition state apparently destabilises the latter.

In the presence of a coordinating salt background, the Co(II) solvate is transformed into complex acidoligands $[CoCl_4]^{2-}$, $[CoCl_5]^{3-}$, etc. The promoting action of the salt background becomes weaker (LiCl) or changes into inhibiting action (LiAc) as a result of stabilisation of the solvate coordination spheres in $[CoX_n]^{2-n}$.

The existence of a concentration dependence in the system $H_2Chl + CoCl_2 + LiCl$ leaves no doubt that the series of acidocomplexes $[CoCl_3]^-$, $[CoCl_4]^{2-}$ and $[CoCl_5]^{3-}$ exists in the presence of LiCl in methanol. These differ little from each other in entropy and enthalpy of activation. Lithium acetate converts the $CoAc_2$ solvate into a single stable coordinated form $[CoAc_4]^{2-}$. This is kinetically 10 times less active in the indicator reaction where Co(Chl) is formed. The lack of a concentration dependence of k_v^{298} in methanolic LiAc is consistent with the lack of other coordinated forms of $CoAc_2$.

However, the effect of background salts on the stability of 3*d*-metal solvates depends strongly on the organic solvent. It has been found[25] that LiCl slows the coordination of the CoX_2 solvate with H_2Chl in *n*-pentanol, in contrast with methanol. However, LiAc accelerates it. This opens wide possibilities for using indicator reactions to study the influence of solvent containing salt on the solvates of a reagent. Even more promising is the use of this method to investigate mixed solvates of 3*d* -metals in binary organic solvents.

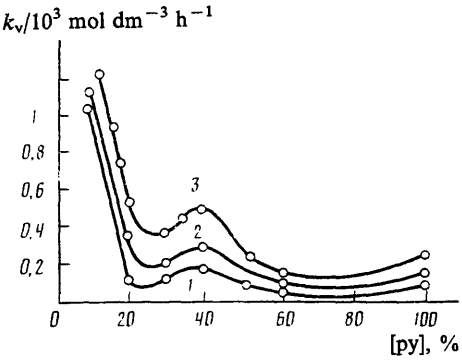


Figure 2. Dependence of formation rate constant of Cu(Chl) in CH_3CO_2H—py on medium composition at: 298 (*1*), 318 (*2*), 328 K (*3*).[30]

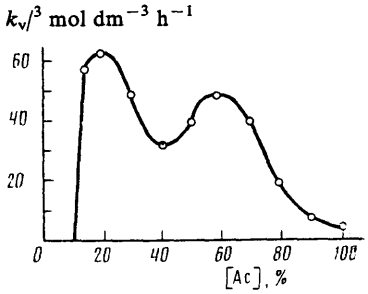


Figure 3. Dependence of formation rate constant of Cu(Chl) in CH_3CO_2H—CH_3COCH_3 on medium composition at 298 K.[30]

Formation of the analogues Cu(Chl) and Zn(Chl) in the systems CH_3CO_2H—coordinating solvent and py—coordinating solvent has been studied.[30] For concentrations of coordinating solvent in CH_3CO_2H from 0 to 100%, kinetic curves of composition *vs.* property were obtained. Lots of composition—rate of indicator reaction (Figs. 2 and 3), composition—activation energy (energy curves), and composition—entropy of activation (structure curves) (Fig. 4) all have peaks.

Concentration dependences of the formation rate of Cu(Chl) from $CuAc_2$ and H_2Chl in the systems CH_3CO_2H–py and CH_3CO_2H–acetone are plotted in Figs. 2 and 3, respectively. These data reflect the change of properties of the binary solvent (its solvating ability) and the change of stability of Cu^{II} solvates as a function of medium composition. Addition of a strongly coordinating component (py, ROH, acetone, dioxane, etc.) to CH_3CO_2H causes a gradual destruction of its dimeric structure $(HAc)_2$, accumulation of solvates $CH_3CO_2H...S$ and a subsequent transition to the structure of the solvent. As the medium composition changes, the mixed solvation sphere of $[MX_2(CH_3CO_2H)_4]$ converts successively to a mixed solvent sphere $[MX_2(CH_3CO_2H)_{4-m}S_m]$†, and then to $[MX_2(S)_{n-2}]$. Formation of $[MX(S)_{n-1}]^+$ and $[M(S)_n]^{2+}$ is also possible.

It is noteworthy that solvates of only divalent cations are examined here. Solvates of MX_3 and MX_4 do not react with porphyrins under ordinary conditions and cannot presently be investigated by porphyrin indicator reactions.

It has been demonstrated[36] that small additions of a second component to a pure solvent greatly changes the structure of the latter, causing either a loss of structure (destabilisation) or higher degree of structure (stabilisation). Destabilisation of the intrinsic solvent structure increases its solvating power whereas stabilisation reduces it.

In our opinion, the increased rate of reaction (15) observed in the majority of cases in CH_3CO_2H with small additions of a strongly coordinating solvent is due to destruction of $(CH_3CO_2H)_2$ dimers and an increased solvation of the transition state [cf. equation (16)] in addition to the destabilisation of the CH_3CO_2H–cation bond that favours reaction (16).

It can be stated that where two or more molecules of a weakly coordinating solvent enter the coordination sphere of *d*-metals they make a poor match. If a strongly coordinating solvent (S_c) enters the inner sphere of MX_2, the effective charge on the metal decreases, the initial M–S bonds are destabilised, and the ability to substitute S increases. In all probability, a similar type of competition for a coordination site arises between any pair of solvents differing in donor–acceptor numbers.

The change of kinetic parameters with large additions of a coordinating component,[20] as demonstrated previously,[31] is caused by substitution of HAc by S_c in the first solvation sphere. Thus, all mixed (HAc–py) $CuAc_2$ solvates are less active than the pure HAc ones. The maximal complexation rate is reached with 40% py. This can be attributed to the special properties of the CH_3CO_2H–py associate that dominates the solvent structure in this range. The second maximum on the curve corresponds to accumulation of the associate and produces a maximum in E and $\Delta S^{\neq}$ (Fig. 4). The first maximum at 20% py represents complete substitution of the very weak ligand CH_3CO_2H by the strongly coordinating py. In HAc and alcoholic solutions, $CuAc_2$ is known[31] to exist as a dimer. However, Cu_2Ac_4 has been found to be unreactive toward porphyrins.

Addition of a strongly coordinating solvent to an HAc solution shifts the equilibrium of the dimer

$$2[CuX_2(S)_{n-2}] \rightleftharpoons [Cu_2X_4(S)_4] + (n-6)S, \qquad (19)$$

where X^- is any carboxylate, toward the monosolvate. As the dimer breaks up, the monosolvate $[CuX_2(S_c)_{n-2-m}(HAc)_m]$ accumulates, i.e. HAC is lost from the inner sphere. This process occurs in parallel with the change in composition of the solvation sphere of the monosolvate, which is present in small quantities in HAc (about 0.1%) and alcoholic solution, and corresponds exactly to this change.

The dimers and their break-up by large amounts of S_c undoubtedly affect k_v. However, they do not change the nature of the dependence of k_v on solvent composition (Fig. 2) and even more the nature of the structure–kinetic curves (Fig. 3) since they do not affect the energy and entropy of activation.

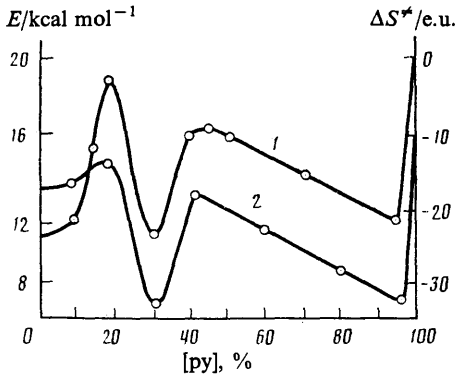


Figure 4. Dependence of energy (*1*) and entropy of activation (*2*) for Cu(Chl) formation in CH_3CO_2H–py on medium composition at 298 K.[20]

This conclusion is also supported by the fact that the curves shown in Figs. 2 and 3 are completely identical if the total concentration of $CuAc_2$ is changed by 10–100 times.

The kinetics of complexation in the mixed solvent HAc–acetone are especially interesting. The reaction sharply accelerates and the rate constant increases three times with even 1% acetone added. In view of the weak basicity and small size of $CO(CH_3)_2$, such an effect cannot be related to a change of properties of HAc as a solvent. The activity of the first mixed acetone–HAc solvate in reaction (15) is so high that even trace amounts cause a large effect. It can be assumed that acetone (ketones) is highly effectively coordinated to copper salts since π-backbonding is possible.

The path of the composition–rate curves suggests that all mixed acetone solvates of $CuAc_2$ are more highly reactive than HAc solvates, which are some of the most reactive solvates (Table 7). It is assumed that the first maximum on curve *1* (Fig. 2) corresponds to the first mixed solvate $[CuAc_2(C_2H_6CO)(HAc)_3]$; the minimum, to the second; and the third, to the third solvate $[CuAc_2.(C_2H_6CO)_3(HAc)]$. The solvate $[CuAc_2(C_2H_6CO)_4]$ is six times less active than $[CuAc_2(HAc)_4]$.

We are inclined to ascribe the elevated reactivity of mixed acetone solvates to the *trans*-effect of acetone in octahedral copper complexes and to its labilising action on bound HAc.[20] The catalytic action of acetone was also observed for Co^{II} salts. The *trans*-effect is proposed to occur in mixed HAc solvates of $CoAc_2$ with py, DMSO and DMF. It can stabilise the transition state of an indicator reaction.

The rate of complexation of tetraphenylporphine (H_2TPP) is slower for all mixed acetone–HAc solvates of $ZnAc_2$ than for the

†The inner coordination sphere is shown in square brackets; the outer sphere is not indicated.

pure HAc solvate. In these instances, there are no maxima on the composition–rate curves. The minima in the energy and entropy on the composition–energy (entropy) of activation curves correspond to the maximal accumulation of mixed acetone–HAc solvates of $CoAc_2$.

Individual rate constants for reactions involving mixed solvates of $ZnAc_2$ and $CoAc_2$ were first obtained by Golubchikov.[31] In these reactions one (k_1) or two (k_2) molecules of HAc in the inner sphere are replaced by a coordinating solvent. The data presented in Table 10 show that entry of one solvent molecule of any kind into the solvation sphere of $ZnAc_2$ instead of weakly bound HAc decreases the coordinating ability by about 2 times; two molecules, by 4–15 times. Under analogous conditions the reactivity of $CoAc_2$ in saturated solvents (excluding monoethanolamine) changes little. The strong catalytic effect in py, DMSO and DMF may be due to a *trans*-effect. Monoethanolamine forms a monosolvate $\{CoAc_2(HAc)_2[NH_2(CH_2)_2OH]\}$ in which the chelate is tightly bound to Co^{II} by the NH_2-group and weakly by the OH-group. In our opinion, the 10-fold increase of rate of coordination to monoethanolamine is explained by the interaction of the OH-group in the transition state with the leaving HAc ligand or an ancillary Ac^- ligand. This enhances the reaction.

Table 10. Individual rate constants of tetraphenylporphine coordination by $ZnAc_2$ and $CoAc_2$ solvates $MAc_2(HAc)_4$, $MAc_2(HAc)_3(S)$ and $MAc_2(HAc)_2(S)_2$ at 298 K.[31]

Reagent salt	Coordinating solvent (S_c)	Rate constants, $dm^3\ mol^{-1}\ sec^{-1}$		
		k_0	k_2	k_1
$ZnAc_2$	HAc	38.5	–	–
	Py	39.0	26.8	6.4
	DMSO	37.8	18.8	2.3
	DMF	39.5	14.1	–
	Butanol	39.0	19.1	8.2
	H_2O	18.7	10.9	5.0
$CoAc_2$	HAc	0.100	–	–
	Py	0.095	0.478	0.670
	DMSO	0.109	0.199	1.21
	DMF	0.079	0.71	–
	Butanol	0.105	0.111	–
	H_2O	0.083	0.064	0.043
	Methanol	0.096	0.096	0.096
	Ethanol	0.106	0.110	–
	Ethyleneglycol	0.105	0.090	0.037
	Monoethanolamine	0.100	0.97	–

A combination of porphyrin indicator reactions and thermodynamic methods is especially effective for investigating the reactivity of individual solvates by the kinetic method. This approach has been successfully used to investigate the state of Cu^{II} carboxylates, including dimers, in binary solvents (consisting of coordinating and weakly coordinating solvents[37,38]).

In conclusion, the special role of solvates in the coordination chemistry of solutions must be emphasised. The chemistry of complexes begins with just these complexes, which are formed during dissolution of metal salts in aqueous and nonaqueous solvents. Methods for preparing the complexes are based on substitution of solvent–ligands by ligands of any other type (molecular, acidoligands, inner-sphere, macrocyclic, etc.). The lack of sufficient data on the structure, stability and reactivity of solvates impedes development of many concepts of the theory of ligand substitution, the theory of their stability in solutions, and the optimal methods of synthesis. Taking into account the importance of solvates to electrochemistry, hydrometallurgy, analytical chemistry of nonaqueous solutions, homogeneous and heterogeneous catalysis, biochemistry and other practically important areas it becomes obvious that efforts need to be focussed on a systematic study of them.

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Translated from *Uspekhi Khimii* 60 1969–1998 (1991) U.D.C. 546.65.386

Features of the complexation of trivalent rare earths

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ABSTRACT. Reasons why chelates of rare earths (RE) do not obey the tetrad 'doublet' effect are discussed. The examination is based on the concept of an ionic metal–ligand bond in RE complexes. The mutual influence of ligands in lower, higher, polynuclear and mixed complexes formed by ligands of low, medium and high denticity is discussed from this viewpoint. Intermolecular interactions in complexes of various structure are examined relative to variations in the volatility of chelates and their selectivity in sublimation and deposition. Structural rearrangement occurring at different points in the RE series for different ligands is proven to be the reason behind the irregular change of properties of RE complexes as a function of RE ionic radius.

A bibliography with 42 citations is given.

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I. Introduction

The predominantly ionic nature of the RE^{III}–ligand bond has been cited as the main feature of RE (Sc, Y, La, Ce–Lu) complexes in previously published reviews.[1,2] The most important consequence of the ionic bonding is a high and variable coordination number (CN) for RE.[3] During the last decade, new evidence supporting such an approach for analysing the nature of the bonding in RE complexes has been gathered. The ionic bond, with a small covalent contribution, does occur. However, questions about the size of the covalent contribution to the metal–ligand bond in such compounds is still actively discussed. A consensus has not been reached. Therefore, in this review we direct special attention to this aspect of RE coordination chemistry.

Problems of RE^{III} complexation are discussed using complexes with organic ligands of various classes as examples (abbreviations for these ligands are given below):

a) Aminocarboxylic acids:

H_4EDTA—ethylenediaminetetraacetic acid
H_5DTPA—diethylenetriaminepentaacetic acid
H_2EDDA—ethylenediaminediacetic acid
H_3NTA—nitrilotriacetic acid
H_2IDA—iminodiacetic acid
Hal—α-alanine
Hgl—aminoacetic acid (glycine)

b) Carboxylic and hydroxycarboxylic acids:

HA—acetylacetone
HDPM—dipivaloylmethane
HPiv—pivalic acid

c) β-diketones:

HA—acetylacetone
HDPM—dipivaloylmethane
HPTFA—pivaloyltrifluoroacetone
HAcim—acetylacetoneimine

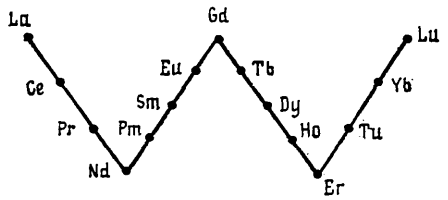
d) Neutral ligands with N and O donors:

phen—*o*-phenanthroline
bipy—α,α′-bipyridyl
py—pyridine
DMSO—dimethylsulphoxide
MESO—methylethylsulphoxide
DMF—dimethylformamide
THF—tetrahydrofuran
HMPA—hexamethylphosphortriamide
TPPO—triphenylphosphineoxide
TBP—tributylphosphate
3(4) – Pic—3(4)-picoline

II. The 'tetrad' effect and the nature of the chemical bond in RE coordination compounds

Let us recall that the tetrad effect consists of the periodic change of properties in the 15-membered RE series La, Ce–Lu.[4,5] This enables the series to be broken into four 'tetrads' corresponding to

the four straight lines in the letter 'W':



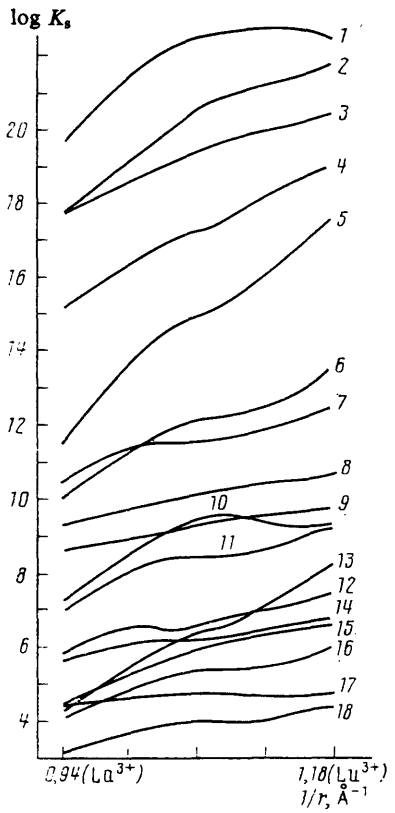


Figure 1. Dependence of lg K_s (K_1, K_2 or β_2) on RE^{III} ionic radius: M(DTPA)$^{2-}$(K_1) (*1*); M(NTA)$_2^{3-}$ (β_2) (*2*); M(DPM)$_2^{+}$(β_2) (*3*); M(EDTA)$^{-}$(K_1) (*4*); M(EDDA)$_2^{-}$ (β_2) (*5*); M(IDA)$_2^{-}$(β_2) (*6*); M(NTA)(K_1) (*7*); M(DPM)$^{2+}$(K_1) (*8*); M(DPM)$_2^{+}$(K_2)(*9*); M(NTA)$_2^{3-}$ (K_2) (*10*); M(EDDA)$^{+}$(K_1) (*11*); M(EDDA)$_2^{-}$ (K_2) (*12*); M(IDA)$^{+}$(K_1) (*13*); M(NTA)(OH)$^{-}$(K_2) (*14*); M(EDDA).(OH)(K_2) (*15*); M(IDA)$_2^{-}$(K_2) (*16*); M(al)$_2^{+}$(K_1) (*17*); M(gl)$_2^{+}$(K_1) (*18*)

Many articles published over the last few years on the chemistry of RE compounds, including complexes, have tried to prove that there is a tetrad effect [or double-u (W) or double–double effect]. It has been assumed that its detection is a direct indication of the reliability of new results obtained. However, such a position is incorrect since the change of properties in RE complexes, especially if their structure is complicated, frequently does not exhibit a W-shaped nature. We read, 'There are only a few ligands for which the rules are observed over the whole RE series and many for which such rules are observed for only a part of the series' (Ref. 6, p. 185).

It must also be noted that even if the dependence in coordinates of property–RE atomic number is W-shaped, in other coordinates, for example property–RE^{III} ionic radius, the dependence is not W-shaped but monotonic.

Let us examine as an example the dependence of lg K_s for RE complexes of polyaminocarboxylic acids on the inverse of the RE^{III} ionic radius. It is clear from Fig. 1 that the W-rule is not obeyed.[7,8] More often than not the curves are smooth and sometimes, for example for EDTA, the dependence of lg K_s on $1/r$ is practically a straight line.

In our opinion, the latter example is of prime importance. It indicates that the bonding in RE complexes is predominantly ionic since the coulombic force itself, which determines the strength of the complexes, is inversely proportional to the distance (its square) between the interacting centres of positive (RE cation) and negative (ligand) charge. This in turn depends on r.

The dependence of the properties of RE complexes not on $1/r$ but on atomic number is plotted in Fig. 2.[6] The similar W-shaped changes of average free energy of complexation ($\Delta\overline{G}$) and ionic radii are interesting. This indicates that the ionic radius itself is the principal factor determining the properties of RE compounds including $\Delta\overline{G}$ of complexation. Since both quantities exhibit a W-shaped change in the RE series, it is obvious that the dependence of $\Delta\overline{G}$ on r will not be W-shaped. In fact, this same conclusion was made before.[6] According to the previous report,[6] since all described properties reflect the lanthanoid† contraction, it follows that this contraction is not a smooth function of Z (atomic number).

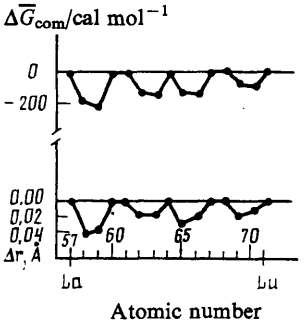


Figure 2. Dependence of average free energy of complexation $\Delta\overline{G}_{com} = \Delta G_{exp} - \Delta G_{int}$ (*a*) and RE ionic radii $\Delta r = r_{exp} - r_{int}$ (*b*) on atomic number.[6]

Therefore, the principal reason for the W-effect is taken to be the controlling influence of changes of radius (atomic, ionic) in the RE series on properties of the compounds. Consequently, the W-shaped dependence on atomic number is seen for those properties that depend on the RE^{III} ionic radius, i.e., have an ionic nature.

† Correctly stated 'lanthanide' and not 'lanthanoid' contraction (Ref. 9 p. 10) (author's note).

The W-shaped dependence can be converted into a smooth one (sometimes linear) by changing the 'atomic number' coordinates into 'ionic radius' (Fig. 1). This indicates that the ionic component predominates in the chemical bonding in RE complexes. Moreover, a deviation from linearity (ideality) in property–radius coordinates can be qualified as a result of the superposition of other factors, primarily, stereochemical hindrances, a covalent contribution and structural changes in the RE series.

In this sense, plotting graphs of any property of RE compounds in property–atomic number coordinates is uninformative since the dependence of the examined property on ionic radius taints all effects. If the plot is made in property–ionic radius coordinates, those factors that are specific for the given system and not for the RE series in general will be identified. Thus, the irregularities in the functions $\lg K_s = f(1/r)$ (Fig. 1) indicate[7,8] at what place in the RE series the structure of the RE complexes changes and how the covalent contribution influences the strength of the complexes if their structure is mainly determined by the ionic contribution.

The dependence of the properties of RE complexes, for example their stability, on ionic radius has a well interpreted physical meaning. It suggests that a decrease of metal ionic radius, makes the metal–ligand bond in the complex stronger. This follows from Fajans simple polarisation theory (for example, cf. Ref. 9, pp 25–40). According to this, the polarising effect exerted on the ligands by RE^{III} cations with a hard rare-gas outer electron shell ($5s^25p^6$) increases from La^{3+} to Lu^{3+} (and from La^{3+} to Sc^{3+}) owing to an increased positive charge density on these cations. As a result, the ligand unavoidably draws nearer to the metal. This increases the metal–ligand electrostatic interaction and simultaneously increases the covalent contribution to the chemical bond (especially if the ligand or its separate functional groups can be polarised).

It is noteworthy that RE^{III} ions, which have a rare-gas configuration, can present only energetically unfavourable vacant 5*d*-, 6*s*- and 6*p*-orbitals and unfilled 4*f*-orbitals, which are highly shielded by the $5s^25p^6$ electrons, to the ligands for formation of covalent donor–acceptor bonds. The small degree of participation of 4*f*-orbitals in complex formation is well documented. For example, the small shifts of absorption bands in RE electronic spectra even on formation of very strong complexes with polydentate ligands provide evidence for this (Ref. 8, pp 5–23, 65–76). This is also supported by the low stability of RE complexes with monodentate ligands (including strong-field ligands such as CN^-, CO, etc.). Only the chelate effect arising on formation of RE complexes with polydentate ligands substantially increases the stability of the RE^{III} complexes. For example, K_s of Nd^{III} complexes with $EDTA^{4-}$ and $DTPA^{5-}$ are 10^{16} and 10^{22}, respectively.

Furthermore, since the ratio between the ionic and covalent contribution to the RE^{III}–ligand bond is often poorly defined, the choice of coordinates for examining the dependence of properties on position of the metal in the RE series is made arbitrarily in many instances.

For example, we learn (Ref. 10, p. 205) that *'additional effects* of stabilisation resulting from the influence of the ligand field and spin–orbit coupling are determined by the number of *f*-electrons. Therefore, the correct correlation for revealing *all effects that determine the bond energy* is the dependence on the number of *f*-electrons, i.e., on the RE atomic number'. The question arises, 'If the 4*f*-electrons influence namely the *"additional"* effects of complex stabilisation (which can be agreed to), then why will it be correct to correlate the strength of *all chemical bonding* with the number of *f*-electrons and not the parameters determining the principal (ionic) contribution to the chemical bonding?' In our opinion, a mistake has been made here since the nature of the chemical bonding in RE complexes must be carefully discussed taking into account recently obtained data.

The semiquantitative nature of the simple polarisation approach based on Fajans rules (or the contemporary but also semiquantitative Pearson concept of hard and soft acids and bases[11]) usually yields the correct prediction of the principal tendencies in the change of properties of one or another series of chemical compounds, if the series is chosen legitimately. In our opinion, the RE series is an ideal subject for demonstrating the fruitfulness of such an approach. Therefore, the concept underlying further examination of the properties and structure of RE complexes can be formulated as follows:

1. Complexes of a given composition in the series La, Ce–Lu and La–Y–Sc are formed mainly by ionic interaction of the RE^{III} and ligands. The strength of the ionic bond increases in these series as the RE^{III} radius decreases.

2. The covalent contribution to the RE^{III}–ligand bond increases according to Fajans rules as the polarising action of the RE^{III} cations increases, i.e., from La^{3+} to Lu^{3+} and from La^{3+} to Sc^{3+}.

3. The presence of a W-effect in the dependence of any properties of RE compounds on atomic number is consistent with primarily ionic bonding in these compounds. The lack of a W-effect for the majority of RE^{III} complexes indicates the existence of effects that complicate the simple ionic model. These are a greater or lesser covalent contribution, a change of structure in one or another part of the RE series, the influence of steric hindrances that weaken the chemical bond, etc.

III. Evidence for a covalent contribution to the RE^{III}–ligand bond

The bonding in RE complexes is undoubtedly primarily ionic. However, it is important to estimate the amount of covalent interaction between the RE^{III} cation and the ligands. The simple polarisation model of Fajans predicts, as already indicated, an increase in the covalent (and ionic) contribution to the metal–ligand bond as the RE ionic radius decreases. However, compounds of the lighter lanthanides, i.e., RE with the maximal radius, are viewed as having the greatest covalent contribution in a number of reports.

Thus, Tananaev et al. (Ref. 6, p. 186) report that 'the *f*-orbitals contract faster in the first half of the series and slower in the second owing to the decrease of exchange interactions (a decrease in the number of unpaired electrons) in the f^7–f^{14} series.' Hence the conclusion was drawn that the *f*-orbitals more actively participate in chemical bonding in the first half of the RE series than in the second half.

This conclusion is supported[6] by data for the faster decrease of average molar volumes of the unit cells in the first half of the RE series than in the second. In our opinion, this conclusion is inaccurate since it is obvious that the rapid contraction of the *f*-orbitals in the beginning of the RE series controls the rapid decrease of molar volumes. This occurs because the ionic radius decreases quickly whereas the covalent contribution takes a different path.

Kostromina has come to the same, in our opinion, inaccurate conclusion.[10] A comparison of the enthalpic and entropic contributions to the thermodynamic stability of *f*- and *d*-element complexes (Ref. 10, p. 195 ff.) suggested that the enthalpic contribution to the formation energy of *d*-element complexes is large

and the entropic contribution to that of the *f*-elements with about the same K_s is large. Then, the conclusion was reached that 'for elements of the Ce subgroup the covalent component provides a substantial contribution to the bond energy' by carrying out multistepped calculations using data from methods of varying accuracy such as electronic spectroscopy, thermochemistry and pH measurements (Ref. 10, p. 216). Such a calculation was not carried out for RE of the Y subgroup. However, the whole discussion by Kostromina[10] leads one to believe that the covalent contribution to the bonding of later RE with polydentate ligands is relatively small.

We have already noted that the simple polarisation approach predicts a rule opposite to that accepted previously[6,10] New experimental data, as will be demonstrated below, confirm the correctness of the polarisation prediction.

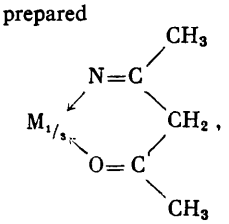
A large number of physical-chemical methods can detect the covalent contribution to the RE^{III}–ligand bond. We will discuss results obtained by photoelectron spectroscopy (PES), IR spectroscopy and kinetics studies.

1. Photoelectron spectroscopy

The principles of the PES method have been developed previously.[12,13] The study of RE β-diketonates by Vovna et al.[14] demonstrated a decrease of metal–ligand covalency as the metal radius increased in the following series of tris-acetylacetonates: ScA_3 > LuA_3 > YA_3. It was noted that an increase of the metal radius in tris-acetylacetonates of the iron subgroup (Fe^{III}–Ru^{III}–Os^{III}) caused the opposite effect, an increase of covalency. It is noteworthy that such a trend agrees completely with Fajans rules, according to which the polarising action of ions with a rare-gas electron configuration, for example RE^{III}, increases with decreasing radius. However, ions with an unfilled (as in the Fe subgroup) or completely filled 18-electron shell polarise (and are polarised) more strongly the greater their radius. Since the covalent bond can be viewed as a polarising perturbation of the ligands by the metal, the series cited above agree with predictions of simple polarisation theory.

The same result as for the RE^{III} tris-acetylacetonates was obtained by PES for RE^{III} tris-dipivaloylmethanates $M(DPM)_3$. The photoelectron spectra of $M(DPM)_3$ are consistent with a greater donor strength of DPM compared with acetylacetone. For $M(DPM)_3$, additional bonding molecular orbitals are detected in the valence band whereas the upper MOs are withdrawn from the valence band. Like for the RE^{III} tris-acetylacetonates, signals in the PES of the RE^{III} tris-dipivaloylmethanates shift by 0.2–0.3 eV to higher ionisation potentials owing to an increase of covalency and a change of $M(DPM)_3$ geometry as the RE^{III} ionic radius decreases (Ref. 14, p. 149). The smallest covalent contribution to the metal–ligand bond among the $RE(DPM)_3$ studied is found for $Pr(DPM)_3$. The MO in its spectrum is not split (splitting is a sign of covalency).

It is also very interesting to compare the PES of RE acetylacetonates and acetylacetoneiminates. As demonstrated previously,[15] where RE acetylacetoneiminates $M(Acim)_3$ with chelate rings were first prepared



substitution of one of the O atoms in the six-membered chelate rings in MA_3 by a N atom in $M(Acim)_3$ causes the PES to change. This is indicative of a relatively large covalent contribution to the M^{3+}–$Acim^-$ bond. It can be seen in Fig. 3 (Ref. 15, p. 87) that the splitting of PES signals of $Lu(Acim)_3$ is much greater than that of LuA_3.

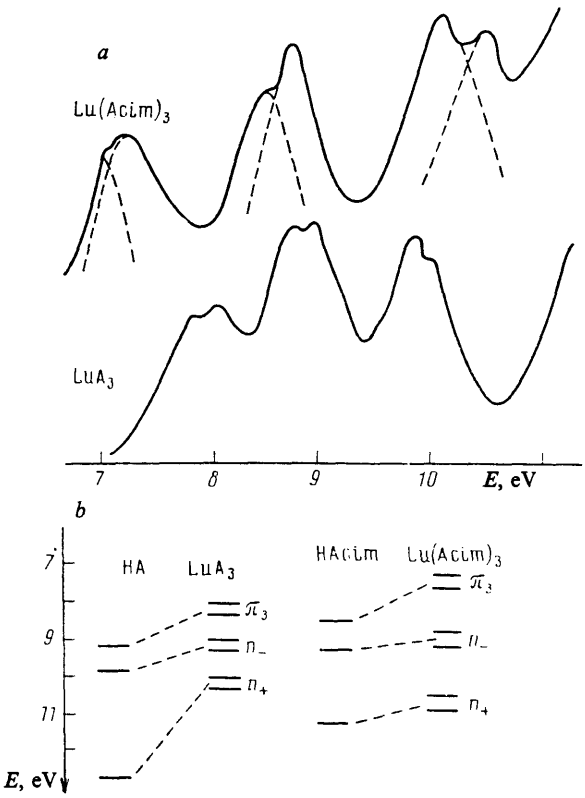


Figure 3. Photoelectron spectra of Lu acetylacetonate and acetylacetoneiminate (*a*); comparison of orbital energy of free ligands (HA, HAcim) and the same ligands in Lu complexes (PES data) (*b*).[15]

This fact agrees well with general concepts of polarisation theory, according to which the N atoms (one of the two donors in $Acim^-$) are more strongly polarising. Consequently, this forms a stronger covalent bond than the O atoms (in A^-) under otherwise equal conditions. However, it is noteworthy that the thermodynamic and, therefore, the chemical stability of $M(Acim)_3$ compounds is less than that of MA_3. Hence, $RE(A)_3$ are unstable in air, quickly hydrolyse, and lose volatility. However, $RE(Acim)_3$ of the Ce subgroup are difficult to isolate pure.[15] Apparently the large covalent contribution (due to substituting O by N) to the bonding in $M(Acim)_3$ is accompanied by a weakening of the metal–ligand coulombic interaction. As already stated, this is the principal component of the chemical bond in all RE^{III} compounds.

As is clear from the preceding, the PES method provides direct evidence for a covalent contribution to the bonding of RE^{III} to

ligands and also indicates that this contribution increases as the RE ionic radius decreases. In our opinion, these data are of prime significance in understanding the coordination chemistry of RE.

2. IR spectroscopy of RE complexes

The literature contains an enormous amount of information on the IR spectra of RE complexes. Unfortunately, the M–O and M–N stretching vibrations are located in the low-frequency IR region (<400 cm^{-1}). As a rule, they are insufficiently characterised due to the mixing of these vibrations with skeletal vibrations of the polydentate organic ligand. The broad contours of these bands make their assignment and analysis difficult. Therefore, the type of metal–ligand bond is usually evaluated by noting how coordination to M^{n+} affects the position of the absorption bands in the spectrum of the free ligand (Ref. 8, pp 76–102). Numerous investigations have demonstrated that the C–O stretches in spectra of RE^{III} complexes with O- and N-donor ligands, as a rule, do not shift compared with their position in the spectrum of the free ligand (for example, in the spectrum of the Na salts, which are usually taken as a model of the ligand with ionic bonds[8]). This is consistent with a RE^{III}–O ionic bond. On the other hand, absorption bands corresponding to the N–H and C–H bonds in the ligand shift in the spectra of chelates with a RE^{III}–N bond. This is consistent with a partially covalent M–N bond. Apparently the N atom is softer than the hard, strongly electronegative O donor and experiences a shift of electron density owing to polarisation by the RE^{III}. This shift extends to the ligand bonds conjugated with the RE^{III}–N bond. The importance of analysing the structure of complexes by IR spectroscopy is supported by the data in Table 1. It is clear that the ν(C–N) and ν(N–H) bands of a RE^{III} complex with IDA shift most in spectra of RE(IDA) compared with their position in ionic NaIDA, less in $RE(IDA)_2$ and least in $RE(IDA)_3$. In the last compounds, the polarising action of the RE^{III} is 'absorbed' by the three IDA ligands and, therefore, is weak.[16]

Hence, IR spectroscopy not only indicates partial covalency in the metal–ligand bond but also enables the relative strength of this bond in series of related compounds to be characterised.

Let us illustrate the capabilities of IR spectroscopy using RE^{III} β-diketonates as an example. As seen in Table 2, the shift of ν(C=O) to low frequencies in the spectra of RE^{III} tris-acetylacetonates is maximal for anhydrous MA_3.

The low-frequency position of the ν(C=O) band indicates that the C=O bond is weakened most where only acetylacetonates enter the RE^{III} coordination sphere. Introduction of additional neutral ligands such as H_2O, phen, DMSO, etc. into the inner sphere weakens the coordination of the principal ligand, acetylacetonate. This strengthens the C=O bond and increases ν(C=O). It is also shown in Table 2 that chelation of acetylacetoneiminate by RE^{III} greatly weakens the N–H bond in the ligand. The greatest weakening occurs in $M(Acim)_3$, the M^{3+} cations of which have the smallest ionic radius, i.e., are the strongest polarisers.

It is interesting that the sensitivity to the size of the RE^{III} polarising action in this instance also (like for RE complexes) is substantially greater for the M^{3+}–N bond than M^{3+}–O.

Structural data confirm the correctness of conclusions about RE chelate structures made on the basis of IR spectra. For example, the average Yb^{3+}–O distance in YbA_3,[17] for which ν(C=O) = 1585 cm^{-1}, is 2.211(8) Å, i.e., slightly less than in $Yb(Acim)_3$ (2.233 Å) and in $YbA_3 \cdot 3H_2O$ (2.23 Å).[19] This agrees with ν(C=O) = 1595 cm^{-1} (Table 2).

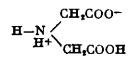
3. Kinetic studies

Systems of ionic compounds are known to be kinetically labile under appropriate conditions (solutions, melts, vapors). However, systems of covalent compounds (organic compounds, Pt complexes), as a rule, are kinetically slow. This can sometimes reach the point where equilibrium is not attained. For example, Pt complexes cannot be characterised by stability constants for this reason. Therefore, it can simply be said that rapid exchange reactions are a sign of ionic bonding whereas slow processes are typical of covalency.

Table 1. IR spectra of RE iminodiacetates[16].

Compound	ν(N–H), cm^{-1}	$\Delta\nu^*$(N–H), cm^{-1}	ν(N–C), cm^{-1}	$\Delta\nu^*$(N–C), cm^{-1}
Na_2Z	3340	–	1140, 1145	–
NdZCl	3250	90	1120	22
ErZCl	3255	85	1118	24
Nd_2Z_3	3270	70	1125	17
Er_2Z_3	3275	65	1125	17
$KNdZ_2$	3280	60	1128	14
$KErZ_2$	3280	60	1127	15
K_3NdZ_3	3290	50	1122, 1148, 1132	9
K_3ErZ_3	3290	50	1111, 1130, 1145	12

Note. Iminodiacetic acid (HIDA, H_2Z) has the structure



*$\Delta\nu$ = ν(RE^{III} complex) – ν(Na_2Z).

Table 2. IR spectra of RE^{III} acetylacetonates and acetylacetoneiminates.[15,17,18]

Compound	ν(C=O), cm^{-1}	ν(N–H), cm^{-1}
(Tb–Lu)A_3·HAcim	1600	3380, 3220
(La–Gd)A_3·2HAcim	1605	3340, 3180
(La–Lu)$A_3 \cdot H_2O$	1615	–
(La–Lu)$A_3 \cdot 3H_2O$	1600	–
(Gd–Lu, Y, Sc)A_3	1585	–
HAcim	1625	3350, 3180
(Tu, Yb, Lu, Sc)$(Acim)_3$	1595	3265
(Dy, Er)$(Acim)_3$	1595	3275
$Gd(Acim)_3$	1595	3290
(Pr–Yb)A_3·DMSO	1600	–
(Pr–Yb)A_3·phen	1625	–

However, there usually is no simple and direct dependence between the kinetic parameters of exchange processes in systems with complexes and the type of metal–ligand bond that determines the

thermodynamic and structural characteristics. Comparison of kinetic, thermodynamic and structural parameters is most often complicated by the different mechanisms of the reactions being compared. However, if subjects with reactions described by identical kinetic equations can be found, such an examination can become valid.

We carried out a special investigation of the kinetic parameters of solutions of RE complexes and proved that the metal exchange in systems with light and heavy RE occurs by the same mechanism (identical kinetic equations) but with different rates. Such a conclusion suggests that the kinetic sluggishness typical of heavy RE complexes (RE of the Y subgroup) is due to a larger covalent contribution to the metal–ligand bond in these chelates compared with the same chelates of light RE (RE of the Ce subgroup).

Results of a study of the metal exchange in aqueous solutions containing RE^{III} and H_4EDTA are presented in Table 3.

Table 3. Metal exchange rate in aqueous solutions of EDTA complexes.[20]

M^{3+}_{leav}	M^{n+}_{ent}	$10^{-2}k'$, $dm^3 mol^{-1} sec^{-1}$	$10^{-2}k''$, $dm^3 mol^{-1} sec^{-1}$
Nd^{3+}	Yb^{3+}	4.67±0.33	18.0±0.20
Nd^{3+}	Tu^{3+}	4.50±0.50	17.6±0.17
Nd^{3+}	Er^{3+}	4.17±0.51	15.6±0.10
Nd^{3+}	Gd^{3+}	4.33±0.17	14.0±0.36
Nd^{3+}	Eu^{3+}	4.00±0.50	13.3±0.20
Nd^{3+}	Pr^{3+}	4.67±0.20	12.3±0.34
La^{3+}	Cu^{2+}	20.2±0.2	(2.2±0.1)·10^2
Pr^{3+}	Cu^{2+}	6.6±0.1	(0.92±0.09)·10^2
Nd^{3+}	Cu^{2+}	4.8±0.1	(0.67±0.01)·10^2
Eu^{3+}	Cu^{2+}	2.3±0.3	(0.22±0.01)·10^2
Gd^{3+}	Cu^{2+}	1.6±0.1	(0.13±0.03)·10^2
Tb^{3+}	Cu^{2+}	0.82±0.04	3.17±0.02
Er^{3+}	Cu^{2+}	(5.5±0.1)·10^{-2}	0.83±0.03
Yb^{3+}	Cu^{2+}	(1.56±0.05)·10^{-2}	0.33±0.01

It was found[20] that the exchange

$$[M_{leav}(EDTA)]^- + M^{n+}_{ent} \rightleftharpoons [M_{ent}(EDTA)]^{4-n} + M^{3+}_{leav},$$

obeys the following kinetic equation:

$$V = V_I + V_{II} = k'[H^+][M_{leav}(EDTA)^-] + k''[M_{leav}(EDTA)^-][M^{n+}_{leav}],$$

where M^{3+}_{leav} and M^{n+}_{ent} are the leaving and entering cations, respectively, and k' and k'' are the exchange rate constants for the dissociative and associative mechanisms. The rate of the dissociative process (V_I), as previously demonstrated,[20] is limited by cleavage of the leaving cation–acetate ($EDTA^{4-}$) bond in the intermediate protonated complex whereas the rate of the associative process (V_{II}) is limited by cleavage of the leaving cation–N($EDTA^{4-}$) bond in the intermediate binuclear complex. Table 3 clearly shows that V_I does not depend on the nature of the entering RE^{III} cation but decreases as the leaving cation shifts towards the heavy RE. The rate V_{II} also is minimal in complexes of heavy RE, which have the minimal ionic radius and, therefore, provide the greatest chance for covalency owing to the large polarising effect.

Fig. 4 shows that the slope of the dependences of rate constants on ionic radius of leaving RE^{III} changes in the middle of the RE series. This can be related[20] to the change of inner-sphere hydration on going through the RE series. Whereas inner-sphere dihydrates $[M(H_2O)_2(EDTA)]^-$ are typical of heavy RE, formation of di- and trihydrates is equally probable for RE in the middle of the series. Thus, the following equilibrium was studied for the system with Eu^{III}

$$[Eu(H_2O)_2(EDTA)]^- \rightleftharpoons [Eu(H_2O)_3(EDTA)]^-,$$

and it was demonstrated[21] that the reactivity of the inner-sphere dihydrate is less than that of the trihydrate $[Eu(H_2O)_3(EDTA)]^-$. Structural data indicate that inner-sphere trihydrates are more characteristic of the light RE. This was found, in particular, for Nd and Eu complexes of EDTA. The structural data suggest (Ref. 8, p. 10) that the RE^{III} draw closer to the ligand if the number of inner-sphere waters of hydration decreases in the RE^{III} complexes of EDTA. In particular, the average RE^{III}–O ($EDTA^{4-}$) and RE^{III}–N ($EDTA^{4-}$) bond lengths in $[Er(H_2O)_2(EDTA)]^-$ are substantially less (2.27 and 2.56 Å) than in $[Nd(H_2O)_3(EDTA)]^-$ (2.53 and 2.83 Å).[22,23] Such a decrease of the bond lengths should certainly increase the polarisation of metal–ligand interactions. This increases the covalent contribution to the bond and affects the rate of electrophilic and nucleophilic substitution in addition to the size of the change of k' and k'' with decreasing RE^{III} ionic radius, as can be seen in Fig. 4.

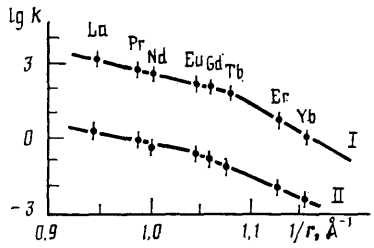


Figure 4. Change of metal-exchange rate constant in solution of RE^{III} EDTA complexes.[20] *I*, lg k'; *II*, lg k''.

Hence, the kinetic data and the PES and IR results confirm the correctness of the hypothesis ensuing from the simple polarisation model that the covalence in the metal–ligand bond increases as the RE^{III} radius decreases in the series La–Ce–Lu and La–Y–Sc.

IV. Mutual influence of ligands and metals in homoleptic and polynuclear RE^{III} complexes

If a complex contains several identical or different ligands in addition to several cations, all of these components of the coordination sphere affect each other. Obviously their mutual influence will be stronger the more labile their bonding in the complex. In our opinion, it is completely justified to assume that the mutual influence of coordination-sphere components is more easily transferred through an ionic metal–ligand bond than through a

covalent one. The reasons for this are the long range and sphericity of coulombic forces in contrast with the directionality and saturation (relatively short range) of covalent forces.

In our work[7,8] in addition to that of others,[6,10] it is possible to find numerous examples in support of the prediction just given, which invokes a strong and rapidly attained mutual influence of coordination-sphere components in RE^{III} complexes. In particular, the regular decrease of successive K_s for RE complexes formed by incorporation into the coordination sphere of one, two, three and more identical (cf. Table 1) or different ligands support the correctness of such an approach. The changes of successive K_s in the RE series of neutral mono-, bis- and tris-IDA complexes of RE [8,24] are plotted in Fig. 5 as an example. It can be seen that the first ligand (formation of the mono-complex) is bound most strongly in the coordination sphere (CS). The energy stored in one metal–ligand bond decreases smoothly on going to the bis- and tris-complexes. The anomalous path of $\lg K_3$ near the heavy RE is due to the generation of steric hindrances owing to the decrease of ionic radius and the approach of the cations and anions in the complex. In general, incorporation of each successive ligand decreases K_s by almost two orders of magnitude. This should be expected if the ionic model of the CS is accepted. According to this model, neutralisation of the positive charge of the RE^{III} cation by each negatively charged ligand should substantially weaken the metal–ligand bond in the CS.

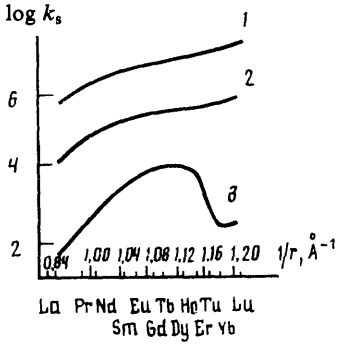


Figure 5. Change of stability of mono- (*1*), bis- (*2*), and tris-IDA complexes (*3*) of RE.[24]

The path shown in Fig. 5 for the successive K_s is normal for an ionic CS.[8] However, these data of themselves do not answer the question of whether the position of ligands in higher complexes is equivalent. For example, is each IDA ligand in bis- and tris-IDA complexes of RE bound with the same strength? In order to answer this question, data obtained by other methods can be used. For example, an IR study of solid RE complexes, as already mentioned above (cf. Table 1), indicates successive weakening of the RE^{III}–N bond on going from the mono- to bis- and tris-IDA complexes and equivalence for the two IDA residues in the bis-complex and three in the tris-complex. This conclusion agrees with PMR spectroscopic results.[11] However, this method detects equivalent ligands in higher RE complexes only for ligands of low denticity (in particular, including tridentate IDA). According to PMR, only one of the ligands remains highly dentate in complexes of ligands with high denticity for example, $[M(EDTA)_2]^{5-}$ with sexadentate H_4EDTA. The second only partially uses its donor atoms. This fact is explained in the monograph of Kostromina[11] by the large energy gained by retaining the configuration of the mono-complex $[M(EDTA)]^-$ in the bis-complex $\{[M(EDTA)](EDTA)\}^{5-}$ compared with the compound where some of the chelate rings of $[M(EDTA)]^-$ are broken and both $EDTA^{4-}$ residues are identically bound, i.e., exhibit decreased denticity of 4: $[(EDTA)\equiv M\equiv(EDTA)]^{5-}$. Apparently such a redistribution of donor atoms opens (breaks) the EDTA ring in the mono-complex. This sharply reduces the entropy of the system.

It is interesting that a similar nonequivalence of the structural components of the CS based on the polydentate complexants H_4EDTA and H_5DTPA is achieved not only in higher complexes (excess of ligand) but also in polynuclear complexes (excess of M^{3+}).

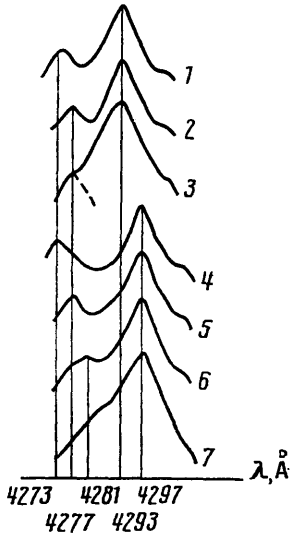


Figure 6. Electronic spectra of Nd complexes with $EDTA^{4-}$ (*1–3*) and $DTPA^{5-}$ (*4–7*).[25] Concentration, M: $[Nd_4(EDTA)_3]$ = 0.04 (*1*); 0.14 (*2*); $[Nd_5(DTPA)_3]$ = 0.02 (*4*); 0.15 (*5*); 0.40 (*6*). Solid complex (*3*, *7*).

As demonstrated in Fig. 6,[25] high-resolution electronic spectroscopy (Ref. 8, pp 65–76] detects nonequivalent positions for the two Nd atoms in the dinuclear complexes $[Nd_2(EDTA)]^{2+}$ and $[Nd_2(DTPA)]^+$. In dilute solutions, one of the two moles of Nd^{3+} used per one mole of complexant forms the mono-complex $[Nd(EDTA)]^-$ or $[Nd(DTPA)]^{2-}$ with absorption bands at 4292 and 4297 Å, respectively. The second mole of Nd^{3+} remains as the aqua-ion $[Nd:aq]^{3+}$ with an absorption band at 4273 Å. Polynuclear complexes form as these solutions are concentrated (Ref. 8, pp 15–18). This produces only a small shift to long wavelength of the absorption band of the aqua-ion (to 4277 and 4281 Å in the H_4EDTA and H_5DTPA systems, respectively). A shift

of this value corresponds to coordination of Nd^{3+} by only one or two of the acetato-groups of the ligand. Therefore, high-resolution spectrography reveals the nonequivalence of the two Nd^{3+} ions in dinuclear complexes. Consequently, here, like in the higher complexes, the ligands and RE ions remain different. Their positions are not averaged. The energy gain from this structure apparently determines the state of the system in polynuclear complexes based on $EDTA^{4-}$ and $DTPA^{5-}$. Such an unaveraged state for the metals and ligands does not contradict the postulated ionic bond in RE complexes. In fact, PMR [10] and kinetic studies[20] detect rapid exchange in such systems so that the discussion is not about the nonequivalence of polynuclear or polyligand CS that presumes metal–ligand covalency but about which arrangement of donors and RE ions is thermodynamically most favorable.

Results of mathematical modelling of equilibria in EDTA solutions of Nd^{III} and Yb^{III} using experimental pH measurements are presented in Tables 4 and 5.[26]

Table 4. Modelled pH-tritration of $2Nd^{3+}-EDTA^{4-}-KOH$ solutions.[26]

Model No.	Model	Sum of squares of experimental deviations
0	H^+; Nd^{3+}; $NdOH^{2+}$; $EDTA^{4-}$; $HEDTA^{3-}$; H_2EDTA^{2-}; H_4EDTA; H_3EDTA^+; $Nd(EDTA)^-$	2.07
1	{0}+HNd(EDTA)	0.12
2	{1}+$Nd_2(EDTA)^{2+}$	0.07

Table 5. Stability of Nd^{III} and Yb^{III} EDTA complexes by mathematical modelling[26].

Compound	ln β	log K_s	pK_a
$[Nd(TDTA)]^-$	36.02±0.08	15.66	–
$H[Nd(EDTA)]$	40.88±0.09	–	2.11
$[Nd_2(EDTA)]^{2+}$	38.46±0.16	1.06	–
$[Yb(EDTA)]^-$	43.01	18.70	–
$H[Yb(EDTA)]$	47.10±0.09	–	1.78
$[Yb_2(EDTA)]^{2+}$	44.04±0.52	0.45	–

Note. β is the overall formation constant. K_s is the step-wise stability constant. K_α is the acid dissociation constant.

The data suggest that the strength of the polynuclear complexes decreases from light RE (Nd) to heavy ones (Yb). The very large difference in successive K_s corresponding to binding of one or two RE^{III} by one $EDTA^{4-}$, respectively, is interesting. For Nd^{III} and Yb^{III} this difference is greater than 14 and 18 orders of magnitude, respectively. Therefore, the thermodynamic efficiency of removing part of the donors from the mono-complex to form the polynuclear compounds is small. The same can be said about the nonequivalence of identical ligands in a system with more EDTA ligands and other RE polyligand compounds based on high-denticity ligands.[7] However, the less stable the mono-complex is (achieved with a low-dentate complexant), the less the difference is in the state of the second and successive ligands in the RE CS and the greater their mutual influence.

V. Mutual influence of ligands in heteroleptic RE complexes

If the principal ligand, i.e., the ligand forming the stronger bond to the RE^{III} in a mixed coordination sphere has high denticity and high donor activity then, as a rule, additional weaker ligands enter the complex with a relatively small K_s. Let the additional ligand be citrate with a comparatively low denticity (equal to 4). Then, RE^{III} form heteroleptic complexes in addition to those with the principal ligand, for example, EDTA. However, these have low stability.[7,27] This agrees well with the low stability (consider the successive K_s) of higher homoleptic complexes of RE with H_4EDTA. However, if the principal and additional ligands are of comparable denticity and donor strength (for example, H_2IDA and H_3Cit), their state in the $RE^{III}CS$ is essentially the same and resembles the situation discussed above for formation of higher homoleptic IDA complexes (cf. Table 1 and Fig. 5).

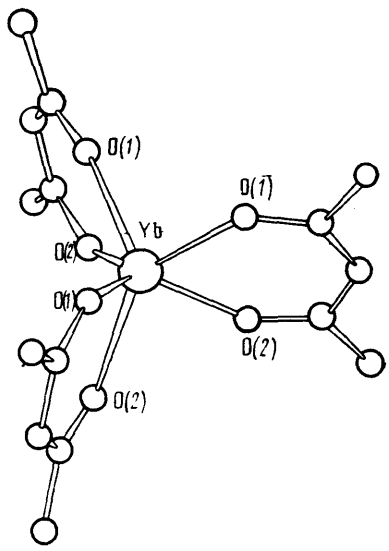


Figure 7. Crystal structure of anhydrous Yb tris-acetylacetonate.[28]

Mixed complexation in systems with principal and additional ligands of comparable strength have been studied by us in connection with adduct formation in RE^{III} tris-β-diketonates. Since RE^{III} characteristically have high and variable coordination number and the denticity of each β-diketonate is 2, only six donors surround the RE^{III} in monomeric tris-β-diketonates (Fig. 7).[28]

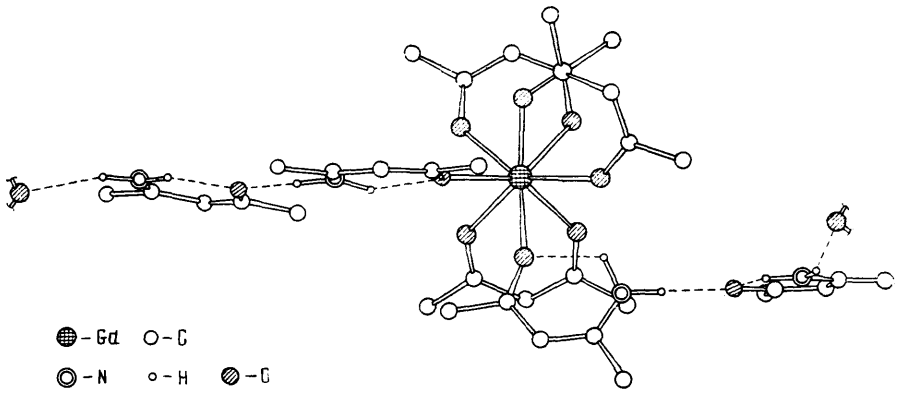


Figure 8. Structure of the adduct $GdA_3 \cdot 4HAcim$.[30]

In general this is clearly insufficient to saturate the $RE^{III}CS$. Therefore, tris-β-diketonates, including RE^{III} tris-acetylacetonates MA_3 and tris-dipivaloylmethanates $M(DPM)_3$, usually polymerise.[29] Polymerisation does not occur if an additional ligand capable of entering the inner CS of the RE^{III} tris-β-diketonate and increasing its CN to 7–9 is present. Mixed complexes based on tris-β-diketonates form. These are called adducts (i.e., addition products) although the additional ligands are inner-sphere and in this sense are equal to the principal ligands. The structure of the adduct of GdA_3 with HAcim of composition $GdA_3 \cdot 4Acim$ is shown in Fig. 8.[30] Of the four HAcim molecules, two are monodentate (through O) and increase the CN to 8. Two HAcim molecules are outer-sphere and bonded through H-bonds.

Incorporation of an additional neutral ligand into the CS of a RE tris-β-diketonate usually lengthens the $RE^{III}-O$ distance owing to partial neutralisation of the metal charge (ion–dipole interaction) and generation of steric hindrances. This can lead to competition with donor atoms of the principal ligand for the CS. This does not open the chelate rings formed by the principal ligand even if the additional neutral ligand is bidentate (bipy, phen, etc.). However, the $RE^{III}-O$ distance in adducts (including hydrates) is always slightly greater than in the monomeric tris-β-diketonates themselves (Table 6).

Apparently this difference in bond lengths would be much greater if data for the monomeric and not dimeric (as in Table 6) tris-β-diketonates were used for comparison in systems with $RE(DPM)_3$ of the Ce subgroup. Polymerisation has the same weakening effect on the $M^{3+}-O$ bond as adduct formation. However, data for the monomers exist only for RE of the Y subgroup where both polymerisation and adduct formation are sterically hindered. The influence of the additional ligand on the strength and length of the $M^{3+}-O$ bond is less than in these same systems with RE of the Ce subgroup. There are no structural data for anhydrous RE tris-β-diketonates (acetylacetonates) of the Ce subgroup. Even for the heavy RE only the one structure mentioned above, YbA_3, has been solved.[28]

Therefore, the mutual influence of identical and mixed ligands in the $RE^{III}CS$ is substantial. It is not determined by any one factor, for example, the nature of the metal, but by several parameters. First of all, a donor strength and steric characteristics must be assigned to the ligands interacting in the inner sphere of RE^{III} complexes.

Table 6. Influence of adduct formation on M–O bond length in chelate rings of RE^{III} tris-β-diketonates.[17,18]

tris-β-Diketonate	M–O bond length, Å	Adduct	M–O bond length, Å
$[Nd(DPM)_3]_2$	2.32	$[Nd(DPM)_3 \cdot bipy]$	
		$[Eu(DPM)_3 \cdot py_2$	2.35
		$[Eu(DPM)_3 \cdot DMF]$	2.36
$[Pr(DPM)_3]_2$	2.41	$[Pr(DPM)_3 \cdot TPPO]$	2.36
$[Er(DPM)_3]_1$	2.21	$[Dy(DPM)_3 \cdot H_2O]$	2.30
		$[Ho(DPM)_3 \cdot (4\text{-}Pic)_2]$	2.27
$[Lu(DPM)_3]_1$	2.19	$[Lu(DPM)_3 \cdot (3\text{-}Pic)_2]$	2.24
$[NdA_3]_1$		$[NdA_3 \cdot 2H_2O] \cdot H_2O$	2.44
		$[NdA_3 \cdot H_2O \cdot DMSO] \cdot DMSO$	2.43
		$[PrA_3 \cdot 2H_2O] \cdot H_2O$	2.44
		$[EuA_3 \cdot phen]$	2.40
		$[GdA_3 \cdot 2HAcim] \cdot 2HAcim$	2.38
		$[YbA_3 \cdot H_2O]$	2.233
$[YbA_3]_1$	2.211	$[YbA_3 \cdot HAcim]$	2.23

Our attempt to determine the stability of $M(\beta\text{-diket})_3 \cdot xQ$ adducts by gas–liquid chromatography (GLC) demonstrates just how complicated it is to predict the result of the mutual influence of ligands in heteroleptic RE complexes, for example, in the CS based on β-diketones. It is clear from Table 7 that the stability of the adducts changes differently in the RE^{III} series depending on the nature of the principal ligand, i.e., the β-diketone. Since HDPM creates steric hindrances in the $M(DPM)_3CS$ owing to the two tert-butyl radicals in each molecule, the probability of incorporating an additional ligand in it decreases as the RE ionic radius decreases. The adducts have minimal stability for the small Lu^{3+} and maximal

Table 7. Effective formation constants (K_{eff}) of RE tris-β-diketonate adducts $ML_3 \cdot Q$[31].

ML_3	Additional ligand, Q	Determination method	K_{eff}						
			Lu	Yb	Tu	Er	Ho	Gd	Nd
$M(DPM)_3$	TPPO	GLC, mathematical modelling	0.9±0.2	1.3±0.2	4.0±0.2	4.0±0.2	7.7±0.3		
$M(DPM)_3$	THF	GLC of additional ligands (Q) on stationary phase with $M(DPM)_3$	0.3±0.1	0.3±0.1		0.3±0.1		0.4±0.1	0.3±0.1
	DMFA		1.4±0.0	1.8±0.4		2.2±0.1		3.8±0.1	3.4±0.6
	DMSO		2.6±0.1	7.0±0.1		7.5±0.3		13.4±0.3	11.7±0.1
	MESO		4.2±0.1	3.9±0.1		7.1±0.3		11.4±0.4	10.4±0.3
$M(PTFA)_3$	THF	ditto		4.3±0.1		3.9±0.1	2.4±0.1	0.5±0.1	

for the large Nd^{3+}. Conversely, $M(PTFA)_3$ are less sterically hindered (Table 7) and add an additional ligand more strongly the smaller the RE^{III} ionic radius. In this instance, the normal relation predicted by Fajans simple polarisation theory is seen.

Table 8. Temperature of maximal thermolysis (T_s) of RE tris-dipivaloylmethanate adducts $M(DPM)_3 \cdot Q \rightarrow M(DPM)_3 + Q$.[18]

M	Q	T_s, °C	M	Q	T_s, °C
–	phen	340	–	DMSO	180
Nd	phen	385	Nd	DMSO	325
Tb	phen	380	Tb	DMSO	325
Yb	phen	380	Yb	DMSO	305
–	bipy	250	–	TBP	240
Nd	bipy	335	Pr	TBP	330
Sm	bipy	335	Sm	TBP	340
Tb	bipy	330	Tb	TBP	335
Yb	bipy	300	Ho	TBP	320

The reversal in the dependence of effective formation constants of the RE^{III} tris-β-diketonate adducts due to steric parameters of the principal ligand (Table 7) is confirmed by chromatography of $RE(DPM)_3$ and $RE(PTFA)_3$ with and without additional ligands. As demonstrated previously,[31] the difference between the retention times (Δt_{ret}) of the tris-β-diketonates and their adducts is greatest for DPM complexes of the light RE. This is consistent with maximal stability of the adducts $M(DPM)_3 \cdot Q$ for the light RE. For $M(PTFA)_3$, the greatest difference in retention time of the tris-β-diketonates and their adducts is seen in the middle of the RE series. At this point, the steric hindrances to adduct formation are still small and the complexing power of the metal (Ho^{3+}) is still significant, in contrast with the light RE^{III}, owing to the 'average' size of M^{3+}.[31]

A study of the thermal stability of the RE tris-β-diketonate adducts also demonstrates the complexity of the competition between the different ligands in the $RE^{III}Cs$. It is evident from Table 8, in agreement with the GLC data (Table 7), that the thermal stability of $M(DPM)_3 \cdot Q$ for all additional ligands studied[18] decreases as the RE ionic radius decreases, i.e., the steric effect of the DPM, the principal ligand, is unfavourable and here has the definitive effect.

The thermal stability changes in the opposite direction for adducts of less sterically hindered RE acetylacetonates. Table 9 shows that the temperature of maximal thermolysis of the adducts does not decrease with decreasing RE^{III} ionic radius [as for $RE(DPM)_3$]. It increases somewhat (Q = phen) or changes little (Q = bipy). The simple explanation is that acetylacetone is not a sterically hindered ligand. Therefore, the normal relation resulting from Fajans polarisation laws is in effect during adduct formation.

Table 9. Temperature of maximal thermolysis of RE tris-acetylacetonate adducts $MA_3 \cdot Q$.[18]

M	Q	T_s, °C	M	Q	T_s, °C
–	phen	340	–	bipy	250
Pr	phen	315	Nd	bipy	235
Eu	phen	357	Sm	bipy	230
Er	phen	383	Gd	bipy	235
Y	phen	385	Y	bipy	235
Yb	phen	388	Yb	bipy	240
Lu	phen	395			

It is interesting (Table 9) that the temperature dependence is much stronger for $MA_3 \cdot Q$ adducts with phen than bipy. This can be explained by the greater rigidity of phen compared with bipy. The latter can rotate fragments around the C–C bond and, therefore, more flexibly than phen fills the voids in the MA_3 structure. Hence, steric effects for systems with $RE(A)_3$ are determined mainly by the structure not of the principal but of the additional ligand.

It is noteworthy that Table 9 includes data for $RE(A)_3$ adducts $MA_3 \cdot Q$ only with bidentate additional ligands (phen, bipy) whereas Table 8 includes data for $RE(DPM)_3$ adducts with monodentate additional ligands. This is due to the fact that $RE(A)_3$ form not only mono- but also bis-adducts with monodentate ligands owing to the lack of steric hindrances on coordination of the principal ligand. As a rule, formation of $MA_3 \cdot 2Q$ is characteristic for light RE, which have a large ionic radius, whereas mono-adducts $MA_3 \cdot Q$ are typical of heavy RE, which have a small ionic radius. Solid $MA_3 \cdot 2Q$ and $MA_3 \cdot Q$ undergo thermolysis by different mechanisms. Therefore, the thermal stability of such adducts over the whole RE series cannot be compared, in contrast with $M(DPM)_3 \cdot Q$, where the RE adducts have a constant composition.

The change of composition of $RE(A)_3$ adducts is sometimes even more complicated. For example, adducts of MA_3 with monodentate (neutral) HAcim reportedly have the following composition:[17]

$$MA_3 \cdot 2HAcim \quad (M = La - Gd);$$
$$MA_3 \cdot 4HAcim \quad (M = Sm - Tu, Y);$$
$$MA_3 \cdot HAcim \quad (M = Tb - Lu).$$

Regions of stability of the different adducts in the RE series overlap. For example, Tb forms all three adducts: $TbA_3 \cdot HAcim$, $TbA_3 \cdot 2HAcim$ and $TbA_3 \cdot 4HAcim$. It is important to note that the mono-adduct is thermally more stable than the bis-adduct.[17]

$$TbA_3.HAcim \xrightarrow[-HAcim]{105\ ^\circ C} TbA_3(s.) + HAcim\uparrow \quad \xrightarrow[sublimation]{110\ ^\circ C} TbA_3(g.),$$

$$TbA_3.2HAcim \xrightarrow[-2HAcim]{95\ ^\circ C} TbA_3(s.) +$$

$$+2HAcim\uparrow \xrightarrow[melting]{105\ ^\circ C} TbA_3(l.) \xrightarrow{160\ ^\circ C} \text{thermolysis}.$$

Thermolysis of only the mono-adduct produces the monomeric sublimable TbA_3. Thermolysis of the bis-adduct leads to melting, polymerisation, and anhydrous $[TbA_3]_n$ that cannot be sublimed.

Therefore, practically each studied series of mixed RE complexes has its own specific type of complicated interaction of numerous factors that often have an equivalent influence on the properties of the complexes. However, it can be confirmed with certainty that such an array of structures and properties of RE^{III} complexes is a consequence of the predominantly ionic interaction in these compounds.

VI. Intermolecular interaction in RE complexes with polydentate organic ligands

The predominantly ionic metal–ligand bonding in RE^{III} complexes frequently leads to catenated structures where one polydentate ligand is shared between two or more RE^{III}. Such a structure is especially characteristic for compounds with a deficit of ligands (of moderate denticity). Therefore, it is very often found in 1:1 complexes. For example, monocitrates $[M(Cit)]_n$ monotartrates $[M_2(tart)_3]_m$ and mononitrilotriacetates $[M(NTA)]_p$ have extensively linked (by polymerisation) chain structures (Ref. 8, p. 11).

As a rule, such compounds are difficultly soluble. However, addition to the RE^{III} coordination sphere of another such ligand can form a monomeric structure with weak intermolecular contacts. This solubilises the initially poorly soluble 1:1 complex:

$$\underset{\text{ppt.}}{[M(Cit)]_n} + n Na_3Ci \rightarrow \underset{\text{solution}}{n Na_3[M(Cit)_2]};$$
$$\underset{\text{ppt.}}{[M(NTA)]_m} + m K_3(NTA) \rightarrow \underset{\text{solution}}{m K_3[M(NTA)_2]} \text{ etc.}$$

If the ligand forming the RE^{III} complex is highly dentate (denticity 6 and greater) and sufficiently flexible to surround the RE^{III} with a spherical (or hemispherical) shield that isolates it from other RE^{III}, the resultant structure is monomeric. As a rule, the intermolecular contacts in it are weak. Such a compound is very soluble in polar solvents, for example, water.[1,2,7,8]

Conversely, the number of donors in 1:1 complexes with ligands of low denticity (1, 2 and 3) is insufficient to saturate the inner CS of RE^{III} even if a bridging structure is formed. Therefore, other ligands must be added (or they are added during synthesis, for example, solvent) to the CS of such complexes to produce monomers. Such CS most often are mixed. Their properties and intermolecular contacts are determined by the stoichiometry of the complex and the relationship among properties of the system components. An example would be RE^{III} chloride–HAcim complexes synthesised and studied previously.[15] The properties of these $MCl_3 \cdot n$ HAcim are exceedingly varied:

$$MCl_3 \cdot 3{,}5HAcim \quad (M = Pr, Nd, Sm);$$
$$MCl_3 \cdot 3HAcim \quad (M = Gd - Yb);$$
$$MCl_3 \cdot 4HAcim \quad (M = Lu, Sc);$$
$$MCl_3 \cdot 6HAcim \quad (M = La, Pr, Nd, Sm, Gd - Er, Lu).$$

Among RE complexes with low-dentate ligands, the most completely studied are the β-diketonates. This is due to practical applications related to their ability to dissolve in low-polarity solvents and to sublime. Therefore, they are suitable for extraction, chromatography and sublimation.

We have already mentioned the coordinative saturation of RE^{III} tris-β-diketonates and their tendency to saturate the CS by adding ligands or by forming bridging O bonds. (This was first found structurally in $[Pr(DPM)_3]_2$.[32]) Intermolecular contacts in such compounds are controlled by the properties of the affected principal and additional ligands in addition to the degree of polymerisation (oligomerisation) of the tris-β-diketonates themselves. Somehow the majority of these compounds can be vaporised by heating under vacuum. They can be distilled or sublimed.

The discovery that RE^{III} complexes can be sublimed at first was surprising since it was generally accepted that ionic compounds were involatile. Attempts to find an appreciable covalent component in tris-β-diketonates and to explain their volatility by their covalent nature were unsuccessful.[33,34] However, it has now been established that the volatility and solubility of tris-β-diketonates in low-polarity solvents are due to their pseudoorganic properties. The hydrocarbon radicals of the β-diketonate ions form a hydrophobic sphere around the ionic core that has little tendency to form associates. This determines the behaviour of RE tris-β-diketonates, which is characteristic for ordinary molecules comprising the world of organic compounds.

The pseudoorganic nature of neutral RE tris-β-diketonates is responsible for the low selectivity in fractional sublimation, gas chromatography and extraction. However, the specific properties of different RE^{III}, no matter how subtle they may be, still cause substantial differences in the thermodynamic characteristics, for example, K_s (cf. Fig. 1). On the other hand, if the compounds do

not decompose or at least the RE CS does not open temporarily during sublimation and extraction, the selectivity leads to differences in the intermolecular interactions.[35] Therefore, fractional sublimation of tris-β-diketonates under ordinary conditions is suitable only for group separation of RE mixtures. For example, dimeric $[M(DPM)_3]_2$ of light RE can be separated by fractional sublimation from monomeric $[M(DPM)_3]$ of heavy RE,[33] whereas intragroup separation of RE^{III} without competing decomposition is ineffective.[35]

Intermolecular interaction of RE complexes explains the important loss of individual properties of complexes in the mixture to be separated. For RE β-diketonates, the mutual influence of individual RE complexes is accompanied by formation of heterometallic oligomers. Preliminary experiments demonstrated that these can be detected by mass spectrometry. However, reliable proof of their existence comes from preparative chemical studies. We will give some examples.

The pioneering work of Sievers and Eisentraut[36] demonstrated that group separation of RE^{III} mixtures by fractional sublimation of $RE(DPM)_3$ of the Ce and Yb subgroups was not complete. The separated components contained an approximately 3% impurity of the other RE subgroup elements even though an apparatus with a gradient heater was used. In our opinion, such a consistent mutual contamination that could not be eliminated by repeated sublimation is due to formation of oligomers that are stable in the vapour.

Another example. It has been found[17,18] that adducts of $RE(A)_3$ of the Ce subgroup with DMSO ($MA_3 \cdot 2DMSO \cdot H_2O$) and HAcim ($MA_3 \cdot 2HAcim$) do not give volatile products containing RE on heating in vacuum. Moreover, as we showed in collaboration with Dzyubenko and Kalinichenko,[37] these compounds in the presence of $RE(A)_3$ adducts of the Yb subgroup do appear in the sublimate. The percent transferred can be significant. Thus, heating in vacuum a 1 : 1 mixture of $[NdA_3 \cdot 2DMSO \cdot H_2O]$ and $[YA_3 \cdot DMSO]$ produced 40% of the starting Nd in the sublimate even though the starting complexes are involatile.

The amount of involatile $MA_3 \cdot nH_2O$ transferred to the vapour and then into the sublimate increases sharply if coordinatively saturated Zr^{IV} tetrakis-acetylacetonate is added to the starting compound, for example, $YA_3 \cdot 3H_2O$.[38]

In the preceding examples, the loss of identity of $RE(A)_3$ on mixing with each other can be linked to formation of oligomers that contain RE of different subgroups in one molecule. However, in our opinion, break-up of YA_3, which tends to oligomerise, by coordinatively saturated ZrA_4 is more probable in the example with ZrA_4. This prevents formation of $[YA_3]_x$ oligomers that are less volatile than YA_3.

Furthermore, the components in a subliming mixture of $RE(A)_3$ have practically no influence on each other if a stable adduct that does not decompose during sublimation is present. Since MA_3 adducts with strong donor ligands such as HMPA and TPPO only partially dissociate on heating in vacuum and partially lose the additional ligand (in contrast with adducts with weaker donors: H_2O, DMSO, HAcim), the coordinative saturation of the RE complexes is preserved during sublimation. This prevents oligomerisation of the individual chelates and interaction of the components with each other. In fact, as demonstrated in Table 10, the separation coefficients of RE mixtures determined experimentally and calculated from the sublimation parameters of the individual components are practically the same for such mixtures. Consequently, coordinatively saturated RE complexes exhibit independent behaviour, retain their integrity, and remain monomeric during separation.

It is noteworthy that multiple repetitions and intricate mathematical treatment of the experimental results is necessary to obtain reliable data for the fractional sublimation of partially dissociated adducts of RE β-diketonates. This happens since small changes in the experimental conditions have a large effect on the results.[39]

Table 10. Separation of RE mixtures by fractional sublimation of $MA_3 \cdot HMPA$.[37]

Sublimed mixture (M', M")A_3.HPMA	Separation coefficient $\alpha^{M'/M''}$	
	experimental data for the mixture	calculated data for individual adducts
(Nd, Pr)A_3.HMPA	1.2±0.1	1.2
(Gd, Nd)A_3.HMPA	6.0±0.1 *	1.2
(Er, Gd)A_3.HMPA	4.4±0.3	5.4
(Er, Nd)A_3.HMPA	35±5 *	6.5
(Er, Ho)A_3.HMPA	1.3±0.1	0.97

*Experimental $\alpha^{M'/M''}$ are greater than calculated since the mixture was separated in a gradient furnace.

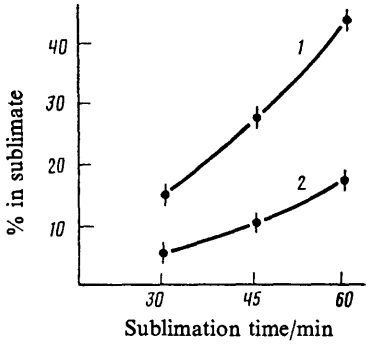


Figure 9. Sublimation of $Nd(Piv)_3 \cdot 3.5HPiv$ (*1*) and $Er(Piv)_3 \cdot 3HPiv$ (*2*) at 360 °C and 10^{-1} torr.

The RE carboxylate system is an example of a sublimation system where the mutual influence of the components is very strong.

The volatility of RE carboxylates was recently discovered by our co-workers at Moscow State University (Kuz'mina et al.[39,40]). Fig. 9 shows that RE pivalates $M(Piv)_3 \cdot nHPiv$ only partially vaporise. The individual RE^{III} pivalates of the Ce subgroup under our experimental conditions sublime more completely than those of the Yb subgroup. The separation coefficient for $Nd^{3+} - Er^{3+}$ from separate sublimation of Nd and Er pivalates is (heating at 360 °C and 10^{-1} torr for 75 min) $\alpha^{Er/Nd} = 68.7$. Such an α value promises

good group separation of RE mixtures. However, an experimental check of the separation gave $\alpha^{Er/Nd} \approx 1.0$, i.e., the sublimate had the composition of the starting mixture. The reason for the lack of separation was the loss of integrity of the components owing to polymerisation of the chelates during sublimation. It can be assumed that the carboxylates act as bridges to form strongly bonded oligomers that are stable in the vapour. Preliminary mass spectroscopic data[40,41] enabled detection of heterometallic RE oligomers that were stable even under the high vacuum of the mass spectrometer.

Instances where the properties of individual RE chelates are suppressed by another component of the mixture are quite common. However, let us recall that this is characteristic for systems in which the complex is not monomeric and oligomers and polymers form owing to coordinative unsaturation.

Such instances are characteristic not only for vapour processes but also for complexation in liquid solutions and solid-state mixtures of chelates. For example, it was found[17] that trihydrates of individual $RE(A)_3$ are isomorphous for the series Pr–Tm and Y whereas $YbA_3 \cdot 3H_2O$ has a different structure. However, coprecipitation from aqueous solutions of $MA_3 \cdot 3H_2O$ and the Yb^{III} complex causes the latter to lose its integrity and form the trihydrate $YbA_3 \cdot 3H_2O$, isomorphous with the other RE $MA_3 \cdot 3H_2O$. It is interesting that addition to the coordination sphere of $RE(A)_3$ of a ligand more bulky than H_2O, for example, HAcim,[17] leads to simultaneous precipitation of crystals of the separate noniso-morphous $NdA_3 \cdot 2HAcim$ and $YbA_3 \cdot HAcim$ with insignificant mutual contamination (2% Nd in $YbA_3 \cdot HAcim$ and 7% Yb in $NdA_3 \cdot 2HAcim$).

This fact suggests that $YbA_3.3H_2O$ in the presence of other RE $MA_3 \cdot 3H_2O$ loses its integrity owing to rather strong intermolecular interaction, possibly with conversion of monomeric structures into catenated ones. The greater bulk of the additional ligand in $MA_3 \cdot HAcim$ than in $MA_3 \cdot 3H_2O$ prevents such a process. The monomeric structure is preserved. The chelate does not lose its integrity.

The mutual influence of components in a precipitated mixture was detected by us[42] during attempted group separation of mixtures of protonated RE EDTA complexes. If $HM(EDTA) \cdot xH_2O$ are prepared separately for RE of the Ce and Yb subgroups, the solubility differs ($\alpha_{calc}^{M'/M''} = 10-1000$). However, coprecipitation under the same conditions gives separation coefficients close to unity. Such a result is consistent with coordinative unsaturation in the RE^{III} mono(EDTA) complexes and polymerisation of the CS.[8]

These data indicate that the behaviour in the presence of other RE can be changed by varying the composition of the complexes and thereby changing the stability of the CS and the degree of coordinative saturation in the RE^{III} chelates. An excess of ligands ensures coordinative saturation and prevents formation of polymers. On the other hand, a deficit of ligands generates polymers, i.e. strong intermolecular interaction.

However, this does not mean that preparation of coordinatively saturated RE chelates guarantees highly effective separation of RE mixtures. Results of sublimation of $RE(A)_3$ adducts with additional ligands of various donor strength are plotted in Fig. 10. It is quite clear that formation of the stable adducts $MA_3 \cdot phen$[18] completely averages the properties of the RE chelates. Conversely, thermolysis of the less thermodynamically and thermally stable chelates $MA_3 \cdot HMPA$ [39] and $MA_3 \cdot HAcim$ [17] reveals certain differences in the sublimation behaviour of RE chelates. Therefore, stable coordinatively saturated compounds are suitable for practical use where the composition of the RE mixture must be preserved without change.[29] Less stable compounds that partially dissociate are promising in separation and purification processes of RE mixtures.

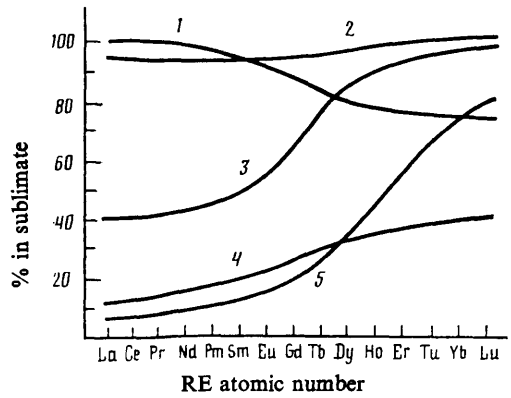


Figure 10. Sublimation of RE^{III} pivalates (*1*) and acetylacetonate adducts (*2–5*) (optimal temperature, 10^{-1} torr): $M(Piv)_3$ (*1*); $MA_3 \cdot phen$ (*2*); $MA_3 \cdot HMPA$ (*3*); $MA_3 \cdot 3H_2O$ (*4*); $MA_3 \cdot n HAcim$ (*5*).

VII. Reasons behind the variation in RE-chelate property changes across the series

One of the most interesting problems in RE chemistry is the variable nature of the change in structural and thermodynamic characteristics of their complexes with ligands of different structure and properties (for example, cf. Fig. 1). This has often been discussed in the literature.[1,2,7,8,10] At the start of this article we prove that the irregularity in the change of RE-chelate properties does not produce a W-effect. We confirm that the principal role in this is played by a ligand of one or another structure that can react flexibly as the ionic radius changes across the RE series. Owing to different flexibilities, each of the ligands has its own limit on permitted interatomic distances and angles for a given structure around the metal.

The greater the ligand geometry deviates from the optimal one in a given RE chelate, the less stable is the structure. In our opinion, it is obvious that the strain that accumulates in the chelate structure surfaces in the details of isostructural complexes across the RE series. When the flexibility of the complex reaches its limit as the RE^{III} radius changes, the chelate rearranges its structure. However, it would be incorrect to assume that the point where the slope changes on the curve of one or another property vs. RE ionic radius (cf. Figs. 1 and 5) corresponds to the place at which the 'old' structure can no longer exist and a new CS structure is formed. Numerous investigations carried out in our laboratory[8,9] and those of others[6,10] of the structure and properties of RE chelates confirm that the old, no longer stable structure continues to exist at one or another break in the RE series, although conditions are favourable for generation of a new structure.

Let us return to Fig. 1 and recall that the slower increase of K_s for RE complexes as the ionic radius decreases usually occurs due to

generation of steric hindrances that prevent a regular approach of the metal and ligand on moving across the RE series. That point for DTPA complexes occurs (cf. Fig. 1) near Sm. Apparently the RE^{III} and ligand in general do not come closer after the octadentate $DTPA^{5-}$ ligand forms a closed sphere around the RE^{III}. Therefore, the strength of the coulombic interaction between the RE^{III} and $DTPA^{5-}$ is practically constant in the series from Sm to Lu and K_s does not change. Ligands of lower denticity change their structural role several times in the RE series. This is reflected in the plots of the dependence of the Cs properties on RE^{III} ionic radius.

Unfortunately, data for isostructural chelates of the whole RE series or several of its members are usually lacking. These could indicate how the ligand strain in a chelate ring increases in an isostructural series and eventually leads to a CS structural change. Therefore, in our opinion, the data on polymorphic transformations in a series of anhydrous $RE(A)_3$ obtained by Trembovetskii[17] in our laboratory are interesting. It was found that anhydrous $RE(A)_3$ (volatile species[29]) synthesised by the reaction

$$MA_3 \cdot HAcim \xrightarrow{T^\circ C} MA_3 + HAcim$$

can exist in four modifications:

I. ScA_3—monomer, octahedron (X-ray structure).[17]

II. ErA_3, TmA_3—unknown structure.

III. YbA_3, LuA_3—monomer, trigonal prism (X-ray structure).[28]

IV. (Y, Tb, Dy, Ho, Er, Tm, Yb)A_3, oligomeric structure (NMR and IR spectroscopy).[17]

Only TmA_3 and YbA_3 are obtained simultaneously in two modifications by sublimation (metastable species are marked with an asterisk): TmA_3^{II}, TmA_3^{IV*}, YbA_3^{III}, YbA_3^{IV*}, respectively. On prolonged heating in vacuum, the following monotropic transitions occur: $TmA_3^{IV} \rightarrow TmA_3^{II}$, $YbA_3^{IV} \rightarrow YbA_3^{III}$. The species ErA_3^{IV} was also metastable. However, it is more stable than TmA_3^{IV*} and TbA_3^{IV*}. Only extended heating (for 23 h) produces the rearrangement $ErA_3^{IV} \rightarrow ErA_3^{II}$. Therefore, the type IV MA_3 structure is metastable for RE^{III} with a small radius. Apparently[17] this is due to steric hindrances to forming the oligomeric species $[MA_3]_n^{IV}$ that are generated by the shielding of the small ions of heavy RE^{III} by the chelate rings.

The metastability of ErA_3^{IV}, TmA_3^{IV} and YbA_3^{IV} is evident in the higher vapour pressure compared with the corresponding type II and III, which condense in the hotter zone of the sublimator. Direct proof of the metastability of (Er, Tm, Yb)A_3^{IV} was obtained by differential scanning calorimetry (DSC). It was demonstrated[17] that the monotropic transition $MA_3^{IV} \rightarrow MA_3^{II,III}$ is an exothermic process. It is clear from Fig. 11 that only the melting endotherm of the chelates is detected on heating all stable MA_3 from 80 to 200 °C. Metastable MA_3^* exhibit also a premelting endotherm and then an exotherm for the monotropic rearrangement (Ref. 17, pp. 99–105). Obviously the MA_3 molecules acquire the mobility (premelting) necessary to rearrange into the stable TmA_3^{II} and YbA_3^{III} near the melting points of the metastable modifications TmA_3^{IV} and YbA_3^{IV}.

The existence of metastable MA_3 for the heavy RE^{III} and their ability on heating to transform into more stable structures support the hypothesis that a new structure gradually replaces an old one on moving across the RE series. Therefore, it is as a rule impossible to find a single point in the RE series where one structure transforms into another. The regions of existence of two or more structures usually overlap.

We have already presented examples of the coexistence under actual experimental conditions of different compounds {for example, $TbA_3 \cdot HAcim$, $TbA_3 \cdot 2HAcim$ and $TbA_3 \cdot 4HAcim$[17] or $[Eu(H_2O)_3(EDTA)]^-$ and $[Eu(H_2O)_2(EDTA)]^-$ (Ref. 11, 26]}. This also supports the presence of a certain range in the RE series where the complex is changing from one structure to another.

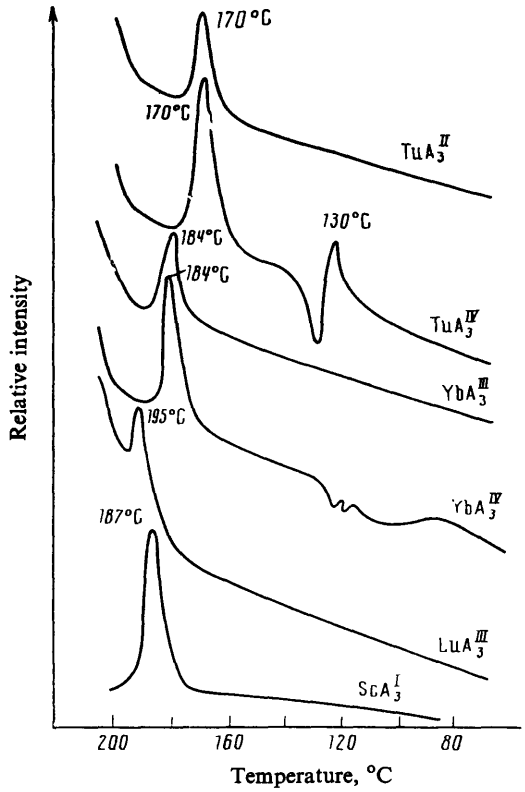


Figure 11. Scanning calorimetry of MA_3.[17]

VIII. Conclusion

The data presented demonstrate the complexity of RE^{III} complexes with organic polydentate ligands and reveal the unwarranted simplicity of the concept of a W-effect. Numerous facts indicate that the crystallographic instability of RE chelates due to small differences in ionic radii of neighbouring RE does not appear in any individual RE but in a more or less broad range of the RE series. Moreover, these ranges can considerably shift in the presence of several RE toward the light or heavy RE. This must be considered in developing industrial separations, purifications and applications of RE compounds since the RE^{III} characteristically lose their integrity in mixtures of coordinatively saturated and unsaturated compounds.

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Translated from *Uspekhi Khimii* **60** 1999–2019 (1991) U.D.C. 542.934.7

Mechanism of heterogeneous oxidation of acrolein to acrylic acid

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ABSTRACT. A summary and analysis is given of results in the literature, and of our own results, of investigations into the mechanism of the heterogeneous oxidation of acrolein on oxide catalysts. The mechanism by which acrylic acid and oxides of carbon are formed from acrolein and oxygen is discussed. General principles for the interaction of acrolein with oxide catalysts are considered, and special attention is given to the nature of adsorption centres and the role of surface compounds of acrolein and acrylic acid, in the course of acrolein oxidation. On the basis of a proposed mechanism, some principles are formulated for the specific selection of catalysts for the selective oxidation of acrolein to acrylic acid.

The bibliography contains 74 references.

Contents

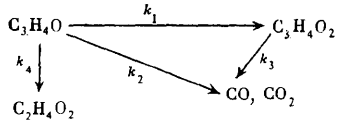
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I. Introduction

The selective oxidation of organic compounds constitutes a large area of heterogeneous catalysis. In a series of monographs and reviews, dedicated to the problem of selective oxidation of hydrocarbons,[1–7] consideration is given to the mechanism of reaction, the nature of catalytic action, and the chemical composition of catalysts. Special attention is given to activation of the oxidised substances and oxygen, the stages of reaction, and the state of the active surface. However, the question of the mechanism of selective conversion of unsaturated aldehydes, in particular acrolein, has received insufficient attention.

Heterogeneous catalytic oxidation of acrolein to acrylic acid is carried out abroad on the industrial scale—it is the second stage in the process for the synthesis of acrylic acid from propylene.[8–12] The practical value of this reaction has stimulated, especially in recent years, a large number of scientific investigations into the mechanism and kinetics of the conversion, and also the selection of catalysts. In the present work we have attempted to summarise the literature data, and also our own data, on the mechanism of the heterogeneous oxidation of acrolein and to reveal some principles for the course of this reaction.

For the oxidation of acrolein to acrylic acid, multi-component oxide catalysts are used. The reaction proceeds by a consecutive-parallel scheme:



The principal products are acrylic acid and the oxides of carbon but, with some catalysts, acetic acid is also obtained. The small number of products and the difference in their acid-base properties from those of the starting material, make this reaction a convenient model for application of the ideas of Boreskov, on the intermediate chemical interaction of the catalyst with components of the reaction mixture, to the selection of catalysts. According to these ideas,[1] the direction of conversion of the intermediate surface compounds (SC), which are formed by interaction of the catalyst with the reaction mixture, is determined by the structure and bond energy of the SC.

Investigation of the reaction mechanism, i.e. defining the forms and energetic characteristics of the SC, the elucidation of their chemical bonding with the catalyst, and their directions of conversion into reaction products, is the most reliable route to an understanding of the nature of the catalytic action and to elaboration of the principles of catalyst selection. It is from precisely these points of view that we consider the available data for acrolein oxidation in the present work.

II. Mechanism by which oxygen takes part in the formation of acrylic acid and products of more deep-seated oxidation

Two mechanisms can be distinguished for the introduction of oxygen into the molecule which is undergoing oxidation: a step-wise mechanism, involving alternating oxidation and reduction of the catalyst by oxygen and the substances undergoing oxidation (the so-called oxidation-reduction mechanism) and a unified (associative) mechanism, with oxygen taking part in the gas phase.[13–16]

At the present time, for many selective conversion reactions of hydrocarbons, the oxidation-reduction mechanism for the participation of oxygen is well established.[17–20]

The question of whether one or other mechanism is in operation is determined by a direct comparison of the independently measured rates of catalysis and of catalyst reduction (or reoxidation), which are found in the stationary state. Equality of these rates indicates

the step-wise oxidation-reduction mechanism, but if the rate of catalysis exceeds the rate of reduction, participation by oxygen in the gas phase is indicated. It should be particularly emphasised that it is important to maintain the stationary state of the catalyst during the process of measurement, since it differs considerably from the initial state and depends on the composition of the reaction mixture.[21] With movement towards the stationary state, there are changes in the oxygen content and in the energy of its bonds with the catalyst, the oxidation state of the cations, and the concentration of the strongly-sorbed form of the substance being oxidised, all of which control change in the rates of the particular reactions and accordingly their selectivity. Hence, it follows that the extent of reduction should not change significantly during measurement of the rate of reduction for the stationary catalyst. If these conditions are not observed the rate of catalysis may exceed the rate of reduction, to an extent that increases as the heterogeneity of oxygen in the catalyst increases.

The overall situation is illustrated graphically in Fig. 1,[22,23] from which it can be seen that the stationary state (the plateau on all curves, Fig. 1*a*), differs considerably from the initial state with respect both to activity and selectivity. Comparison of Fig. 1, which shows movement of the catalyst towards the stationary state in the reaction mixture (0.2% C_3H_4O, 0.4% O_2, the remainder He), with Fig. 1*b*, which shows the changes observed in the reducing mixture (0.2%, 99.8% He), leads to the conclusion that the catalyst is reduced by the reaction mixture with the formation of strongly-bonded surface compounds. The latter follows from the absence of a carbon balance for the first pulses. Fig. 1*b* also indicates that even a few percent increase or decrease in the extent of reduction of the surface of the catalyst causes a sharp change in the rate of formation of acrylic acid and oxides of carbon. This picture is typical of catalysts for the oxidation of acrolein.[21] It is therefore necessary to maintain a constant surface composition of the catalyst during measurement of the rates of catalysis and reduction.

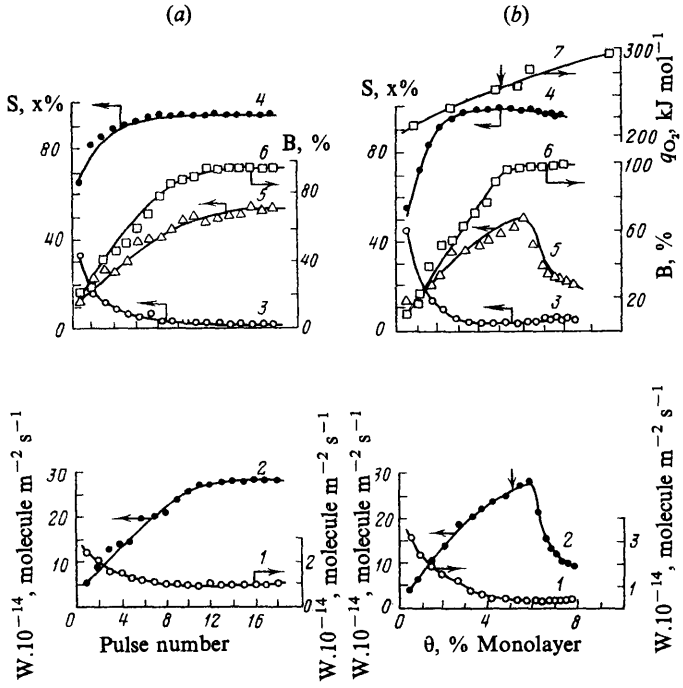


Figure 1. Dependence of the rate of formation of products of deep-seated oxidation (*1*), rate of formation of acrylic acid (*2*), selectivity for CO + CO_2 (*3*) and for $C_3H_4O_2$ (*4*), the extent of conversion of acrolein (*5*) and the carbon balance (*6*) on the impulse number of the reaction mixture (*a*) and on the extent of reduction of the surface (*b*); *7*, heat of adsorption of oxygen. Catalyst $V_2O_5.MoO_3/SiO_2$, T_r = 260 °C. Vertical arrows on Fig. 1*b* indicate the stationary state of reduction.

Table 1. Catalytic properties of vanadium- and cobalt–molybdenum catalysts for the oxidation of acrolein under the conditions of catalysis (mixture of C_3H_4O, 0.1%; O_2, 0.2%; He, 99.7%) and reduction (C_3H_4O, 0.1%; He, 99.9%).[21–24]

Catalyst *	*T*, °C	Working conditions	Conversion %	Reaction rate W.10^{-14} molecule m^{-2} s		Selectivity (%) for		Heat of adsorption O_2 kJ mol^{-1}
				C_3H_4O	$CO+CO_2$	C_3H_4O	$CO+CO_2$	
$V_2O_4 \cdot 9MoO_3/SiO_2$ **	260	Catalysis	54.0	29.0	1.07	96.5	3.5	255
		Reduction	48.0	27.0	0.60	97.8	2.2	
		Oxidation	–	–	0.40	–	–	
$V_2O_4 \cdot 9MoO_3/SiO_2$ **	300	Catalysis	49.1	12.5	1.50	89.3	10.7	247
		Reduction	48.5	11.8	1.20	91.0	9.5	
$V_2O_4 \cdot 9MoO_3 \cdot 1CuO/SiO_2$	300	Catalysis	58.1	14.1	1.20	92.1	7.9	226
		Reduction	56.5	14.5	1.20	93.6	7.4	
$V_2O_4 \cdot 9MoO_3 \cdot 0{,}2Cs_2O/SiO_2$	300	Catalysis	24.4	1.10	0.12	89.8	10.2	326
		Reduction	22.2	1.10	0.10	91.3	8.7	
$V_2O_4 \cdot 9MoO_3 \cdot 0{,}06P_2O_5/SiO_2$	300	Catalysis	22.4	8.20	1.58	83.5	16.5	335
		Reduction	19.8	7.30	1.10	86.6	14.3	
β-$CoMoO_4$	260	Catalysis	55.0	11.0	2.5	75.5	17.1	259
		Reduction	44.5	9.5	2.0	76.5	16.0	
		Oxidation	55.0	10.8	2.4	75.5	16.6	
α-$CoMoO_4$	260	Catalysis	44.5	0.98	6.05	11.8	73.5	259
		Reduction	36.0	0.87	4.80	9.4	68.0	
		Oxidation	—	–	2.00	–	–	

*Methods and conditions for the preparation of catalysts and their physico-chemical characteristics are described in Ref. 21.
**Samples obtained by different methods and differing in disperison.

Table 1 gives the rates of formation of acrylic acid and products of more deep-seated oxidation on vanadium- and cobalt-molybdenum catalysts.[21–24] As can be seen from Table 1, the rates of formation of acrylic acid for catalysis and reduction are close, indicating the oxidation-reduction mechanism for its formation. In the formation of products of more deep-seated oxidation, oxygen of the catalyst also participates; there is, however, a definite contribution by oxygen in the gas phase, as indicated in some cases by an appreciably higher rate of catalysis than the rate of reduction and the formation in the oxidising pulses of CO and CO_2. An analogous correlation of the rates of catalysis and reduction is also observed at other temperatures.

Table 2. Catalytic properties of tin–molybdenum catalysts for the oxidation of acrolein under conditions of catalysis and reduction.[27]

Catalyst	Working conditions	Contact time, s	Conversion %	Selectivity (%) for		
				$C_3H_4O_2$	$CO+CO_2$	Decomposition products
SnMoBiVO	Catalysis	0.54	34.2	5.0	95.0	0.0
	Reduction	0.54	32.2	5.3	94.4	0.7
	Catalysis	1.07	64.4	3.3	96.7	0.0
	Reduction	1.07	52.5	3.8	96.1	0.1
SnMoBiFeO	Catalysis	1.07	34.5	7.9	91.4	0.7
	Reduction	1.07	34.5	8.1	91.9	0.0
	Catalysis	0.54	30.5	12.8	86.2	1.0
	Reduction	0.54	31.0	11.3	88.0	0.7
SnMoBiFeNiO	Catalysis	0.54	18.6	14.0	84.2	1.8
	Reduction	0.54	17.4	18.2	81.8	0.0
	Catalysis	1.07	28.2	13.5	86.8	0.3
	Reduction	1.07	25.4	12.1	87.2	0.7

The oxidation-reduction mechanism for the formation of acrylic acid on a vanadium–molybdenum catalyst has also been confirmed by the relaxation method.[25] The oxidation-reduction mechanism for the formation of acrylic acid and the associative mechanism for the formation of CO and CO_2, were shown to occur on vanadium–molybdenum oxide catalysts, promoted by Na, Mn, Zn, and Cu.[26] This conclusion was drawn on the basis of kinetic data, which indicated that oxygen has different effects on the mild and deep-seated oxidation of acrolein and on the basis of the change in catalytic properties of samples by treatment of them with reaction mixtures with different oxygen contents.

An analogous conclusion that acrylic acid is formed exclusively by the oxidation-reduction mechanism, and that CO and CO_2 are formed primarily by the oxidation-reduction mechanism, follows from a comparison of conversion and selectivity under the conditions of catalysis and reduction, on promoted tin–molybdenum catalysts (Table 2).[27]

In the opinion of Yakubovich,[28] a step-wise oxidation-reduction mechanism is involved in the formation of acrylic acid and products of deep-seated oxidation, on molybdates of Cr, Cd, Ni, Ba, Co, Mn, Mg, Cu, Zn, Fe, and Ca.

The step-wise oxidation-reduction mechanism can therefore be considered to be established for the preparation of acrylic acid on catalysts of various composition. Products of deep-seated oxidation may be formed by the oxidation-reduction mechanism, with varying contributions from the associative mechanism.

The oxidation-reduction mechanism assumes that oxygen of the latice, generally considered[29–32] to be in the charged state, O^{2-}, takes part in the catalysis. Participation of lattice oxygen in the formation of acrylic acid and the oxides of carbon was demonstrated by isotopic labelling with ^{18}O in reduction experiments with acrolein and phosphomolybdic heteropoly acid.[33] The same is shown by other data.[34] On exposure of $K_3PMo_{12}O_{40}$ to acrolein vapour at catalyst temperatures of 150–300 °C, an ESR signal was observed, as a result of reduction to give an oxygen-deficient Keggin unit, with the gain of two electrons. From the IR spectrum it was established that the oxygen lost was a bridging oxygen atom (Mo–O–Mo). The same view that bridging oxygen participates in the formation of acrylic acid from acrolein, is held by other authors.[33]

It should be noted that the role of bridging or doubly bonded oxygen in the oxidative conversion of acrolein is scarcely discussed in the literature. But in the series of molybdates of elements of group II and period 4, it is those which contain molybdenyl bonds that are chosen.[28,35] The lowest selectivity for acrylic acid is observed for the molybdates of Ba, Ca, and Cd, which are exactly those for which molybdenyl doubly bonded oxygen (Mo=O) is absent.

In connection with the course of reaction by the oxidation-reduction mechanism and the participation of oxygen in the stage at which acrylic acid and products of deep-seated oxidation are formed, a question arises concerning the effect of the bond energy of oxygen to the catalyst on the direction of acrolein conversion and the rates of particular reactions.

For reaction by the two-stage oxidation-reduction scheme, a plot of the dependence of rate on the oxygen-catalyst bond energy shows a maximum, corresponding to optimum bond energy.[36] The ascending part of the curve corresponds to the case when reaction is limited to oxidation on the surface, and the descending part when its rate is determined by the loss of oxygen. A quantitative dependence of activity on bond energy has been found for a series of oxide catalysts in the oxidation of hydrogen, nitrous oxide, and ammonia, and also for the deep-seated oxidation of some hydrocarbons.[37] For all these reactions, the dependence of rate on the bond energy of oxygen with the catalyst follows a descending curve, i.e. the activity of the catalyst is lower, the higher the energy of its bonds with oxygen.

For complex reactions which include a series of parallel and consecutive stages, for each of which there is an optimum strength for the metal–oxygen bond (M–O), its influence on the activity of the catalyst, and especially on its selectivity, is not obvious.

Boreskov[38] has formulated the general requirements for catalyst selectivity: "The energy of the bond between oxygen and the surface of the catalyst must be sufficiently low to provide the required rate of oxidation of the starting material, but at the same time be sufficiently high to ensure that further oxidation of the useful products of incomplete oxidation does not occur".

This position is convincingly confirmed by the way in which selectivity depends on the extent of reduction of the surface, as found for many oxide catalysts in partial oxidation reactions of hydrocarbons.[21,39] Thus, for each catalyst, the selectivity for mild oxidation products invariably increases with the extent of oxygen removal but for products of deep-seated oxidation the selectivity falls. Also, since oxygen as a rule is not homogeneous on the catalysts investigated and its bond energy with the surface increases as a result of reduction, it is generally recognised at the present time that the absence of weakly-bonded oxygen is a requirement for

selectivity. In the oxidation of acrolein, the dependence of selectivity on the extent of reduction for each catalyst is analogous to that described for hydrocarbons and the same rule is applicable, requiring the absence of weakly-bonded oxygen for the course of reaction to be selective. However, the search for a correlation of selectivity and activity, with the bond energy of oxygen in a series of oxide catalysts, has led to complex and even contradictory results. Thus for simple oxides, the rate of formation of acrylic acid and products of deep-seated oxidation was seen to depend on the bond energy with oxygen (Fig. 2), but selectivity was not dependent on this parameter.[40] In contrast, it is established[28,35] that the energy of the M–O bond in a series of molybdates of Mg, Ni, Zn, Mn, Fe, Cr, Cu determines the selectivity precisely and does not influence activity. It should be noted that in the latter case the bond energy of oxygen was determined from the initial rate of reduction by samples of hydrogen. This rate undoubtedly characterises the initial state of the catalyst but since, as shown above, this differs considerably from the stationary state, it is doubtful whether the conclusions of the authors[28,35] can be considered to be sound.

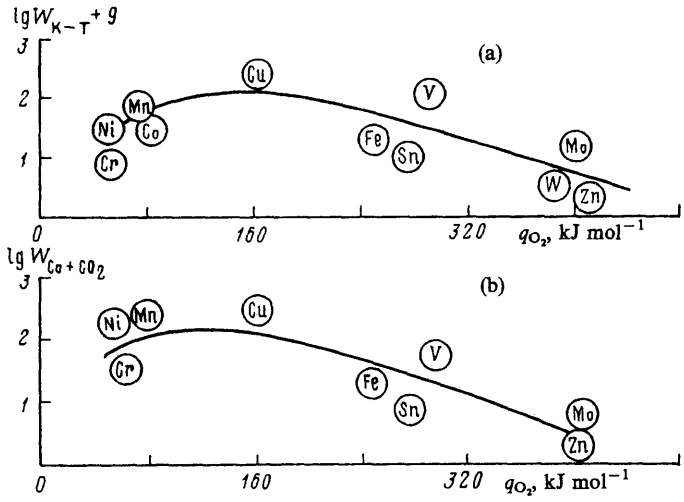


Figure 2. Dependence of the rate of oxidation of acrolein to the acid (*a*) and to Co + CO_2 (*b*) at 300 °C, on the bond energy of oxygen with the surface of oxide catalysts.[40]

An attempt has been made[28,35,40] to find a dependence of catalytic properties on the electronegativities of the cations, which determine the acidity of the catalyst. In the case of molybdates, the acidity of the catalyst does not influence selectivity but it affects the activation energy of the reaction.[28,35] For simple oxides, on the other hand, the selectivity depends on electronegativity.[40]

It is also very difficult to find any correlation of activity and selectivity with the bond energy of oxygen in the cases of V–Mo- and Co–Mo-catalysts. For these examples, as a measure of the bond energy, the heats of the adsorption (q) on the catalysts were determined in the stationary state, either by adsorption of oxygen on the previously reduced surface,[23,24,41] or *in situ*.[42]

As seen from Table 1, for the series of binary and promoted V–Mo-catalysts, only a fall in the rate of acrylic acid formation can be seen to occur with increase in the oxygen bond energy, whereas for the α- and β-modifications of $CoMoO_4$, which have identical values for the oxygen bond energy, the rates differ considerably. All catalysts in the stationary state are characterised by the presence of strongly-bonded oxygen (q_{O_2} = 225–335 kJ mol^{-1}) and with the exception of α-$CoMoO_4$ show high selectivity, but no quantitative correlation of selectivity with q_{O_2} is found.

The oxygen bond energy thus plays an important role in the oxidation of acrolein to acrylic acid but it is not possible to show a dependence of catalytic properties on q_{O_2} as the only parameter. In the oxidation of acrolein, and with the aim of selective oxidation,[36,38,43] it is therefore necessary to take account of other important factors, i.e. specific interaction of the substance being oxidised and the product of reaction with the catalyst surface.

III. Surface complexes of acrolein and acrylic acid and their role in the formation of reaction products

At the present time, basic information on the structure of surface compounds (SC) is obtained by the method of IR spectroscopy. Thermal desorption measurement has previously been widely used to provide evidence of the involvement of SC in the formation of reaction products but in recent years the use of spectroscopic methods *in situ*[44] has also made it possible to study the kinetics of conversion of the SC, and to measure the rate of the catalytic reaction simultaneously.

In Table 3, a summary is given of literature data on the structures of surface compounds of acrolein. Table 4 contains information on the catalysts on which these SC have been observed, together with their catalytic properties in the reaction of acrolein oxidation.

We have attempted on the basis of the literature data to reveal some general principles for the interaction of acrolein with oxide catalysts, giving special attention to the nature of the centre of adsorption and the role of surface complexes in the oxidation of acrolein. We do not dwell on the spectroscopic identification of SC, since this question is considered in detail elsewhere.[58,59]

Centres of adsorption on the surface of oxide catalysts may be protons, H^+ (Brønsted acid centres, BAC), coordinatively-unsaturated cations of transition metals (Lewis acid centres, LAC), and oxygen. These probably give rise to the diversity of the adsorbed forms of acrolein on the surface of oxide catalysts.

The presence of BAC on the catalyst surface, in the form of OH groups or delocalised protons, H^+, leads to the formation of a H-bonded complex with acrolein [SC (I), Table 3]. As a rule, this complex is weakly bonded with the surface and easily decomposes at room temperature as a result of brief pumping, or purging with helium, with the release of acrolein into the gas phase. It is therefore thought that hydrogen-bonded acrolein is not an intermediate in the process by which oxidation products are formed. However, in the presence of strong BAC, more strongly bonded SC (I) may be formed, which are able to participate in the reaction, and this also possibly occurs in the case of heteropoly acids (HPA) and heteropoly salts (HPS).[53]

The interaction of acrolein with aprotic centres (LAC) is accompanied by the formation of a coordinatively-bonded π-complex of acrolein (II), a surface acrylate (IV) and a carbonato-carboxylate complex (V). A number of workers have also observed the

formation of a σ-complex of acrolein (VI) at aprotic centres.[51,55] Surface ions of oxygen, O^{2-}, may also act as centres of adsorption, at which carbonyl-bonded acrolein (III) is stablised (Table 3).

Table 3. Surface complexes of acrolein.

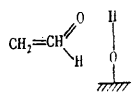
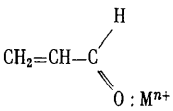
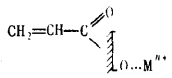
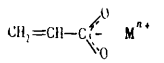
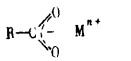
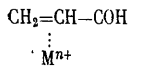
Structure	Name	IR absorption bands cm^{-1}	References
	Hydrogen-bonded acrolein	ν_{O-H} =3500 $\nu_{C=O}$ =1690–1705 $\nu_{C=C}$ =1625 δ_{C-H} =1370	[45–47]
	Coordinatively-bonded acrolein (II)	$\nu_{C=O}$ =1660–1690 $\nu_{C=C}$ =1625 δ_{C-H} =1370	[47–52]
	Carbonyl-bonded acrolein (III)	$\nu_{C=O}$ =1710–1730 $\nu_{C=C}$ =1625	[47–51, 53]
	Acrylate (IV)	$\nu_{as\,COO^-}$ =1520–1560 $\nu_{s\,COO^-}$ =1420–1460 $\nu_{C=C}$ =1640 δ_{C-H} =1370	[47–51, 54–57]
	Carbonato-carboxylate (V)	$\nu_{as\,COO^-}$ =1530 $\nu_{s\,COO^-}$ =1360	[50, 52]
	π-complex (VI)	$\nu_{C=C}$ =1490–1520	[51, 55]

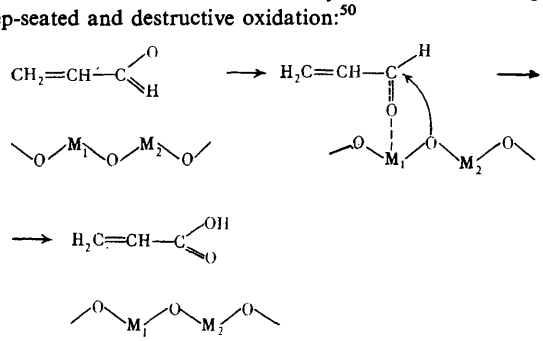
Table 4. Forms of adsorption of acrolein on oxide catalysts.

Chemical composition of the catalyst	Observed SC	Oxidation products	References
MoO_3/SiO_2	(II)	CO, CO_2, $C_3H_4O_2$	[52, 57]
Co–Mo=1 : 2	(II)	$C_3H_4O_2$, CO, CO_2	
Co–Mo + 2% MoO_3	(II)	$C_3H_4O_2$, CO, CO_2	[48, 50]
Co–Mo + 2% Co_3O_4	(II)	CO, CO_2	[48, 50]
Co–Mo + 7% V_2O_5	(II)	CO, CO_2	[48, 50]
Co–Mo + 10% V_2O_5	(II)	$C_3H_4O_2$, CO, CO_2	[49]
Co–Mo + 80% V_2O_5	(II)	$C_3H_4O_2$, CO, CO_2	[49]
V–Mo/SiO_2	(I) (II) (III) (IV)	$C_3H_4O_2$, CO, CO_2	[58]
V-Mo (solid solution of V in MoO_3)	(II) (III) (V)	$C_3H_4O_2$, CO, CO_2	[49]
Cr–Mo	(IV)	$C_3H_4O_2$, CO, CO_2	[54]
Cr–Mo–Te	(IV)		
Bi–Mo/SiO_2	(I)	–	[46]
SiO_2	(I)	–	[45]
MgO	(IV)	CO, CO_2, C_2H_4O $C_2H_4O_2$	[24, 56]
CuO	(V)	CO, CO_2	[24, 57]
Co–Mo/MgO	(II) (III) (IV) (VI)	–	[51]
Cr_2O_3	(V)	CO, CO_2	[52]
ZnO	(V)	CO, CO_2	[54]
$K_3PMo_{12}O_{40}$	(III)	$C_3H_4O_2$, CO, CO_2	[53]

*For name of the corresponding SC see Table 3.

As seen from Table 4, it is very difficult to link any form of surface complex directly with the defined chemical composition of the catalyst and with its catalytic properties: one and the same SC, for example coordinatively-bonded acrolein or acrylate, may be observed on a catalyst for the selective, deep-seated, or destructive oxidation of acrolein. Furthermore, on some catalysts, in spite of the rather diverse composition of the products of oxidation, only one surface complex was identified.

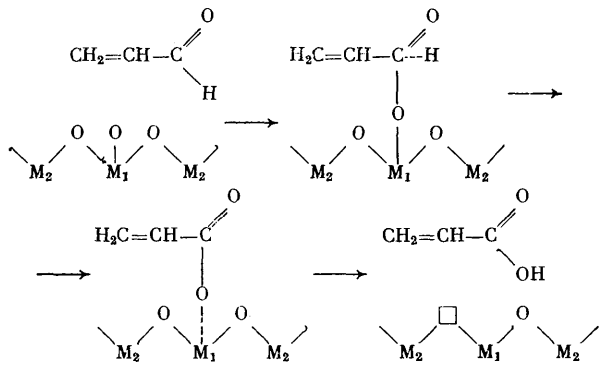
There are various opinions on the role of SC in the course of reaction. Thus, it is assumed that coordinatively-bonded acrolein is an intermediate in the formation of acrylic acid and also of products of deep-seated and destructive oxidation:[50]



where $M_1 = Mo^{6+}(T_d)$, $Mo^{5+}(T_d)$; $M_2 = Mo^{6+}(O_h)$, $Co^{2+}(O_h)$. The initial interaction presumably occurs with Mo^{6+} in either tetrahedral (T_d) or octahedral (O_h) coordination, or with Mo^{5+}.

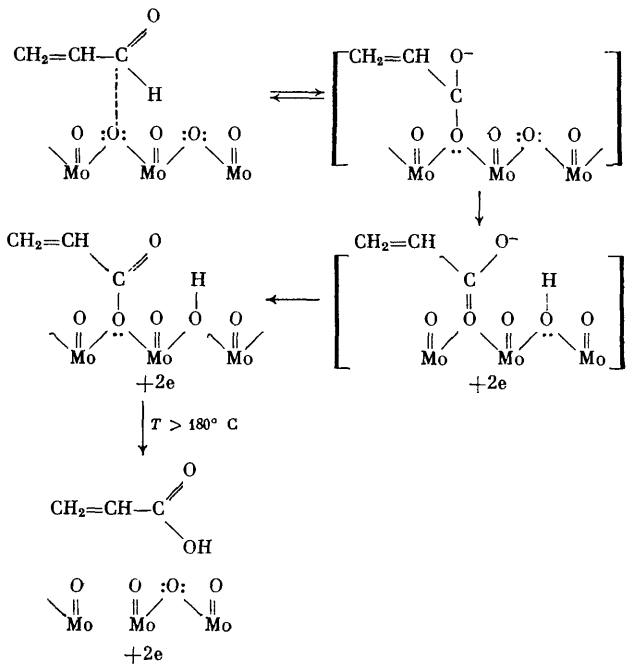
Coordinatively-bonded acrolein, for which the centres of adsorption on Co–Mo–V-oxide catalysts are Co^{2+} or Co^{3+} ions, in octahedral coordination, is thought[50] to be an intermediate in the formation of products of destructive oxidation. Certain authors believe[48–50] that surface acrylates [SC (IV)] are blind-alley forms for the adsorption of acrolein on Mo-containing oxide catalysts, whereas others[54] recognise acrylates as intermediate compounds both in the partial and the deep-seated oxidation of acrolein. The literature data allow a more definite judgement to be made on the direction of conversion for carbonyl-bonded acrolein (III) and surface carboxylates (V): almost all authors hold the opinion that (III) is an intermediate SC in the formation of acrylic acid, but (V) in the formation of deep-seated oxidation products.

The mechanism for the formation of acrylic acid through carbonyl-bonded acrolein is presented in the following scheme:[50]



$M_1=V^{5+}$, Mo^{6+} (*Oh*); $M_2=V^{4+}$

An analogous mechanism is also proposed for the oxidation of acrolein on phosphomolybdic heteropoly acids (HPA):[53]



This mechanism is confirmed by the results of an investigation into the adsorption of acrolein on $K_3PMo_{12}O_{40}$ by the methods of IR spectroscopy and ESR *in situ*.[53]

Another mechanism has been proposed[33] for the oxidation of acrolein and methacrolein on HPA, similar to the mechanism for the oxidation of aldehydes by chromic acid or permangante in solution.

The scatter of opinions on the mechanism of acrylic acid formation is due, first of all, to the use in most cases of insufficiently selective catalysts, with the result that several reaction products are obtained. Furthermore, the forms of adsorption were investigated under the conditions of pre-catalysis, when it is impossible to make a direct comparison between the rate for decomposition of the SC and the formation of reaction products. Such a comparison provides the most convincing evidence of the participation of one or other SC in the formation of reaction products.[60]

These conditions were observed in a study of the mechanism of acrolein oxidation by the method of IR spectroscopy *in situ* on a V–Mo–Si-oxide catalyst.[61,62] This catalyst possesses high selectivity: for acrolein conversions of less than 20%, acrylic acid is virtually the only reaction product, and with high conversions, further oxidation is also insignificant. Furthermore, good IR transmission of the sample made it possible to investigate the decomposition of surface compounds in the temperature range 25–350 °C, under the conditions of catalysis. Adsorption of acrolein on this catalyst led to the identification of a hydrogen-bonded SC (I), coordinatively-bonded SC(II), carbonyl-bonded SC (III), acrolein, and acrylate SC (IV).[58]

The hydrogen-bonded complex does not take part in the reaction; it is weakly bonded with the surface and is removed after brief pumping at room temperature. Prolonged standing at 25 °C, or increase of the temperature to 100 °C, converts the surface complex (II) into SC (III), an unsymmetrical acrylate which is converted into the symmetrical acrylate SC (IV) with further increase in temperature.

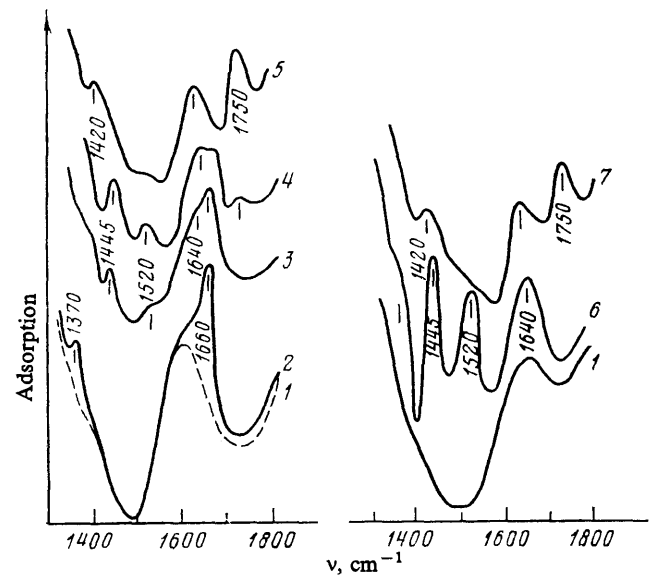


Figure 3. IR spectra of the initial V–Mo–Si–O-catalyst (*1*) and with passage of the reaction mixture containing 0.2 vol.% C_3H_4O; 0.4 vol.% O_2; 99.4 vol.% He at 25 (*2*), 125 (*3*), 160 (*4*), and 280°C (*5*) and after adsorption of acrylic acid at 80 °C (*6*) and 280 °C (*7*).[62]

Under the conditions of the catalytic reaction, with partial oxidation on a V–Mo–O-catalyst, in the temperature range 75–300 °C, the method of high-temperature IR spectroscopy *in situ* identified three surface complexes: coordinatively bonded acrolein (II), acrylate IV) and a molecular form of the adsorbed reaction product, acrylic acid (VII).[61,62]

Because of the high rate on conversion of SC (III) into (IV) under the conditions of reaction it is not possible to observe the change in concentration of SC (III).

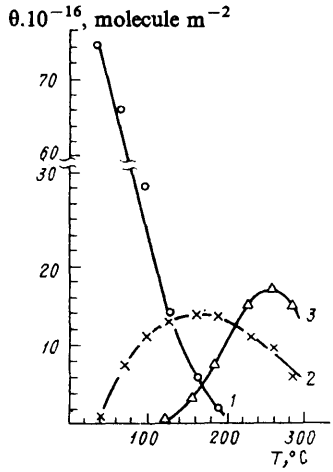


Figure 4. Dependence of the stationary concentrations of SC (II) (curve *1*), (IV) (*2*), and (VII) (*3*), on reaction temperature.[62]

Fig. 3 presents the IR spectra which are obtained by passing the reaction mixture, containing acrolein, through a reaction cell with the V–Mo–Si–O-catalyst, and after the adsorption of acrylic acid. In the temperature range up to 100 °C, only the σ-complex of acrolein [SC (II)] is formed on the surface: $\nu_{C=O}$ = 1660, $\nu_{C=C}$ = 1620, δ_{C-H} = 1370 cm^{-1} (Fig. 3, spectrum *2*). With increase of the temperature to 160 °C, the intensities of the absorption bands at 1370 and 1660 cm^{-1} decrease and absorption bands appear, related to acrylate [SC (IV)]: $\nu_{C=C}$ = 1640, $\nu_{as\,COO^-}$ = 1520, $\nu_{s\,COO^-}$ = 1445 cm^{-1} (Fig. 3, spectra *3* and *4*). Further increase in temperature to 250 °C leads to a decrease in intensity of the absorption bands characteristic of acrylate, and to the appearance of absorption bands at 1420 and 1750 cm^{-1} (Fig. 3, spectrum *5*), which are caused, in our opinion, by re-adsorption on the SiO_2 carrier of acrylic acid, formed at the stage of disintegration of the acrylate. This was confirmed by the formation of SC (VII), by the adsorption of acrylic acid (Fig. 3, spectrum *7*). Acrylate is another surface compound, formed by the adsorption of acrylic acid on the V–Mo–Si–O-catalyst (Fig. 3, spectrum *6*).

The dependence of the stationary concentrations of surface complexes of acrolein on reaction temperature is given in Fig. 4.

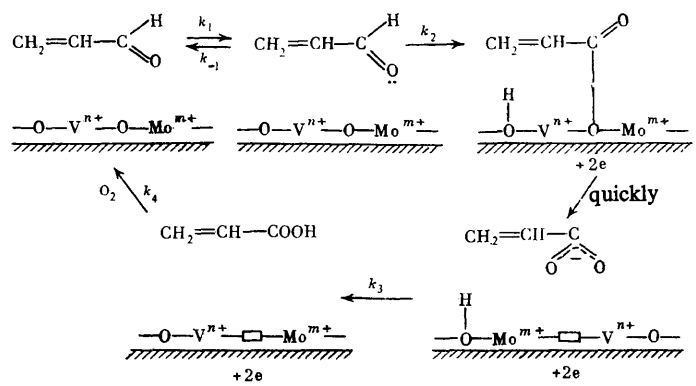
In order to resolve the question of the participation of the observed SC in the course of reaction, a comparsion was made of the rates of formation of reaction products and the rates of destruction of the SC (Table 5). On the basis of such a comparison, it was concluded that acrylic acid is formed by decomposition of the surface acrylate. In the temperature range for which the re-adsorption of acrylic acid on SiO_2 [SC (VII)] is observed, the rate of formation of acrylic acid is close to the sum of the rates of decomposition of SC (IV) and SC (VII).

The active component of the investigated V–Mo–Si–O-catalyst is the chemical compound VMo_3O_{11}, in which vanadium is found in the V^{4+} state and the charge on Mo is close to 6+.[63] It has been shown[58] that the centres of stabilisation for SC (II) on this catalyst are the molybdenum ions, but the centres of stabilisation for acrylate are V^{4+} ions.

Table 5. Comparison of the rates of formation of products of desorption and decomposition of surface compounds.

T, °C	Stationary concentration of SC, $\theta.10^{-16}$ molecule m^{-2}			Rate of decomposition of SC, $W.10^{-14}$ molecule $m^{-2}\,s^{-1}$			Rate of formation desorption products, $W.10^{-14}$ molecule $m^{-2}\,s^{-1}$	
	(II)	(IV)	(VII)	(II)	(IV)	(VII)	$C_3H_4O_2$	$CO+CO_2$
125	14.6	11.3	trace	4.5	0.4	–	0.5	trace
190	2.5	13.0	8.0	–	0.6	0.3	1.1	0.03
230	trace	11.0	16.0	–	1.0	1.4	2.7	0.08
260	–	8.0	17.3	–	1.2	2.2	4.7	0.20
285	–	5.0	14.0	–	0.5	5.2	7.2	0.30

The stated mechanism for the formation of acrylic acid on a V–Mo–Si–O-oxide catalyst can be presented as follows:



A study[62] has been made of the kinetics of conversion for the SC of acrolein, and a non-stationary kinetic model was proposed for the oxidation of acrolein to acrylic acid on a V–Mo–Si–O-catalyst, describing the change in concentration of the SC and the gaseous components of the reaction mixture with time in the temperature range 25–300 °C.

Values of rate constants for the separate stages are given below:

$$k_1 = 23\ atm^{-1}\cdot s^{-1};\ k_{-1} = 1.0\cdot 10^2 \exp\left(-\frac{10\,000}{RT}\right) s^{-1};$$

$$k_2 = 4.5\cdot 10^6 \exp\left(-\frac{19\,000}{RT}\right) s^{-1};$$

$$k_3 = 2.1\cdot 10^3 \exp\left(-\frac{13\,000}{RT}\right) s^{-1};$$

$$k_4 = 1.8\cdot 10^{-14} \exp\left(-\frac{8000}{RT}\right) m^2.molecule.atm^{-1}s^{-1}.$$

Thus, the first stage of reaction in the oxidation of acrolein on a V–Mo–Si–O-catalyst is a donor-acceptor type interaction, with transfer of an electron pair to a vacant orbital of the highly charged and electronegative Mo^{n+} cation. The formation of the σ-complex (II) is accompanied by activation of the C–H bond which undergoes heterolytic fission in the presence, on the surface, of nucleophilic oxygen, with formation of a fragment $(CH_2=CH-C=O)^-$ possessing a formal charge $Q = -1$. This fragment is a good electron donor and restores the catalyst by sharing the electrons of the carbonyl group, with consequent formation of an electrophilic species $(CH_2=CH-C=O)^+$. Calculation shows that the positive charge is almost totally localised on the carbon of the carbonyl group ($Q = 0.8$),[58] so that the species is highly reactive to nucleophilic attack by oxygen of the catalyst, leading to the formation of SC (III). The change from SC (III) to (IV), a symmetrical acrylate with equivalent oxygen atoms, does not apparently present energetic difficulties and occurs rapidly. Decomposition of the surface acrylate (IV), resulting in the formation of acrylic acid, is the slowest step. This mechanism is also confirmed by experimental data, obtained for the stationary state in the course of the reaction. The corresponding kinetic equation:[64]

$$W_{aa} = k_1 C_{acr}/(1 + k_2 C_{acr} + k_3 C_{acr}/C_{O_2}) ,$$

where C_{acr} and C_{O_2} are the concentrations of acrolein and oxygen respectively, describe the experimental data well over a wide range of temperatures and concentrations.

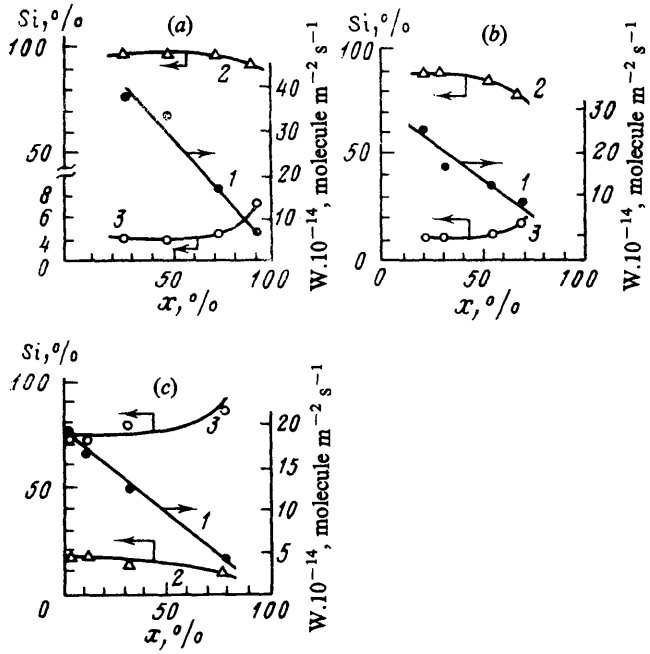


Figure 5. Dependence of catalyst activity (*1*), and its selectivity for C_3H_4O (*2*) and CO + CO_2 (*3*), on the extent of conversion of acrolein at 260 °C, on: *a*, $V_2O_5.3MoO_3/SiO_2$; *b*, β-$CoMoO_4$; *c*, α-$CoMoO_4$.[24] Composition of the reaction mixture: 0.2 vol.% C_3H_4O; 0.4 vol.% O_2; 99.4 vol.% He.

IV. Bond energies of intermediate compounds and the direction of acrolein conversion

The formation of coordinatively-bonded acrolein [SC (II)], appears to be the general form of its interaction with oxide catalysts, on the surface of which there are aprotic centres. It is probably the precursor of the other oxidised SC, namely SC (III), (IV), and (V). However, for selective oxidation of acrolein to acrylic acid, it is insufficient that a σ-complex of acrolein should be formed, followed by its oxidation to a surface acrylate by oxygen of the catalyst. As seen in Table 4, surface compounds of types (II), (III), and (IV) may be formed on inactive and unselective catalysts. The direction of conversion of the surface compounds is influenced more decisively by the strengths of their bonds with the centres of stabilisation and the reactivity of oxygen of the catalyst.

The influence of the bond strengths of the surface complexes of acrolein and its oxidation product, acrylic acid, on the direction of the reaction is confirmed graphically, by comparison of the catalytic properties of vanadium– and cobalt–molybdenum catalysts, and also by their thermal desorption data.[58]

Fig. 5 shows the dependence of the selectivity of these catalysts for acrylic acid and products of deep-seated oxidation, on the conversion of acrolein. The reactions in all cases are described by the consecutive-parallel scheme (Scheme 1) and by first order equations, so that it is possible to express the initial selectivity (S^0) and the constant of (further) oxidation (*b*) as follows:

$$S^0_{aa} = \frac{k_1}{k_2 + k_1} , \quad S^0_{CO+CO_2} = \frac{k_2}{k_1 + k_2} , \quad b = \frac{k_3}{k_1 + k_2}$$

Table 6. Catalytic properties of various catalysts for the oxidation of acrolein (composition of the reaction mixture, vol.%: C_3H_4O—0.2%, O_2—0.4%, He—99.4%, reaction temperature—260 °C.

Chemical composition	Specific surface $m^{-2}\,g^{-1}$	Reaction rate, $W.10^{-14}$, molecule $m^{-2}\,s^{-1}$, for x=50%		Initial selectivity %		Further oxidation constant, *b*, mol fraction
		Overall conversion of acrolein	Formation of acrylic acid	$C_3H_4O_2$	$CO+CO_2$	
$V_2O_4 \cdot 9MoO_3/SiO_2$	44.0	8.85	8.43	96.0	4.0	0.01
β-$CoMoO_4$	9.0	14.60	11.00	88.0	10.0	0.04
α-$CoMoO_4$ *	9.0	8.20	0.97	18.0	75.0	0.20
$V_{0.05}Sb_{0.95}$ **	78.0	0.53	0.20	90.0	10.0	1.70

*Acetic acid present in the reaction products.
**Reaction temperature 300 °C.

In Table 6, the values of S^0_{aa} and *b* are given for the catalysts under investigation. In Fig. 6, the results of chromatographic analysis are shown for the products of thermal desorption for acrolein (Fig. 6*a*) and acrylic acid (Fig. 6*b*) on the V–Mo–Si–O-catalyst.[24] In both cases, in the temperature range 70–350 °C, the

desorption of acrolein and acrylic acid is not accompanied by destruction of the carbon skeleton. In the 350–500 °C region the products of thermal desorption are CO and CO_2. On α- and β-$CoMoO_4$, the thermal desorption curves have a similar appearance, yet acetaldehyde and acetic acid are also present among the products of decomposition.[24]

In Fig. 7*a*, the initial selectivities for acrylic acid and for products of deep-seated oxidation are compared with the relative amounts of the weakly sorbed (T_{des} = 70–350 °C) and strongly sorbed (T_{des} = 350–500 °C) acrolein (θ^{acr}_{weakly} and $\theta^{acr}_{strongly}$ respectively), and Fig. 7*b* shows the dependence of the further oxidation constant (*b*) on the relative amount of strongly sorbed (T_{des} = 350–500 °C) acrylic acid. The correlation of these values clearly indicates the participation of a weakly bonded form of acrolein in the formation of acrylic acid, but strongly bonded forms of acrolein and acrylic acid in the formation of products of destructive oxidation by parallel and consecutive pathways. The proportions of these forms also determine the selectivity. It should be noted that revelation of such a clear correlation was favoured by the purely fortuitous closeness of the bond energies for oxygen on these catalysts (see Table 1).

From Figs. 4 and 6*a*, it follows that the weakly bonded forms of acrolein are coordinatively-bonded acrolein [SC (II)] and acrylate [SC (IV)]. The structure of strongly bonded acrolein on the V–Mo–Si–O-catalyst could not be identified by IR spectroscopy, the amount being very small because of the high selectivity of the catalyst.

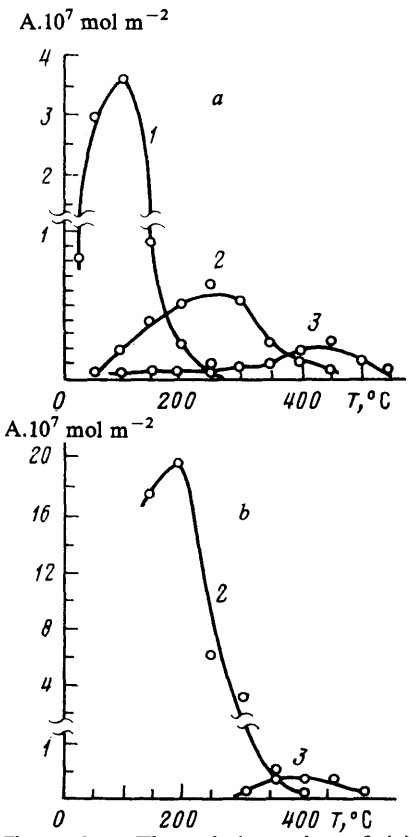


Figure 6. Thermal desorption of (*a*) acrolein and (*b*) acrylic acid with V–Mo–Si–O-catalyst.[24] *1*, acrolein; *2*, acrylic acid; *3*, CO + CO_2.[24]

Surface compounds of the acrylate type are formed by the adsorption of acrylic acid on both selective and non-selective catalysts for the oxidation of acrolein (see Table 4). It has been shown[65] that the properties of the surface acrylates, in particular the strength of the bond with the surface, can be judged by the temperature of decomposition by thermal desorption, and that the composition of the products of desorption on various catalysts differ considerably. Weakly bonded arylates that are formed for example, by the adsorption of acrylic acid on the V–Mo–O-catalyst and on MoO_3, are decomposed by an increase in temperature to 200 °C, with release of acrylic acid into the gas phase. Acrylate, formed on MgO, is strongly bonded with the surface and undergoes practically no change up to 400 °C. Further increase in the temperature leads to its destructive oxidation to give surface carboxylate, containing no C=C bond [SC (V)], and further decomposition occurs above 500 °C with release into the gas phase of acetic acid, acetaldehyde, and oxides of carbon. On CuO, a typical catalyst for deep-seated oxidation, further oxidation of the surface acrylates occurs at only 200 °C to give carbonato-carboxylate complexes, which decompose at 250 °C with the release into the gas phase of oxides of carbon. The low temperature at which further oxidation of SC (IV) occurs in this case is due, apparently, to the presence of weakly bonded oxygen in CuO.

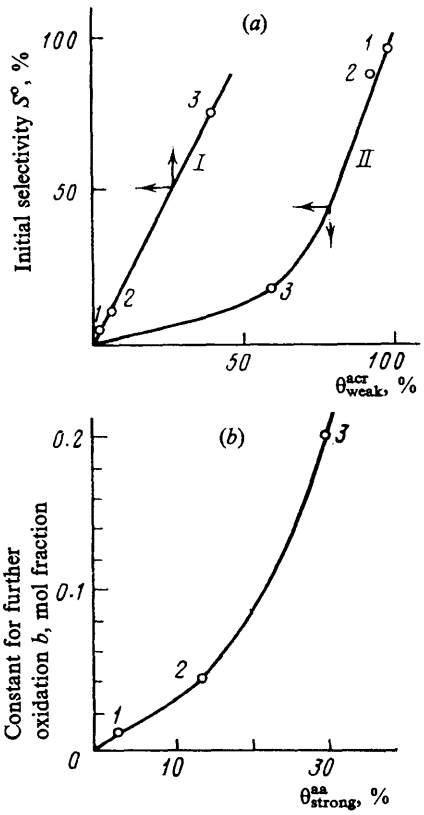


Figure 7. Dependence of initial selectivities for strongly adsorbed acrolein (curve *1*), and for acrylic acid (curve *2a*) in relation to weakly adsorbed acrolein; and the dependence of the constant for further oxidation on the relative quantity of strongly adsorbed acrylic acid (*b*). Catalysts used: *1*, $V_2O_5.9MoO_3/SiO_2$; *2*, β-$CoMoO_4$; *3*, α-$CoMoO_4$.

Thus, from all accounts, it follows that the bond strength of the intermediate surface compounds determines the direction of conversion of acrolein, but the simultaneous requirement of high activity and selectivity dictates that the SC should have an optimum bond energy. Evidently, the higher the bond energy of oxygen and the lower the bond strength of the SC of the adsorbed acrolein, the more selective the catalyst but the lower is its activity.

In Table 7 the heats of adsorption are given for acrolein and acrylic acid on promoted V–Mo–O-catalysts, measured *in situ* by a calorimetric method[66] together with the heats of adsorption for oxygen.[42]

Table 7. Catalytic properties of modified V–Mo-oxide samples, supported on SiO_2 (70 mass% SiO_2).

Composition of active material	$W.10^5$, mol m^2 h^{-1} for $x=70\%$	S^o_{aa}, %	Further oxidation constant, b mol fraction	Heat of adsorption, q kJ mol^{-1}		
				C_3H_4O [66]	$C_3H_4O_2$ [66]	O_2 [42]
$V_2O_4 \cdot 9MoO_3$	10.6	96.5	0.011	84	75	255
$V_2O_4 \cdot 9MoO_3 \cdot 1CuO$	12.3	98.3	0.005	84	75	226
$V_2O_4 \cdot 9MoO_3 \cdot 0.2Cs_2O$	0.3	97.5	0.058	84	96	326
$V_2O_4 \cdot 9MoO_3 \cdot 0.06P_2O_5$	6.3	88.0	0.014	117	75	335
$0.5 \cdot V_2O_4 \cdot 9MoO_3 \cdot 0.5SiO_2$	10.6	97.0	0.007	–	75	274

As seen from Table 7, the most active and selective catalysts (the binary and copper-promoted V–Mo–O-catalyst) are characterised by heats of adsorption $q_{O_2} = 230-250$, $q_{acr} = 75$, and $q_{acr} = 84$ kJ mol^{-1}. These values are apparently close to the optimum.

The influence of the energetic characteristics of the intermediate compounds on the rate of formation of acrylic acid on V–Mo-catalysts can be seen from Fig. 8. The slow stage of the oxidation reaction of acrolein is desorption of acrylic acid.[62,64] In accordance with the Brønsted–Polanyi equation, the rate of formation of acrylic acid is described by the following expression:

$$W_{aa} = A \exp \frac{-\alpha q_{aa} - \beta q_{O_2}}{RT} [V^{4+}],$$

where $A = k_0 \exp(-E_0/RT)$. The applicability of this equation is confirmed by Fig. 8. A coincidence is observed between the experimentally found number of V^{4+} centres for the stabilisation of acrylate and that calculated from the given equation, with $\beta = 0.07$ and $\alpha = 0.4$. These values for the coefficients α and β correspond to the limiting stage of the reaction; they allow a judgement to be made about the relationship of oxidation-reduction (β) and acid-base (α) properties of the catalyst.

From the mechanism of reaction we turn to a consideration of the principles underlying the choice of catalyst for the oxidation of acrolein to acrylic acid. The basic factor which determines the direction of reaction is the energy of the bond with the SC. Acrolein and the product of its oxidation, acrylic acid, differ in acidic properties and it is therefore possible to influence the strengths of the bonds of the intermediate compounds by regulation of the acid-base properties of the catalyst. For a selective course of reaction, optimum acidity is required: on the one hand, it is necessary to ensure the possible adsorption of acrolein as an organic base with a high velocity of conversion but on the other, to prevent the re-adsorption of acrylic acid to avoid further oxidation. Increase in the acidity above the optimum, gives rise to the formation of a strongly bonded SC of acrolein and leads to an increase in the proportion of products of deep-seated oxidation which are formed by a parallel route, lowering the initial selectivity for acrylic acid. A multistage mechanism for the formation of acrylic acid assumes the existence, in selective catalysts, of a number of centres, differing in their donor–acceptor properties and in their ability to form weakly bonded σ-complexes of acrolein (II) and acrylate (IV).

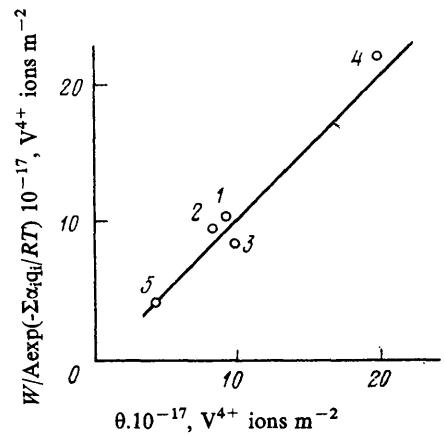


Figure 8. Comparison of the calculated and experimental numbers of V^{4+} centres. Catalysts used: *1*, $V_2O_4.9MoO_3/SiO_2$; *2*, $V_2O_4.9MoO_3.1CuO/SiO_2$; *3*, $0.5V_2O_4.9MoO_3.0.5TiO_2/SiO_2$; *4*, $V_2O_4.9MoO_3.0.06P_2O_5/SiO_2$; *5*, $V_2O_4.9MoO_3.0.2Cs_2O/SiO_2$.

Since acrylate, i.e. the surface complex from which acrylic acid is formed spontaneously, is a salt-like compound, the optimum composition of the catalyst must include elements such as V^{4+}, Mo^{4+}, or Ti^{4+}, which possess amphoteric properties in the oxidation state that is realised under reaction conditions. At the same time, the first stage, the formation of a σ-complex of acrolein, [SC (II)], requires the catalyst to contain highly electronegative ions of the Mo^{6+} type. Nevertheless, an important requirement for catalyst selectivity is the presence of oxygen with a sufficiently high energy bond. Although oxygen participates in all stages of conversion of the surface compounds, its energetic characteristics in the first place affect the stage at which the σ-complex undergoes conversion, since it is precisely on this that the subsequent structure of the SC depends: oxygen, possessing high reactivity, forms surface complexes with high oxygen content, thus promoting the destruction of adsorbed molecules and, consequently, their non-selective conversion. The sum total of these conditions also determines the influence of the acid-base and oxidation-reduction properties. The catalyst which best satisfies these requirements is the V–Mo–O-catalyst, which has energetic characteristics (q_{O_2}, q_{aa}, q_{acr}) that are apparently near to the optimum.

Knowledge of the detailed reaction mechanism allows the catalytic properties of the sample to be changed by the introduction of appropriate additives. Thus, the V–Mo–O-catalyst, on which the limiting stage of reaction is the conversion of the surface acrylate, can be improved by the introduction of a weakly basic additive such as Cu.[67] The introduction of strongly basic additives (Cs, Na, K) or an acidic additive, P, causes a sharp deterioration in the properties.[68] On the contrary, for the V–Sb–O-catalyst, the surface of which does not contain highly electronegative ions, the limiting stage is the formation of coordinatively-bonded acrolein [SC (II)].[69] This catalyst is improved significantly by the introduction of acidic additives, for example phosphorus:[70] its activity is increased and its selectivity is also increased, on account of the suppression of further oxidation of the acrylic acid.

The optimum combination of acid-base and oxidation-reduction properties may only be achieved by the use of a multi-component catalyst. This is confirmed by the low efficiency of individual oxides for the formation of acrylic acid.[40] Molybdates of group II metals of the periodic system[28] are also far from being optimum catalysts: with the reaction proceeding by the mechanism described above, acrylate must be stabilised on these compounds at highly basic ions, i.e. it must be strongly bonded with the surface; this, however, favours an increase in the temperature of the catalyst and destruction of the acrylate, as observed experimentally.

It should be noted that the views described here indicate only the general direction of the search for the chemical composition of a catalyst. In each particular case it is necessary to take account of the structure, coordination sphere, valency state, and proportions of the chemical elements in the catalyst, since these are all reflected in the oxidation-reduction and acid-base properties which determine the structure and strength of the various surface compounds. The examples of α- and β-$CoMoO_4$ are object lessons in this respect. These two polymorphous modifications, differing in the coordination of the Mo, and in the presence of Co^{3+} ions in α-$CoMoO_4$ but not in β-$CoMoO_4$, possess different catalytic properties in the reaction of acrolein oxidation:[24] α-$CoMoO_4$ in practice is a catalyst for the deep-seated oxidation of acrolein, but β-$CoMoO_4$ is a selective catalyst.

In conclusion, it should be noted that the oxidation of acrolein to acrylic acid is not an exception in the large number of reactions of partial oxidation. The role of the acid-base and oxidation-reduction properties of the catalyst in such reactions was shown for the first time in an earlier publication[71] and later by other workers.[72,73] At the present time, it is suggested that reactions and catalysts should be classified by their type of acid-base and oxidation-reduction activity.[74]

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73. T Seiyama, M Egashira, M Iwamoto *Some Theor. Probl. Catal. II Japan–Soviet Catalysis Seminar*, Tokyo, 1973, p. 35
74. G I Golodets *Mekhanizmy Kataliza* (Mechanisms of Catalysis), Nauka, Novosibirsk, 1978, **2** 142

Translated from *Uspekhi Khimii* **60** 2020–2046 (1991) U.D.C. 547.421

gem-Polyols — a unique class of compound

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ABSTRACT. The formation and conversions of *gem*-polyols have been examined together with their chemical and physical properties.

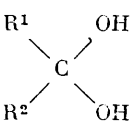
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I. Introduction

Polyalcohols with a geminal structure (I), i.e. *gem*-polyols, are an ill-defined class of organic compound.

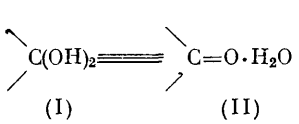


(I)

where R^1 and R^2 = OH or another group of atoms or a specific atom.

In his time, A M Butlerov was puzzled by the fact that "...methyl[ene] glycol was not only unknown but that its existence seemed unlikely: it was not obtained in reactions where its formation might have been anticipated. At present, theory cannot adequately explain this phenomenon..."[1] Although, today, a large number of stable compounds with structure (I) are known, including methylene glycol as the primary form of formaldehyde in aqueous solution,[2] *gem*-polyols more usually play a secondary, incidental role in chemistry as the hydrated form of carbonyl compounds. In the *Universal Decimal Classification* of recent years,[3] it is stated under the entry 547.421.2 that structure (I) represents 'Hypothetical geminal glycols'. In a standard text-book,[4] it is said that on formation of *gem*-diols they are immediately converted into the corresponding aldehyde or ketone.

The fact that the *gem*-polyol structure (I) has not been recognised is evident in nomenclature and formulae which chemists have adopted. Even specialists in this field have referred to such as hydrated carbonyl compounds with structure (II), which clearly is far from a true representation.



(I) (II)

Thus, doubt on the authenticity of (I) has existed since the early days of organic chemistry and remains today. This is, in part, because of their unique properties, which are quite different from those of simple alcohols, and, in part, because little research has been carried out in this field. The chemistry of their formation and subsequent conversions cannot be generalised. Rather, it is dependent on the particular structure of the molecule, the medium, and other factors. Specific information on the nature of *gem*-polyols is still needed in all areas.

In spite of the fact that new data on the properties of (I) are currently being reported in the literature, reviews on this subject are sparse. From the period 1966 to date, the key cited reference is still that on the reversible hydration of aliphatic aldehydes[5] (Russian version see Ref. 6). Monographs have been devoted to the important analytical reagent, ninhydrin, and its analogues, which are stable *gem*-diols.[7,8] Furans with a *gem*-polyol group, and related compounds, have been discussed as part of a review.[9]

Derivatives of (I), especially acetals[10] and orthoesters,[11,12] have been reviewed much more. However, such compounds, which today are readily available, are not normally prepared from *gem*-polyols and therefore have no direct bearing on the theme of the present review.

The study of the chemistry of *gem*-polyols is important for the understanding of a whole range of reactions, certain of which pertain to quite unrelated aspects of organic and inorganic chemistry. These include the hydration of carbonyl-containing compounds and oxides, the interconversion of pyro-, meta- and ortho-acids, the hydrolysis of esters, the condensation of carbonyl-containing compounds, catalysis and isotopic exchange, hydride transfer and other redox conversions of polyhydroxides, etc. Significantly, *gem*-polyols or their derivatives are invariably cited as intermediates in any mechanistic analysis of the above reactions.[13–20] However, in most instances, the representation of *gem*-polyol intermediates is purely symbolic and does not imply the existence of molecules of structure (I) as real compounds.

The present review is devoted strictly to *gem*-polyols and reactions which are specific to them. From the accumulated experimental data, it has been possible to distinguish and consider (I) as a distinct class quite apart from carbonyl-containing compounds.

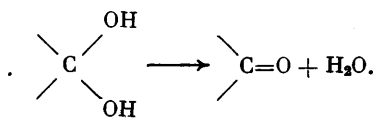
For convenience, *gem*-polyols can be subdivided into three groups: 1) stable, normally crystalline compounds; 2) less stable compounds which exist only in solution; and 3) very unstable intermediates. The first two groups refer essentially to *gem*-diols as a distinct class, while the third embraces all forms of *gem*-polyol. In certain instances, the salt form is more stable than the neutral molecule.

A whole range of modern techniques has been utilised for structural analysis of (I) and for the elucidation of the nature of the species in solution. A number of these have been discussed before.[5,6] They include UV-, IR-, and NMR-spectroscopy, circular dichroism,

polarograph, isotopic exchange, and chemical analysis. Each of these methods has its limitations, so that alternative analyses are always required. Thus, polarographic data on the hydration of aldehydes has, in certain instances, been disputed because of the inherent speed of the methodology, while others argue the obvious benefits of being able to regulate the pH and voltage accurately.[21]

II. The reality of 'hypothetical' compounds

Doubt on the authenticity of geminal polyols is basically groundless. In reality, these compounds are in equilibrium with the corresponding carbonyl compounds and water:



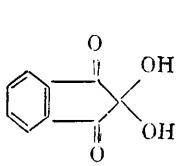
Normally, dehydration is facile, although in certain instances difficulty has been encountered. References in the literature to stable *gem*-diols first appeared in 1910 with reports on the synthesis of ninhydrin,[7] in which one of its three keto groups is hydrated with ease. Today, the list of such compounds is significant, and many authors have studied the factors which control the equilibrium between the *gem*-polyol (*gem*-diol in most instances) and carbonyl form. One elementary fact has been established: electron-accepting groups adjacent to the *gem*-diol group tend to stabilise, and electron-donating groups destabilise, the function. However, this is a complex issue since many other factors have to be considered. The requirements of listing all known *gem*-polyols (I) is clear, as also is the examination of their behaviour in different media and the results of structural analyses, etc.

1. Crystalline *gem*-diols

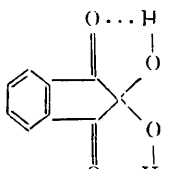
For convenience, these compounds have been subdivided into the following categories: 1) products obtained by hydration of aliphatic α-halogeno-ketones and -aldehydes, 2) aldehydo- or keto-hydrates of a number of α-aldehydo- and α-keto-acids, polyketones and α-keto-aldehydes, 3) hydrates of pyridylcarbonyl compounds, 4) conjugated cyclic ketone hydrates, and 5) *gem*-diols stabilised by intramolecular hydrogen bonds. The latter is evidently a factor to consider with all *gem*-diols.

a) Carbonyl-containing dihydroxymethylenes

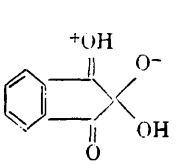
Ninhydrin is a well-known reagent for detection of amino groups (especially amino-acids). It exists in the very stable *gem*-diol form (III), both in the crystalline state and in solution.[7,8] Rukhman[7] was first to study the stability of (III), and proposed that either hydrogen bonding, as in (IV), was responsible or that stabilisation was gained by the formation of a zwitter ion (V).



(III)



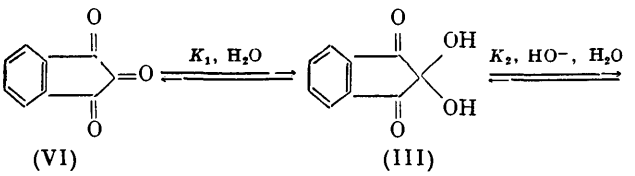
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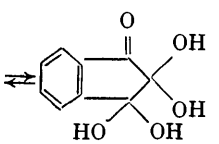
(V)

The formation of (III) proceeds readily even on dissolving 1,2,3-indantrione (VI) in water. A second carbonyl group is hydrated under base catalysis.[22] It is proposed that the anionic form (VIII) of ninhydrin is involved in the formation of the dihydration (VII). The relative amounts of the three forms (III, VI and VII) have been calculated as follows:

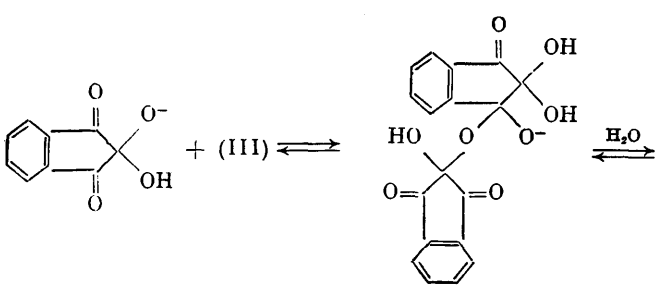
$$K_1 = \frac{[III]}{[VI]} = 2.9 \cdot 10^3; \quad K_2 = \frac{[VII]}{[III]} = 0{,}31 \pm 0.04;$$



(VI) (III)



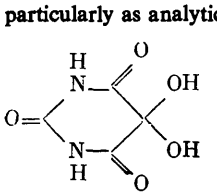
(VII)



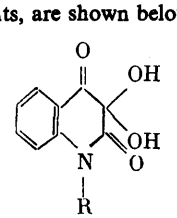
(VIII)

(VII) + (VIII).

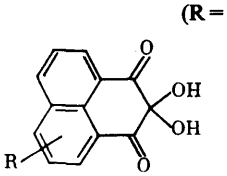
The 'ninhydrin phenomenon' pioneered research into the synthesis of other cyclic polyketones capable of forming *gem*-diols on hydration.[8] Certain of these compounds which have proved useful, particularly as analytical reagents, are shown below.



Alloxan



Quinisatin and its derivatives (R = H, CH_3, Ph)

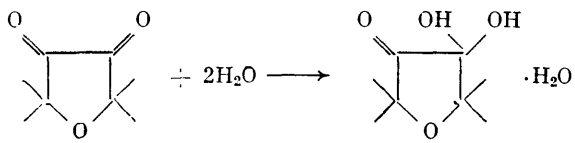


Perinaphthindantrione hydrate and its nitro derivative (R = H, NO_2)

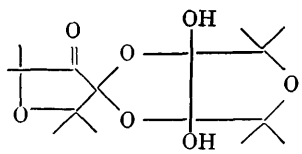
Multi-step syntheses of oxirene [sic (Ed. of Translation)] and phenalene *gem*-diols have been reported.[23] The hydration of cyclic 1,2,3-tricarbonyl compounds has also been studied[24,25] and reviewed over a long period of time in monographs.[7,8]

Dehydration normally requires harsh conditions: distillation *in vacuo* or heating in oleum in methylene chloride.[25] For reactions proceeding via dehydration of *gem*-diols, syntheses have also been carried out in concentrated sulphuric acid.

Studies of the hydrated forms of 2,2,5,5-tetramethylfuran-3(2*H*)-4(5*H*)-dione have shown that two structures exist in the crystalline state.[26,27] One incorporates 2 molecules of water for each molecule of the diketone and the other 0.5 molecules of water. In the 'dihydrate' structure, one of the two molecules of water is involved with *gem*-diol formation while the other is associated as a crystal hydrate:



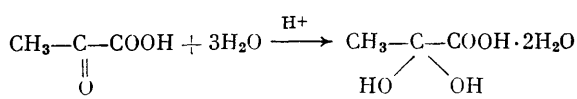
The authors propose a hydrated dimeric structure for the other crystalline form:



Significantly, the non-hydrated form of this diketone is coloured, while the hydrate is colourless. This is unusual and thought to be a consequence of strain in the non-hydrated furan skeleton and the presence of hyperconjugation with the keto-groups. Neither is possible in the *gem*-diol form.

There is reference to a large number of acyclic analogues, formed by hydration of ketones or aldehydes functionalised in the α-position by the carbonyl group of another aldehyde or ketone function or of a carboxyl function or derivatives thereof (e. g. an ester group).

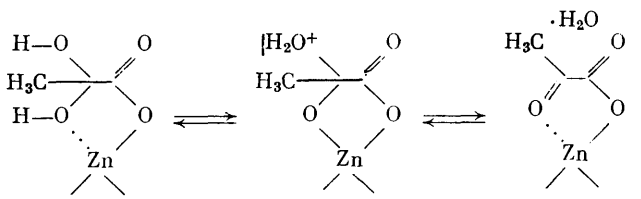
Much research has been devoted to pyruvic acid since this is important biologically. It has been shown that in the crystalline form the hydrate incorporates three molecules, only one being involved with *gem*-diol formation.[28] This hydration is catalysed by protic acids:



For the hydration of pyruvic acid by metalloenzyme complexes [sic (Ed. of Translation)],[29] the order of catalytic activity is as follows:

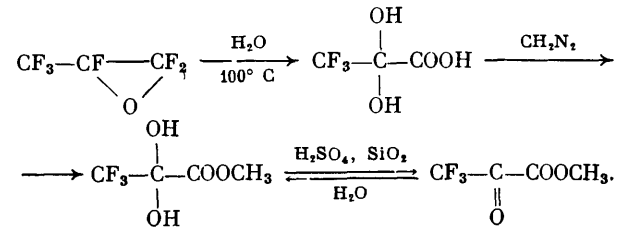
$$Cu^{2+}>Zn^{2+}>Ni^{2+}>Co^{2+}>Cd^{2+}>Mn^{2+}\ .$$

This order is in keeping with the ability of the metal to form a chelate complex with pyruvic acid. For the zinc-catalysed hydration in the presence of carbonic anhydrase, the following scheme has been proposed:

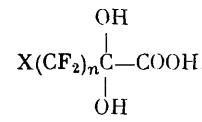


The hydration of pyruvic acid esters has also been reported.[30]

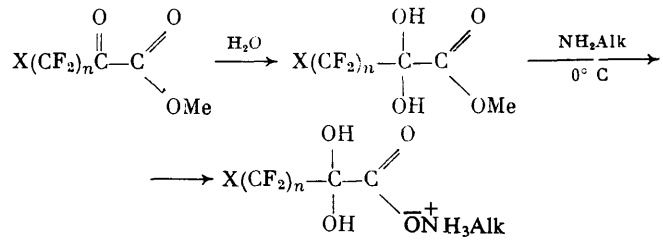
Hydration of halogenated pyruvic acids to the corresponding *gem*-diols is noticeably enhanced. Thus, hydrolysis of perfluoropropylene oxide affords directly trifluoropyruvic acid in the hydrate form (m.p. 124–126 °C; b.p. 156–158 °C).[31] Subsequent treatment with diazomethane gives the corresponding methyl ester. The resulting *gem*-diol dehydrates on heating in sulphuric acid containing silica gel to give methyl trifluoropyruvate, which readily reverts to the *gem*-diol on addition of water.



This research has been extended to the preparation of related fluorinated α,α-dihydroxycarboxylic acids,[32,33] their esters and various alkylamine salts.[34]



X = H, F, n = 1–4.



Structural analyses have been carried out by IR-spectroscopy (ν_{OH} = 3300–3370 cm^{-1}) and NMR-spectroscopy (^1H and ^{19}F).

b) Halogenated dihydroxymethylenes

In a review of their own work on polarographic and spectroscopic (UV) studies,[35] the authors pointed out the correlation between the stability of α-halogenated aldehyde hydrates and the number of halogen atoms. It was also noted that chlorinated hydrates are more stable than bromo derivatives. On the other hand, the stability of the hydrates decreases with increase in length of the alkyl chain. Many systematic analyses published in recent years[5,6] have shown that the stability of halogenated *gem*-diols obtained by hydration of aliphatic fluoro-, chloro- and bromo-aldehydes and -ketones decreases in the order F > Cl > Br. Trihalogeno derivatives are crystalline compounds while most other halogenated *gem*-diols exist only in solution. Chloral hydrate, which has a large number of practical applications, is clearly the best known of these halogenated *gem*-diols. NMR-spectroscopy and circular dichroism both confirm its structure as $CCl_3CH(OH)_2$ rather than the free hydrate, $CCl_3CH{=}O.H_2O$.[6]

It is interesting here to note one of the methods of preparing chloral from chloral hydrate.[36] Commercial 'chloral hydrate', comprising 73.5% chloral hydrate, 6.2% chloral and a mixture of acetals and hemiacetals, is heated for 20 min at 110–120 °C at 1.5–2 atm under nitrogen. The upper layer of the resulting product mixture contains 99% chloral.

Studies have shown that, even with polyhalogenated derivatives, the equilibrium between *gem*-diol and carbonyl form is markedly dependent on the medium.[37,38] ^1H NMR spectroscopy has indicated

that chloral hydrate and related compounds spontaneously dehydrate in non-polar media (Table 1). An increase in the polarity, which has been equated with the basicity (B),[38] leads to a shift in the equilibrium in favour of the *gem*-diol form:

$$\underset{\text{(A)}}{CCl_3-CH(OH)_2} \rightleftharpoons \underset{\text{(B)}}{CCl_3-CH=O} + H_2O.$$

From the data in Table 1, the stability constants (K) for the *gem*-diols in nitromethane have been calculated from the proportion of carbonyl form in the mixture.

$$K = A/B.$$

Thus, for chloral hydrate, bromal hydrate and α,α-dichlorobutyral hydrate, K = 4.9, 0.45 and 0.89, respectively.

Table 1. The proportion of the aldehyde form (%) of α-halogenoaldehydes in different solvents.[37]

Solvent	Compound			B*
	$CCl_3CH=O$	$CBr_3CH=O$	$C_3H_7CCl_2CH=O$	
CCl_4	82	100	100	0
$CHCl_3$	60	67	88	4
CH_2Cl_2	35	69	100	23
$ClCH_2-CH_2Cl$	34	66	79	40
C_6H_6	60	100	100	48
CH_3-NO_2	17	69	53	63
CH_3-CN	0	20	41	160
D_2O	0	0	0	156
CD_3OD	0	0	0	218
$(CD_3)_2C=O$	0	12	29	224
$(CD_3)_2S=O$	0	2	7	312

* B — the relative value of solvent basicity.

A kinetic study of the hydration of trichloroacetaldehyde in aqueous dioxane[39] has shown that four molecules of water may be associated with the aldehyde in the form of a cyclic complex. IR-spectroscopy and circular dichroism spectroscopy indicate that the hydrates of hexachloroacetone, other halogenated acetones, and chloral form adducts with dioxane, cyclohexanone, cyclopentanone, dimethyl sulphoxide, and other bases.[40] The hydrate of hexachloroacetone also incorporates four molecules of water.

There is a reference[41] to the preparation of chloral hydrate by chlorination of ethanol in water under irradiation:

$$CH_3CH_2OH + 4Cl_2 + H_2O \rightarrow CCl_3CH(OH)_2 + 5HCl.$$

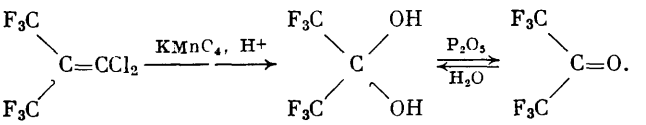
The product, in hydrate form, is distilled from the reaction mixture (b.p. 97.5 °C, m.p. 53 °C) and dehydrated by heating with concentrated sulphuric acid.

Aldehydes with a trifluoromethyl group in any location other than the α-position do not form crystalline hydrates.[42] They may be prepared by routine oxidation of the corresponding primary alcohols.

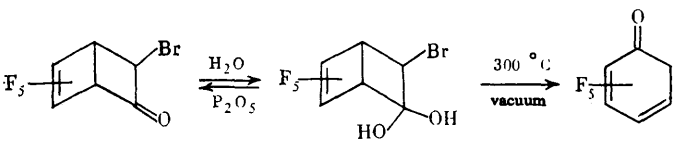
$$CF_3CH_2CH_2OH \xrightarrow{K_2Cr_2O_7,\ H_2SO_4} CF_3CH_2CH=O.$$

Trifluoroacetaldehyde cannot be prepared by this route. However, there is an indirect synthesis based on the conversion of trifluoroacetamide to the corresponding nitrile, followed by treatment with ethereal $LiAlH_4$ and concentrated HCl. The crystal hydrate of fluoral is dehydrated over P_2O_5.

Hexafluoroacetone was prepared for the first time in 1941 by direct fluorination of acetone in the gas phase over a copper gauze (m.p. −129 °C, b.p. −28 °C).[43] A more convenient method[44] involves oxidation of 1,1-dichloro-2,2-bis(trifluoromethyl)ethene in aqueous media, followed by cautious addition of the resulting hydrate (b.p. 57 °C at 93 mmHg) to P_2O_5:



The involvement of a hydrate form in the chemical conversion of a complex fluorinated ketone has also been reported:[45]

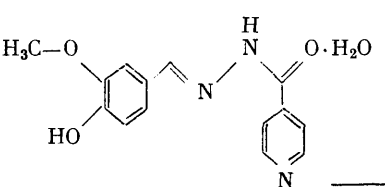


ν_{OH} 3440 см$^{-1}$
m.p. 55–57 °C

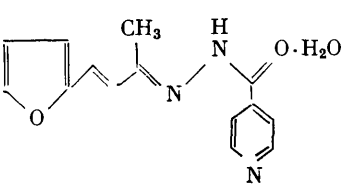
c) Pyridyl-substituted dihydroxymethylene compounds

Pyridinecarboxaldehydes, in particular 2-pyridyl and 4-pyridyl derivatives, are readily converted to crystalline hydrates.[46–49] Thus, 4-pyridinecarboxaldehyde hydrate is obtained by mixing the aldehyde itself with a 15-fold excess of water at 10–15 °C.[46] The resulting hydrate is a white, crystalline powder, m.p. 64–68.5 °C. Quinoline analogues have similar properties.[49] On the other hand, benzaldehydes and other compounds[50] are only hydrated in solution, provided that there is an electron-accepting substituent in the molecule.

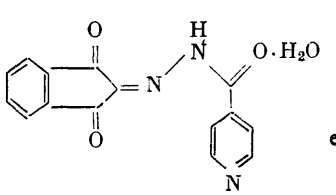
According to one reference book,[51] and elsewhere,[52] it is also reported that tuberculostatic isonicotinoylhydrazones also form crystal hydrates:



Ftivaside

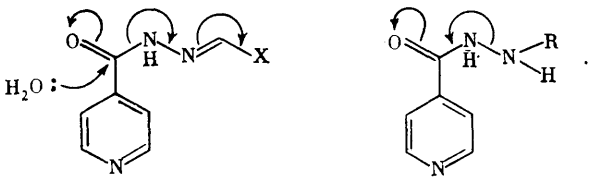


Larusan



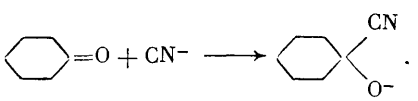
etc.

The precise nature of the hydrate form has not yet been established.[52] Significantly, isonicotinic acid hydrazides do not form hydrates. Thus, it can be assumed that hydration is primarily determined by the electron-accepting effect of the hydrazone residue on the carbon atom of the carbonyl group. Such stabilisation is absent in the free hydrazide:

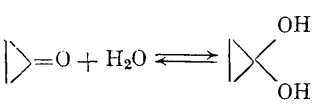


d) Dihydroxymethylene derivatives of strained ring systems

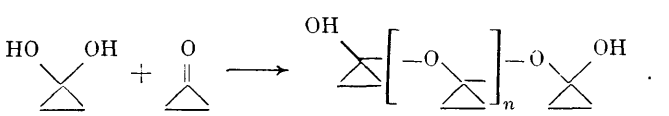
For cyclic systems, the interconversion between planar (sp^2) carbonyl structure and tetrahedral (sp^3) *gem*-diol form is associated with a structural modification of the whole molecule. In such compounds, neither form is especially favoured by neighbouring substituents. Strain in the ring system essentially determines the course of such (de)hydration, as well as other related reactions. Thus, while cyclohexanone interacts smoothly with cyanide ion (see below) and semicarbazide, there is no such reaction with cyclopentanone and cyclobutanone.[53]



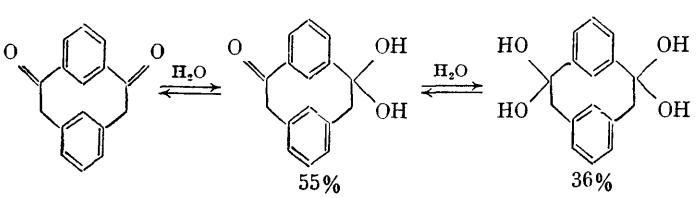
Cyclopropanone is readily hydrated to give the stable 1,1-dihydroxycyclopropane[53–56] (m. p. 82–84 °C).



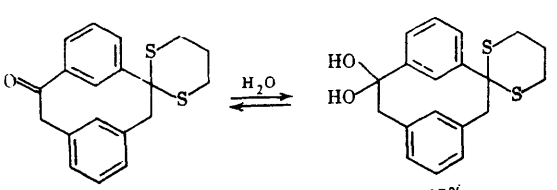
Ring strain also activates the hydroxyl groups of the *gem*-diol, leading to the formation of polymers:



Ketone derivatives of [2,2]metacyclophane are also readily hydrated to give crystalline *gem*-diols:[57]



55% 36%

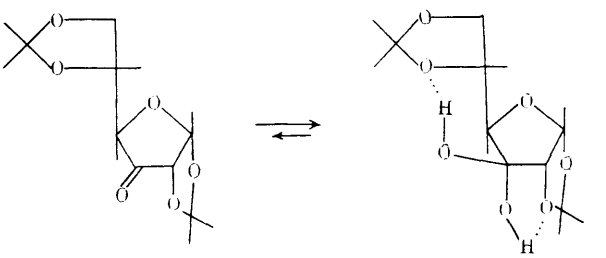


45%

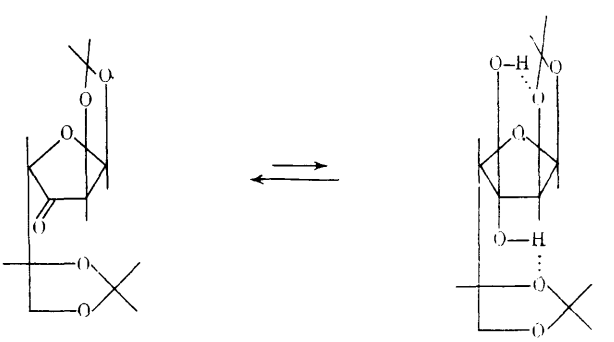
The fact that ring strain may be responsible for the readiness to form hydrates, as in the cyclic compounds shown above, may in part explain why aromatic compounds, such as benzaldehyde and acetophenone, do not exist in the hydrate form.[9]

Ring strain and the influence of electro-accepting groups within the same molecule may contribute together in stabilising the *gem*-diol form. This clearly explains the high stability of ninhydrin[7,8] as well as the facile hydration of tetrahydrofuran-3,4-diones[26,27] and fluorinated bicyclo[2.2.0]hexenones,[45] which change colour on hydrate formation.

There is also the possibility of stabilisation of the *gem*-diol structure in a tetrahydrofuran system by both ring strain and hydrogen bonding with adjacent groups. This is evident in isomeric 1,2:5,6-di-*O*-isopropylidene-*D*-hexafuranoses having a keto group in the 3-position.[58–60]



m.p. 109–111 °C



Studies have shown that *gem*-diol intermediates play an important role in the interconversion of these isomers, as well as in various syntheses based on these compounds.

The data presented in this section support the view that *gem*-diols are a genuine class of compound, contrary to established belief. However, the list of known *gem*-diols is not great, so that it is not yet possible to make theoretical generalisations. The number of less stable *gem*-polyols is significantly greater, but, in contrast to those mentioned above, they exist only in solution.

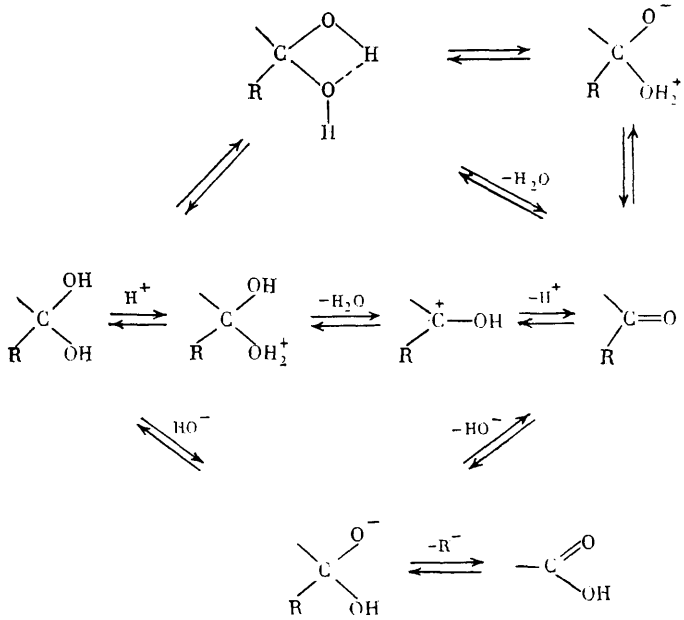
2. *gem*-Polyols in solution

The formation of *gem*-diols (I) can take place in water, or media containing water, by a number of routes: by hydrolysis of halogenoalkanes, hydration of carbonyl compounds, carboxamides, etc., and by exchange of various functions by hydroxyl groups. *gem*-Diols may also be converted into other functional groups in such aqueous media. Studies of the products formed by certain reactions of carbonyl and other compounds[13–20] often indicate that *gem*-diols are short-lived intermediates. However, it may not always be possible to trap them by established techniques.

a) Stability and acid-base properties of *gem*-diols

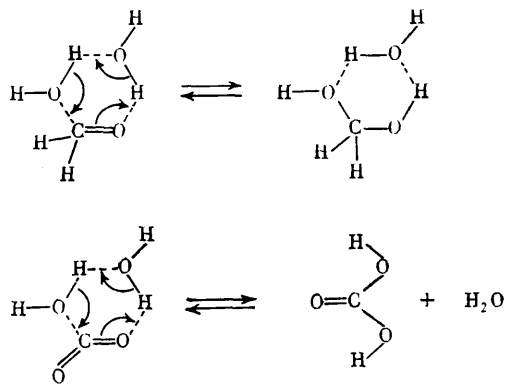
The recognition[5,6] that *gem*-diols are formed reversibly on hydration of aldehydes and ketones has had a profound effect on subsequent studies in this area and has been generally accepted by those who have undertaken theoretical analyses of the chemistry of carbonyl compounds.[13–20,47] Scheme 1 outlines the three possible routes for the formation and cleavage of *gem*-diols: in neutral media and under basic or acidic catalysis. However, conditions may be such that a clear distinction between these pathways cannot always be made.

Scheme 1



R = H, Alk, Ar, OH, NH_2 etc.

By considering the carbonyl form as starting material, only one process is involved: nucleophilic addition of oxygen at the carbon atom of the carbonyl group. Acid catalysis increases the developing positive charge at this carbon atom, thereby facilitating nucleophilic attack, in the same manner as a Lewis acid. Under basic catalysis, nucleophilic attack proceeds with direct participation of an alkoxide anion. It has been shown[61,62] that in neutral media, molecules of water are associated in a cyclic complex, thereby polarising the carbonyl group in the same manner as an acid catalyst.

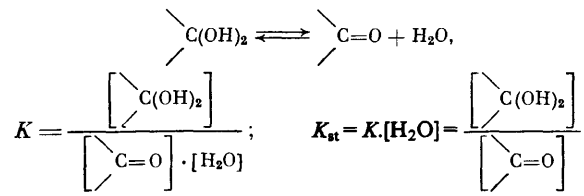


The above-described mechanism of carbonyl group hydration is essentially the same for aldehydes and ketones of various type as well as for carbon dioxide. All the possible catalytic pathways for hydration of the latter have been discussed in a review article.[63]

The pathways outlined in Scheme 1 have also been examined from the side of the *gem*-diol. In this case, the catalytic and 'non-catalytic' routes are more distinct. The instability of *gem*-diols in water at pH 7 is thought to arise by self-protonation.[64] Acid catalysis is effectively the same since the initially formed species is an unstable hydroxonium salt. Under basic catalysis *gem*-diols may often become more stabilised in such a way that subsequent conversions may be determined by secondary reactions, for example by transfer of hydride ion[18] or heterolytic cleavage of a carbon–carbon bond.[19]

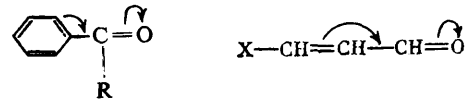
It is clear from the above discussion that the aspect of *gem*-diol stability is a very complex one. In aqueous media, *gem*-diols may be highly stable but impossible to isolate as such. On the other hand crystalline compounds may undergo a variety of conversions on dissolution. *gem*-Diols may not always be cleaved on acid catalysis. In studying the conditions for hydration of pyruvic acid it has been found that the rate of hydration increases in the presence of an excess of propionic acid.[65] The latter thus serves as a mild acid catalyst for the conversion of carbonyl compounds to *gem*-diols.

In order to compare the stability of *gem*-diols, the stability constants, K_{ST} where $K_{ST} = 1/K_d$), for a number of compounds have been listed in Table 2.



The data presented in Table 2, selected from known sources, have in the main been evaluated from the constants K_d (or K_h) or determined from the reported concentrations of the carbonyl and *gem*-diol forms. The value of K_{ST} in these examples is a more meaningful indication of the stability of the *gem*-diol, while K_d (K_h) has been used for an indication of the relative amount of the carbonyl (non-hydrated) form.

For aliphatic compounds it has recently been established that aldehydes are hydrated more easily than ketones. The stability of *gem*-diols increases as electron-accepting groups are introduced into the molecule and decreases on introducing electron-donating substituents. The ready hydration of α-ketocarboxylic acids and their salts is an obvious example to support this point. For aromatic and α,β-unsaturated aldehydes and ketones, there is less likelihood of forming *gem*-diols, even in neutral aqueous media, since the electron deficit of the carbonyl carbon is effectively neutralised by conjugation with the π-electron system.[5,6]



At the same time, dihydroxymethylene derivatives of [2,2]metacyclophane in aqueous solution have quite a high stability, although they can be regarded as analogues of hydrated aromatic ketones.[57] Acetone hydrate and other aliphatic ketone hydrates are

the least stable ketone hydrates. Carbonic acid is somewhat of an anomaly: it has a very unusual dihydroxymethylene structure and a low stability constant, K_{ST}.

Table 2. Stability constants (K_{ST}) for *gem*-diols.

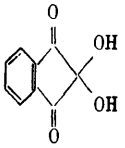
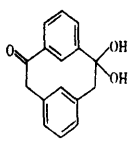
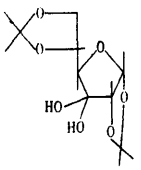
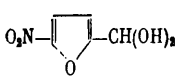
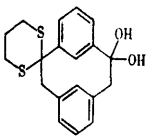
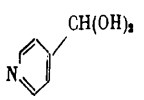
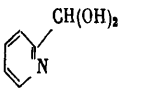
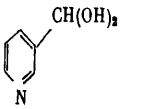
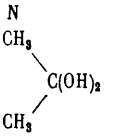
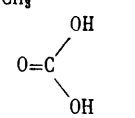
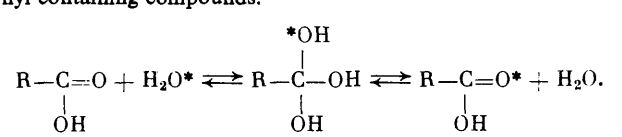
Compound	Method of analysis	K_{st}	Refs.
CCl_3—$CH(OH)_2$	a	$2.78 \cdot 10^6$	[5, 6]
	a	$2.9 \cdot 10^5$	[22]
$H_2C(OH)_2$	a, b	$1.9 \cdot 10^5$	[5, 6]
O=C—$CH(OH)_2$ | OH	b	$1.8 \cdot 10^5$	[21]
CH_2Cl—$CH(OH)_2$	a	$3.7 \cdot 10^3$	[5, 6]
O=C—$CH(OH)_2$ | O^-	b	$6.2 \cdot 10^3$	[21]
	c	10	[57]
	a	5.25	[58]
O=C—C(OH)$_2$ | | HO CH_3	a	2.4	[5, 6, 66]
O=C—C(OH)$_2$ | | H_3C CH_3	c	2.1	[67, 68]
CH_3—$CH(OH)_2$	a, c	1.43	[5, 6]
O=C—C(OH)$_2$ | | HO C_2H_5	a	1.40	[5, 6]
	c	~1.26	[50]
	c	0.82	[57]
	a, b	0.80–0.96	[21]

Table 2 (continued).

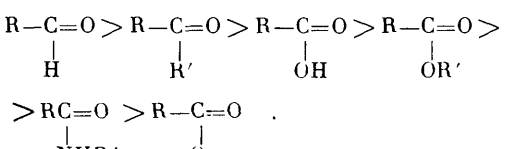
Compound	Method of analysis	K_{st}	Refs.
	a, b	0.20–0.67	[21]
	a	0.11	[21]
	c	$2 \cdot 10^{-3}$	[66]
	d	$2.6 \cdot 10^{-4}$	[5, 6]

Note. a, UV- and IR-spectroscopy; b, polarography; c, NMR spectroscopy; d, electrical conductance.

There is no reference in the literature to the hydration of carboxyl groups to give 1,1,1-triols, sometimes referred to as orthocarboxylic acids. Derivatives of the latter, however, are well defined.[11] Indirectly, the formation and cleavage of 1,1,1-triols from carboxylic acids in water can be inferred by studying isotopic exchange of oxygen with the solvent; this has also been applied to other carbonyl-containing compounds.[69–73]



This mechanism is supported by the fact that no such oxygen exchange takes place with aliphatic alcohols or with phenols which display no tendency to undergo keto-enol tautomerism. With glucose only the carbonyl group is exchanged. The rate of oxygen exchange in acetone is very low compared with that of acetaldehyde. However, in the presence of aluminium oxide or silicon dioxide, the rate of oxygen exchange in acetone is enhanced due to the participation of the oxygen atoms of the catalyst.[74] Carboxylic acids exchange oxygen with the solvent more slowly than aldehydes. The rate of oxygen exchange of various carbonyl compounds decreases in the following sequence:[73]



For a given class of carbonyl compound, the rate depends to a large extent on the nature of the substituents. Thus, for substituted acetic

acids, the rate of exchange, as determined by IR-spectroscopy, is in the order:[75]

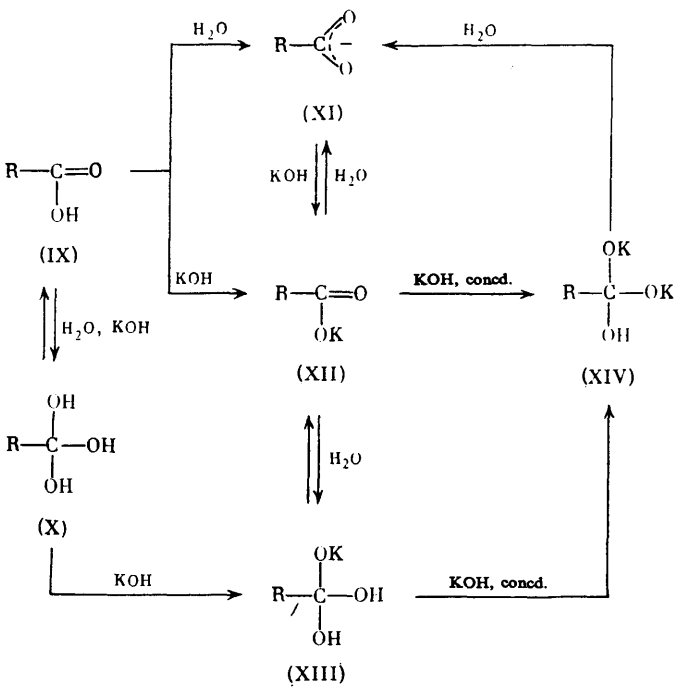
$$CF_3{-}COOH > CCl_3{-}COOH > CH_3{-}COOH > C(CH_3)_3{-}COOH$$

Benzaldehydes also readily undergo isotopic exchange by oxygen.[72] Electron-accepting substituents enhance the process while electron-donating groups have the opposite effect. Such evidence confirms that aromatic aldehyde hydrates have low stability: a fact that may not be apparent by other analytical techniques.

Thus, isotopic oxygen exchange, which has been studied with both carbonyl-containing compounds and inorganic oxide analogues.[70,71] can demonstrate the formation of all theoretically possible *gem*-polyol structures in solution. A dynamic equilibrium is set up, the position of which depends on many internal and external factors. In this context, it is interesting to study the reality of orthocarboxylic acids.

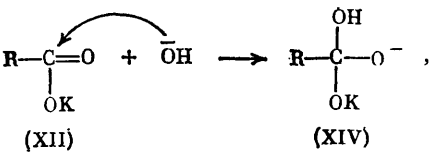
During the last few years a number of acid salts of orthocarboxylic acids (XIV) have been prepared by treatment of aqueous solutions of the corresponding carboxylic acid with concentrated base (>5 *N*). Such derivatives of benzoic furoic, sorbic, methacrylic acid, and others, have been prepared by this route.[9,76–78]

Scheme 2

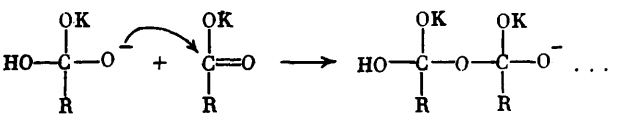


It is possible that what chemists have assumed to be simple potassium carboxylates (XII), formed in routine syntheses, are in fact orthocarboxylic acid salts (XIV). With either salt, routine hydrolysis with mineral acid would give the corresponding carboxylic acid (IX). Salts (XIV) are colourless compounds which are not readily soluble in >5 *N* base. In water, such orthocarboxylic acid salts are converted into the carboxyl forms (XI) and (XII).

Scheme 2 illustrates the various pathways leading to the formation of orthocarboxylic acids and their salts. While the dissociated acid and its salts are converted in water to the carboxyl anion (XI), which is normally unaffected by base, treatment with highly concentrated base provides suitable conditions for the formation of the undissociated salt (XII) as well as the corresponding orthocarboxylic acids (X) and orthocarboxylic acid salts (XIII) as a result of catalytic hydration. The formation of orthocarboxylic acid salts (XIV) may proceed either by nucleophilic addition of hydroxide ion to the carbonyl carbon of the carboxylate salt form (XII),



or by acid-base interaction of the monopotassium salt (XIII) with base in a second deprotonation. It is not possible to form the corresponding tripotassium orthocarboxylates under these conditions, presumably because of the weak acidity of the third hydroxy group. The structures of salts (XIV) have been confirmed by elemental analysis, IR spectroscopy (the absorption corresponding to $\nu_{C=O}$ being absent and that corresponding to ν_{OH} being present), and by potentiometric titration of the mixture of carboxylic acid salts and base obtained after cleavage of (XIV) in water. By the latter technique, it has been possible to determine the molecular weight and the proportion of inorganic anion and base in adduct (XIV). Thus, for salts of unsaturated carboxylic acids (cinnamic, acrylic, sorbic acids) it has been found that the adduct has a more complex structure in which one molecule of base is shared by 2–3 molecules of anion as a result of polymerisation.



Thus, although orthocarboxylic acids have not been demonstrated as stable species, their existence and properties have been inferred through the acid-base conversions of carboxylic acid salts in basic media.

Bases, as either reagents or catalysts, markedly accelerate hydration of carbonyl compounds relative to hydration in neutral media. A relationship has been established between the equilibrium constant for hydration (K_{H_2O}), the constant K_{OH}, for the adduct formation from aromatic aldehydes and hydroxide ion, and the acid dissociation constant, K_a, for the corresponding *gem*-diols (K_w being the dissociation constant for water).[79]

The final product of the reaction is the acid salt of the corresponding metacarboxylic acid (XVI), the formation of which may arise by interaction of base with the metacarboxylic acid itself

or its anhydride, i.e. the aldehyde form. Much work, principally undertaken by Zuman et al., has been devoted to a study of this equilibrium and its mechanism.[80–85]

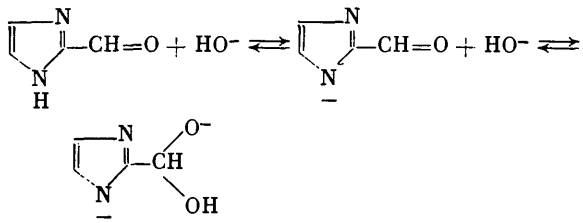
$$ArCH{=}O + HO^- \overset{K_{OH}}{\rightleftharpoons} ArCH(OH)O^-$$
(XVI)

$$H^+ \updownarrow K_w \qquad K_a \updownarrow H^+$$

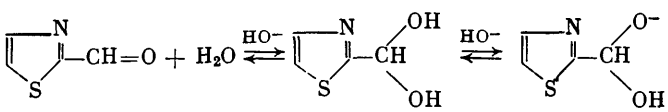
$$ArCH{=}O + H_2O \overset{K_{H_2O}}{\rightleftharpoons} ArCH(OH)_2$$
(XV)

$$K_a = K_{OH}\frac{K_w}{K_{H_2O}}$$

The reactions of a number of aromatic and heteroaromatic aldehydes with base have been reported.[80,81] Benzaldehyde and its derivatives, as well as furan-, thiophene- and *N*-methylpyrrole-carboxaldehydes, add hydroxide ion directly in one step to give the corresponding salt (XVI). Pyrrole- and pyrazole-carboxaldehydes react with base in two steps, the initial step being *N*-deprotonation.

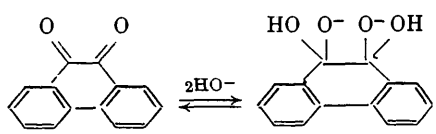


Thiazole-2-carboxaldehyde is initially hydrated, and then reacts with base as follows:



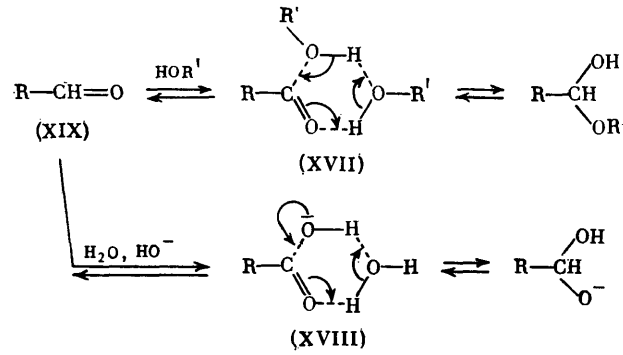
Evidently pyridinecarboxaldehydes also interact with base according to this scheme since a polarographic study in media containing a high concentration of base has established that three forms exist: a carbonyl, a *gem*-diol and an anionic form (XVI).[83]

While hydration of α-polyketones usually involves only one carbonyl group, addition of water or hydroxide ion to a second keto group may take place in the presence of base. This is evident with ninhydrin[22] (see above). It has also been shown that 9,10-phenanthrenequinone forms a stable dianion:[84]



The pK_a values for a number of structurally varied *gem*-diols, given in Table 3, confirm the weakly acidic nature of these compounds. From these values for benzaldehyde derivatives, the corresponding values, J_-, J_{m-} and H_-, H_{m-}, have been calculated.[81,82,85] These denote, respectively, the readiness of the OH and OR group to add to the carbonyl group, (C=O), and the interaction of these with protic solvents.

All of the examples studied are characterised by a final step involving the formation of the corresponding *gem*-polyol and its salt form. However, as has already been noted in review articles,[61,62] the formation of complex cyclic solvates or transition states precedes this stage. By studying the UV spectra of aromatic and heteroaromatic aldehydes in polar and non-polar solvents, an attempt has been made to analyse the spectra of solvate complexes, (XVII) and (XVIII), and calculate their stability constants.[89,90]



As solvation is reversible in polar media, aldehydes may exist in at least two forms—an unassociated carbonyl form (XIX) and a solvated form (XVII or XVIII)—as is the case with many other compounds which are solvated. This mixture of the two forms has been studied by measuring their light absorption properties. In particular, it has been established that benzaldehyde, as a dilute solution in water, is solvated to the extent of 70%, while the figure in ethanol is 54%. The corresponding values for *p*-nitrobenzaldehyde are 61 and 45%. Solvate complexes have well-defined UV-spectra so that the proportion of free and solvated forms in the mixture can be determined quantitatively. It cannot for certain be inferred that solvate complexes are necessarily converted into *gem*-diols or their derivatives, but their formation does represent an integral stage in the overall process.

b) Characteristic reactions of *gem*-polyols

Differences in the reactivity of hydrated and non-hydrated carbonyl complexes have, up to now, not been considered. It has been thought that these reactions are one and the same, except in certain instances. It is now clear, from the evidence presented, that carbonyl compounds and *gem*-diols are distinct functional groups, and that the latter, just as acetals, may in part fulfil the role of a masking group for the former. However, apart from their masking, accelerating and inhibiting properties towards the carbonyl function, *gem*-polyols do undergo reactions which are uniquely their own.

It has been argued that the degree of hydration of the carbonyl group may be an indication of its reactivity.[91] Thus, glutathione (GSH) only forms hemimercaptals with readily hydrated aldehydes and ketones. Glyoxal, which exists as a dihydrate in aqueous solution, affords two types of hemimercaptal, while methylglyoxal monohydrate forms only a ketohemimercaptal:

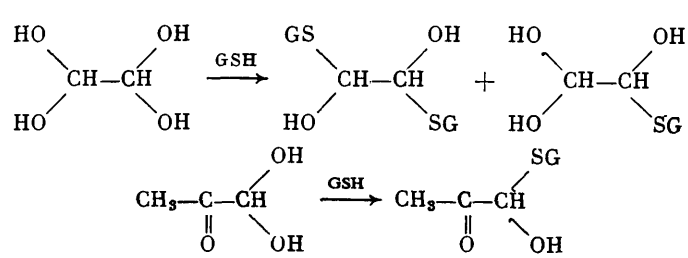
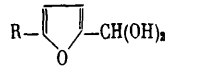
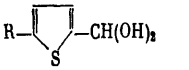
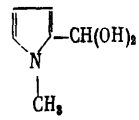
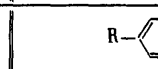
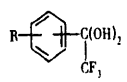
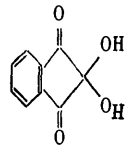


Table 3. Values of the first dissociation constant (pK_a) for *gem*-diols.

Compound	pK_a	Refs.
R-CH(OH)$_2$		
R=H	12.70	[5, 6, 86]
CH_3	13.57	[5, 6, 86]
$(CH_3)_2CH$	13.77	[5, 6, 86]
CCl_3	10.44	[5, 6, 86]
$CH_3C(=O)$	11.00	[86]
	12.05	[86]
	13.00	[86]
		
R=H	14.75	[80, 87]
CH_3	15.65	[80, 87]
NO_2	11.82	[80, 87]
		
R=H	15.21	[80, 87]
Br	14.64	[80, 87]
		
CH_3	17.50	[80]
		
R=H	14.90	[86]
CH_3	15.39	[86]
OCH_3	15.96	[86]
NO_2	12.79	[86]
		
R=H	10.00	[86]
p-CH_3	10.15	[86]
p-OCH_3	10.18	[86]
m-Br	9.51	[86]
m-NO_2	9.18	[86]
	8.6	[8]
$O{=}C(OH)_2$	3.7	[88]

It has also been established that the formation of pyrazines by condensation of *o*-phenylenediamine with trifluoromethylglyoxal proceeds with participation of a hydrated carbonyl group.[92] X-Ray structural analysis and NMR spectroscopy indicates that, of the three possible hydrated forms of the ketoaldehyde, the ketone hydrate (XX) is directly involved.

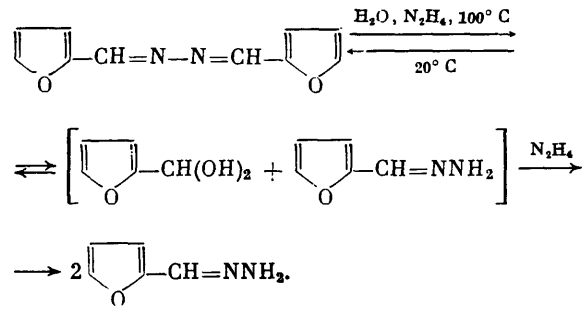
$$F_3C{-}C(=O){-}CH(=O) \overset{H_2O}{\rightleftharpoons} F_3C{-}C(OH)_2{-}CH(=O) \overset{H_2O}{\rightleftharpoons} F_3C{-}C(OH)_2{-}CH(OH)_2$$

(XX)

Initially, condensation takes place with the free aldehyde group; the hydrated keto group is then slowly dehydrated over 18 h at 23 °C prior to ring closure.

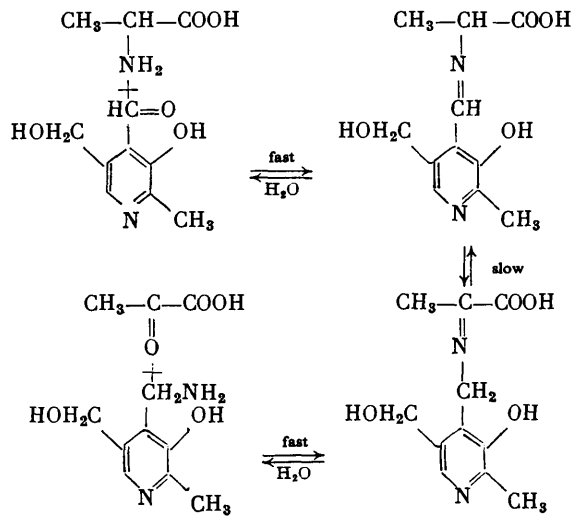
While in the above reaction it is apparent that the hydrated form hinders condensation, in other instances quite the reverse occurs, i.e. hydration facilitates condensation with amino groups. This is well illustrated in the review articles devoted to the chemistry of ninhydrin and analogues.[7,8] 4-Pyridinecarboxaldehyde hydrate has been recommended as a highly sensitive analytical reagent for phenylhydrazine and other unsymmetrically substituted hydrazines.[46] Interestingly, the analysis is not complicated by the presence of such reactive compounds as ammonia, hydroxylamines, aliphatic amines and aldehydes, acetone, etc.

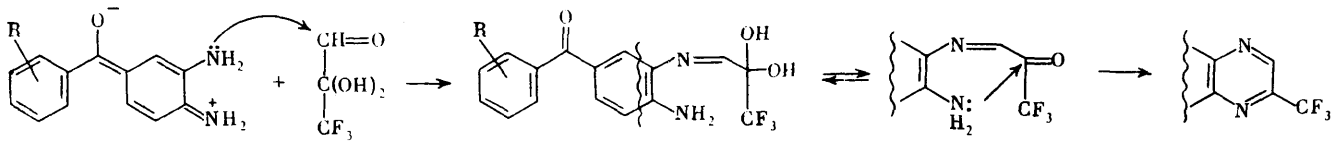
Evidently, the fact that aldehydes are not readily hydrated is reflected in the hydrolytic cleavage of the azomethine group. Thus, furfural hydrazone is obtained by heating the corresponding azine in aqueous hydrazine:[93]



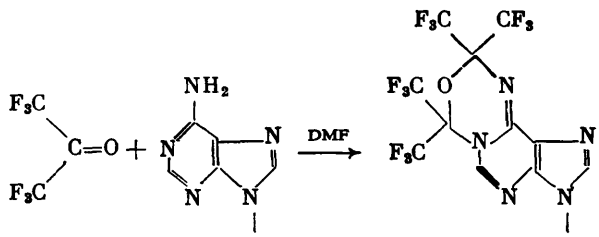
At 20 °C the equilibrium is shifted towards the azine.

Such conversions have a direct bearing on biological processes, as has been demonstrated.[94,95] Thus, in model studies of transferase-catalysed transamination,[94] the authors have discovered a reversible isomerisation of Schiff bases which, on hydrolysis, are converted [in the example below] to pyruvic acid or a substituted pyridine-4-carboxaldehyde. Both products are readily hydrated carbonyl compounds (a fact which the authors did not heed).

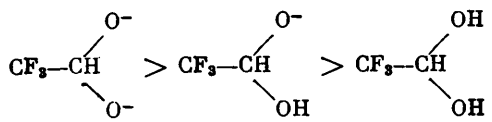




Hexafluoroacetone, which is also readily hydrated,[31,42–44] interacts with adenine and its derivatives to give a product derived by condensation with both the amino group and an endocyclic nitrogen atom.[95]

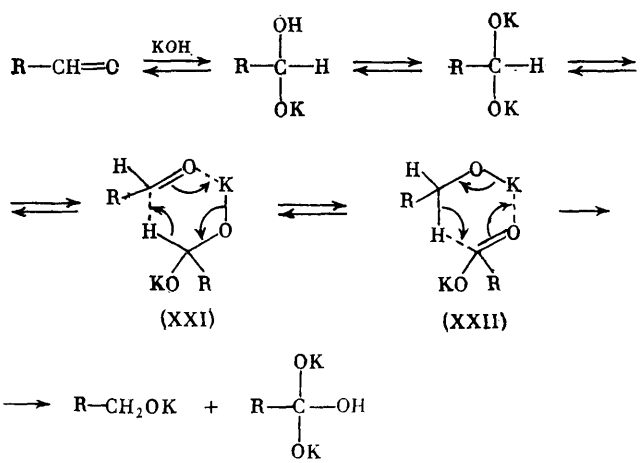


In heterogeneous redox reactions, carbonyl compounds and *gem*-diols perform opposing roles: the former as an oxidant and the latter as a reductant (i. e. as a typical alcohol). In the case of fluoral hydrate, it has been shown that the reducing power increases as the concentration of base increases since the anionic form of the diol is a better oxidant than the neutral molecule:[88]



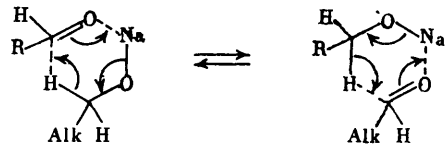
Oxidation of *gem*-polyols is accompanied either by loss of hydride ion[18,96] or, under more forcing conditions, by heterolytic cleavage of a carbon–carbon bond.[19]

For the disproportionation of furancarboxaldehydes on the surface of base granules under an inert atmosphere (in toluene, benzene or diethyl ether [not absolute]), it has been suggested that reaction proceeds via a cyclic complex (XXI) formed from one molecule of aldehyde and one of the corresponding *gem*-dialkoxide. This is converted to (XXII) by hydride transfer, in much the same way as a tautomeric rearrangement. It is an established fact that aromatic alcohols are formed from various aromatic aldehydes in the presence of formaldehydes.[2,18,96] The latter, functioning as a stable *gem*-diol, serves as a reductant, being oxidised by the same type of bond reorganisation depicted in complex (XXI).



(XXI) (XXII)

Simple aliphatic alcohols may perform the same function. Thus, a similar redox interaction has been proposed for the reaction of furfural with simple alkoxides:[97]



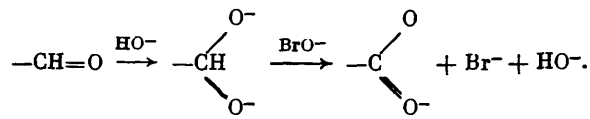
The familiar Meerwein–Pondorff–Verley–Oppenauer conversion with aluminium alkoxides[99] can thus be effectively performed with sodium alkoxides. The resulting aliphatic aldehyde may take part in a subsequent aldol condensation in the presence of an excess of aromatic or heteroaromatic aldehyde.[100]

Evidently, many established routes to carboxylic acids by oxidation of aromatic or heterocyclic aldehydes in basic media (notably Ref. 101) proceed via oxidation of a *gem*-dialkoxide. This has been confirmed for the hypohalite-mediated oxidation of furfural and its 5-methyl derivative.[102,103] A previously reported oxidation of furfural with sodium hypobromite[104] proved unsuccessful with 5-methylfurfural. However, 5-methyl-2-furoic acid was obtained in up to 95% yield by significantly increasing the amount of base (> 1 molar equivalent).

$$Br_2+2NaOH\rightarrow NaOBr+NaBr+H_2O,$$

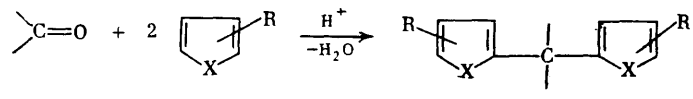
$$-CH=O+NaOBr+NaOH\rightarrow -COONa+NaBr+H_2O.$$

This would suggest that oxidation by hypobromite ion proceeds via the *gem*-dialkoxide rather than directly on the aldehyde:



Excess of base enhances hydration of the carbonyl group, especially in 5-methylfurfural, where the methyl group reduces the polarisation of the carbonyl function.

Under acidic catalysis, all forms of the carbonyl compound (hydrated or non-hydrated ketones and aldehydes) condense with aromatic systems to give polyaryl- or polyheteroaryl-alkanes:[105–107]

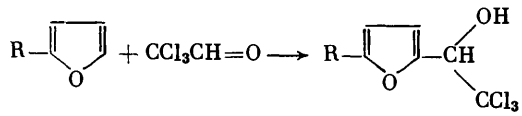


(XXIII)

X = CH = CH, O, S etc. R = H, Alk, OH, OAlk, Hal etc.

Reaction proceeds in two stages with the intermediate formation of secondary or tertiary alcohols (as is the case with alkylation). Termination of the reaction at this intermediate stage is relatively easy for carbonyl compounds which are readily hydrated, while reaction goes to completion in all other cases. In the case of chloral, condensation with various arenes affords the insecticide DDT and its analogues (XXIII, where X = CH = CH),[107] i. e. reaction goes to completion; however, the reaction of anhydrous chloral with furan

derivatives in the presence of $AlCl_3$ yields the corresponding secondary alcohol in up to 75% yield:[108]

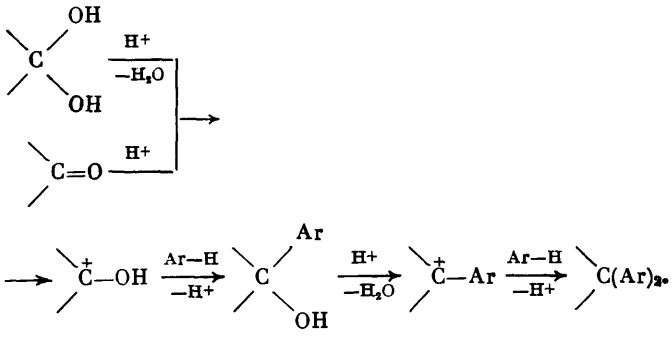


R = H, CH_3, COOAlk.

The same product is obtained from chloral hydrate in sulphuric acid.

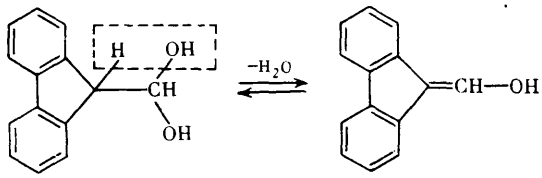
Trifluoropyruvic acid[109] and hexafluoroacetone,[110] which are even more readily hydrated, react in the same way with furan, thiophene, and *N*-methylpyrrole, even in the absence of catalyst.

It is known that electron-accepting (polyhalogeno) groups not only stabilise *gem*-diols but also inhibit the subsequent condensation of the intermediate secondary or tertiary alcohols with a second arene molecule. In the absence of such groups, the process continues (stage B), in the same way as aromatic alkylation with alcohols.



(A) (Б)

The formation of enols from *gem*-diols is interesting. Thus, 9-formylfluorene hydrate, having a labile α-hydrogen at C_9, dehydrates to give the corresponding enol.[111,112] In aqueous solution the *gem*-diol : enol ratio is 1 : 3.



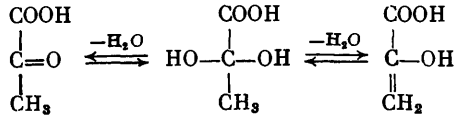
The enol group may be hydrated to reverse the reaction. Hydroxide ion accelerates the process. By comparison with simple alkenes, hydration of enols is four times faster.

$$(CH_3)_2C{=}CH{-}OH + H_2O \overset{K_1}{\rightleftarrows} (CH_3)_2CH{-}CH(OH)_2,$$

$$(CH_3)_2C{=}CH_2 + H_2O \overset{K_2}{\rightleftarrows} (CH_3)_2CH{-}CH_2{-}OH,$$

$$\lg(K_1/K_2) = 3.9.$$

Aqueous solutions of pyruvic acid contain three forms: a carbonyl, an enol and a *gem*-diol.[87] The *gem*-diol is considered to be an intermediate structure.

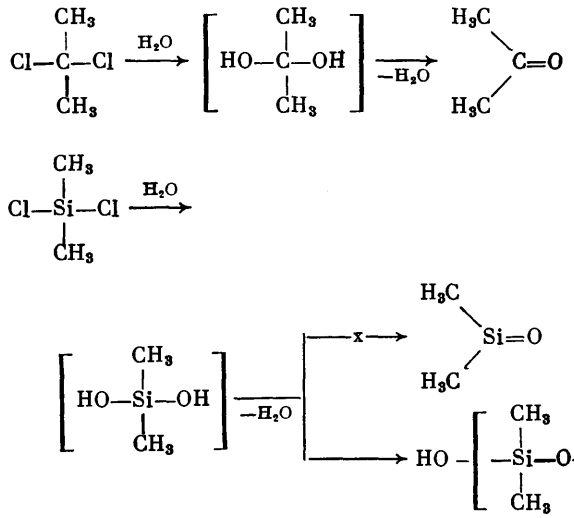


That *gem*-diols may be implicated in enolisation has been noted, especially by Toullec.[113]

III. *gem*-Polyols as members of the *gem*-polyhydroxide family

The reversible hydration of carbonyl groups is in many respects identical with the interconversion of oxides and hydroxides, and effectively is a special case of the latter. The stability and reactivity of *gem*-polyols can be examined in a whole series of related structures by taking into account the characteristics of each system as determined by the central atom. Such comparative studies, however, have rarely been reported. In recent years, quantum mechanics has shed light on the configuration, energy, bond lengths and other parameters pertaining to polyhydroxides of general structure $T(OH)_n$, where T = C, Si, B, Al, Sn and others; $n = 2-4$.[114,-117]

Of group IV elements, only carbon is reluctant to form polyhydroxides. Thus, hydrolysis of 2,2-dichloropropane affords acetone, while dichlorodimethylsilane gives a polysiloxane.[118]



In aqueous ammonia, stannic chloride is hydrolysed to $Sn(OH)_4$ — stannic acid.[119] However, hydrolysis of carbon tetrachloride, like the hydration of carbon dioxide,[63,120] affords dihydroxycarbon monoxide, i.e. carbonic acid

$$O{=}C{=}O + H_2O \rightleftharpoons O{=}C(OH)_2.$$

At the same time, the possibility of forming tetrahydroxycarbon (tetraol) in solution has been indicated by studies of isotopic oxygen exchange.[70,71] These have revealed that the rate of oxygen exchange increases with the atomic number of the central atom, which coincides with an increase in the stability of the polyhydroxide.

The fact that carbon dioxide is only partially hydrated, and anomalies in the hydration of carbonyl compounds, can be viewed with the properties of a large number of polyoxides, which also interact with water to give a variety of hydrated compounds, notably polybasic inorganic acids. The possible factors responsible for the formation of such compounds have been examined earlier.[120,121] The stability of polyhydroxides increases with the atomic number of the central atom and with the Periodic Group number. This is determined by the strength of the T—O bond. Thus, for the halogens in the maximum oxidation state, chlorine forms a monohydroxide, i.e. perchloric acid [$HOCl(=O)_3$], whereas iodine forms $(HO)_3I(=O)_2$. For sulphur, the dihydroxide is known (H_2SO_4), but for tellurium the analogue is $Te(OH)_6$. For nitrogen,

the monohydroxide (HNO_3) is known, but phosphorus forms both meta- and ortho-acids [$HOP(=O)_2$, $(HO)_3P=O$, and others] as the corresponding anhydride, P_2O_6, can be hydrated to various degrees. The stability of these polyhydroxides is determined by many factors inherent in the structure of the central atom. In this respect, a key role is played by vacant orbitals,[122] which give rise to partial double character as a result of a shift of a lone pair of electrons from oxygen:



For carbon compounds which lack vacant orbitals, such stabilisation can be achieved by neighbouring electron-accepting groups which lower the electron density at the carbon atom. Other factors, such as the anomeric effect[123] also have a stabilising effect. The fact that many *gem*-diols are stable only in solution, and are formed as reaction intermediates, would also argue in favour of another stabilising factor: the formation of complex solvates. The full analysis of this aspect would require a separate review.

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Translated from *Uspekhi Khimii* 60 2047–2063 (1991) U.D.C. 547.586.2

Fluorine-containing aromatic aminoacids

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ABSTRACT. **Methods of preparing the following fluorine-containing aromatic aminoacids are reviewed: racemic and optically active phenylalanine and tyrosine derivatives with fluorine atoms or fluoroalkyl groups in the benzene ring or in the side chain. Possible bio-medical applications of these compounds are examined.**

The bibliography contains 100 references.

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I. Introduction

The aromatic aminoacids—phenylalanine and tyrosine—are members of the essential aminoacids. They are constituents of important biologically active peptides, such as oxytocin, enkephalins, and kinins. The products obtained by metabolism of these aminoacids play a key role in processes which take place in the central nervous system and elsewhere in the living organism.

By replacement of atoms of hydrogen by fluorine in aminoacids, one can prepare compounds which are structurally very similar to the corresponding natural aminoacids since the size of the fluorine atom does not differ greatly from that of hydrogen. However, as the energy of the C–F bond is greater than that of the C–H bond, there is a significant change in the metabolism of derivatives containing fluorine. Furthermore, as a consequence of the electronegativity of the fluorine atom, there is a marked shift in electron density which has an affect on the physical chemical properties. With the development of organofluorine chemistry, new methods of selective fluorination have been designed and new fluorinating agents, as well as simple reactive fluorine-containing synthons, have become available. These have been usefully applied to the preparation of fluorine-containing aromatic aminoacids having atoms of fluorine or fluoroalkyl groups in various positions of the molecule. Interest in fluorine-containing phenylalanine and tyrosine is evident from the volume of publications in this area and from the applications of fluorine-containing aminoacids in biochemical studies and in medicine.

In 1970 a review was published on the synthesis of fluorine-containing aminoacids, including phenylalanine and tyrosine derivatives.[1] However, there is little mention of the biological activity of these compounds. A recent review covers the synthesis of aminoacids having a fluorine atom in the β-position of the hydrocarbon chain, including α-polyfluoromethyl derivatives.[2]

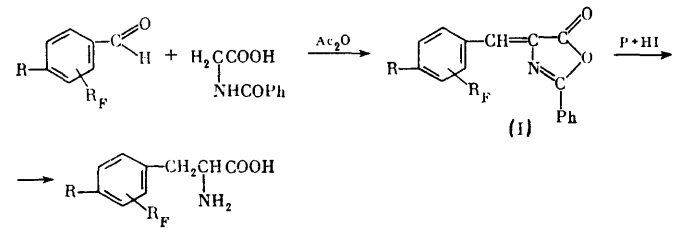
In the present literature survey, a systematic study has been made of synthetic routes to fluorine-containing derivatives of phenylalanine and tyrosine in both racemic and optically active form. The effect of fluorine substitution on biological activity has also been examined, and potential applications of these compounds in biochemical and medical research have been highlighted.

II. Synthesis of racemic fluorine-containing aromatic aminoacids

Various methods are available for preparing aromatic aminoacids with fluorine or fluoroalkyl substituents. These are based on either direct introduction of fluorine into the aminoacid molecule or syntheses from fluorine-containing residues and synthons. The latter methodology has been applied to the preparation of racemic fluorine-containing phenylalanine and tyrosine derivatives, which may be resolved into their enantiomeric forms by a variety of methods.

1. Methods based on the condensation of carbonyl compounds

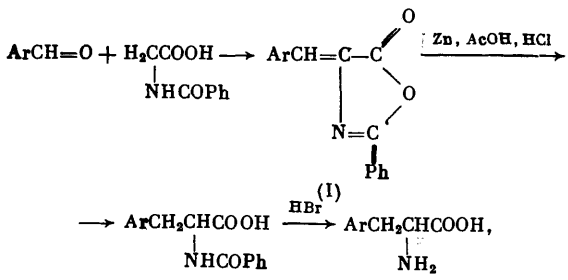
Phenylalanine and tyrosine derivatives with up to five fluorine atoms or trifluoromethyl groups in the benzene ring are usually prepared by the classical route from the corresponding fluorinated benzaldehydes and *N*-acetylglycine.[1] Normally, an oxazolone intermediate (I) is formed in high yield irrespective of the number of fluorine atoms in the aromatic nucleus. Subsequent reduction and hydrolysis (notably with a mixture of red phosphorus and HI) affords the desired fluorine-containing aromatic aminoacids.[1]



R = H, F, CF_3, MeO, OH; $R_F = F_n$, CF_3; $n = 1-5$

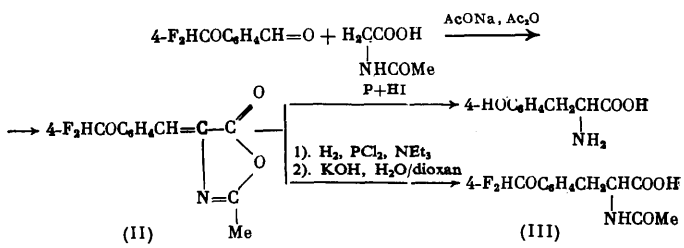
Fluorinated phenylalanine derivatives containing two, three or four atoms of fluorine at various positions of the benzene ring have also been prepared from the corresponding benzaldehydes via reduction of the intermediate oxazolones (I) under mild conditions (with Zn/AcOH). After acidic hydrolysis, ion-exchange resins have

been used to isolate the free aminoacids in higher yield and purity without contamination by inorganic salts.[3]

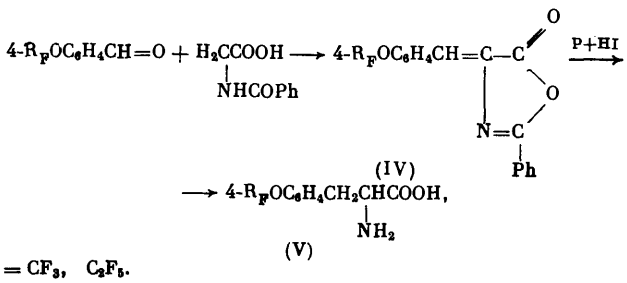


Ar = 2,4-$F_2C_6H_3$; 3,4-$F_2C_6H_3$; 3,5-$F_2C_6H_3$; 2,5-$F_2C_6H_3$; 2,6-$F_2C_6H_3$; 2,3,5,6-F_4C_6H; 2,3,4,6-F_4C_6H; 2,4,6-$F_3C_6H_2$; 3,5-Cl_2-2,4,6-F_3C_6.

4-Difluoromethoxybenzaldehyde, readily obtainable by treatment of 4-hydroxybenzaldehyde with chlorodifluoromethane, reacts with aceturic acid under the conditions of the Erlenmeyer azlactone synthesis to give the corresponding fluorine-containing unsaturated oxazolone (II). However, reduction of the latter with HI/P proceeds by cleavage of the difluoromethyl group to give tyrosine as the only isolable product. On the other hand, hydrogenation in the presence of Pd and NEt_3 affords methyl *N*-acetyl-4-difluoromethoxyphenylalanate which is converted to the *N*-acetyl derivative (III) on basic hydrolysis.[4]

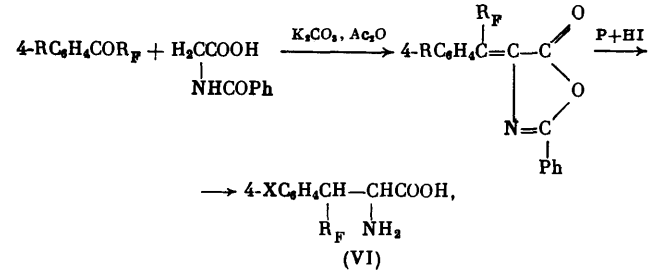


Benzaldehydes substituted by trifluoromethoxy and pentafluoroethoxy groups reacts with hippuric acid to give the corresponding fluorine-containing oxazolones (IV) which, in contrast to azalactone (II), is reduced by HI/P to the corresponding fluorine-containing aminoacids (V). Thus, perfluoroalkoxy groups remain intact under these conditions.[4]



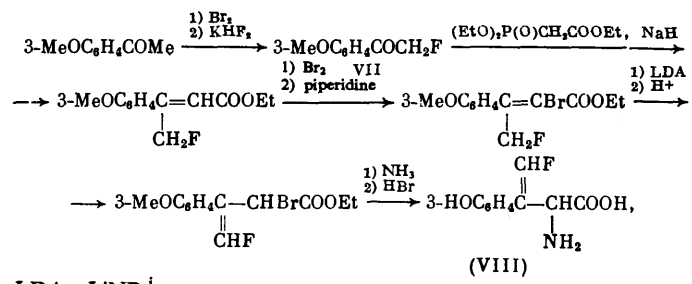
R_F = CF_3, C_2F_5.

The Erlenmeyer condensation of ω-polyfluoroacetophenones with hippuric acid affords the corresponding β-(polyfluoromethyl)-phenylalanines and -tyrosines. It should be pointed out that oxazolones are not formed under these conditions from acetophenone itself or from ω-monofluoroacetophenone.[5] Amino-acids (VI) have two chiral centres and are formed as a mixture of diastereoisomers.



R = H, OCH_3; X = H, OH; R_F = CHF_2, CF_3.

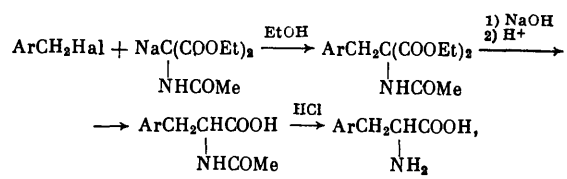
ω-Monofluoro-3-methoxyactophenone (VII) has been used as the key starting material for the synthesis of β-fluoromethylene-*m*-tryosine (VIII). Thus, Horner reaction with (VII) provides the corresponding substituted cinnamic acid ester which is converted by the route shown below to the *m*-tryosine (VIII)—an effective irreversible inhibitor of monoamineoxidase—in an overall yield of 32%.[6]



LDA – $LiNPr^i_2$.

2. Methods based on alkylation

The reaction of benzyl halides with *N*-acylaminomalonic acid esters has been generally applied to the synthesis of fluorine-containing aromatic aminoacids. Aminoacids may be obtained in high yield by this route. However, the sensitivity of the condensation to traces of moisture is a limitation which has a significant effect on the overall yield. In an earlier review,[1] there is reference to the synthesis of fluorine-containing phenylalanines and tryosines by reaction of the sodio-derivative of diethyl acetylaminomalonate with fluorine-containing benzyl halides.

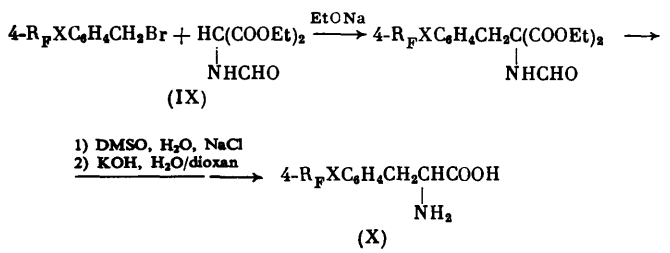


Hal = Cl, Br; Ar = 2-, 3- and 4-FC_6H_4, C_6H_4, C_6F_5, 4-HOC_6H_4, 3-$CF_3C_6H_4$.

As hydrolysis takes place in two steps, it is possible to isolate both the free aminoacid and its *N*-acetyl derivative. By alkylation with variously substituted fluoro- or trifluoromethyl-benzaldehydes,

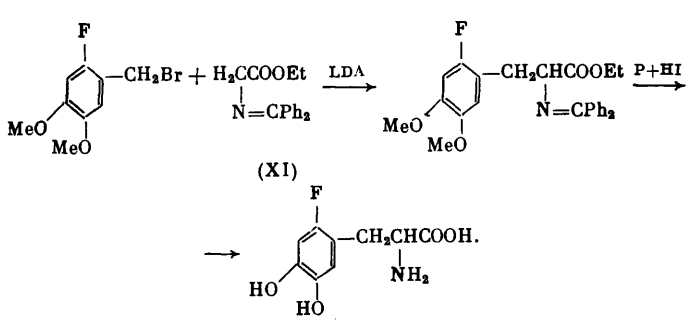
the following fluorine-containing aromatic aminoacids have been prepared: phenylalanine derivatives, $ArCH_2CH(NH_2)COOH$, where Ar = 2-FC_6H_4, 3-FC_6H_4, 4-FC_6H_4, 2,5-$F_2C_6H_3$, 3-$CF_3C_6H_4$, 2-Cl-5-$CF_3C_6H_3$, 4-Cl-3-$CF_3C_6H_3$;[7–9] tryosine analogues, where Ar = 2-F-4-$MeOC_6H_3$, 2-F-4-HOC_6H_3, 2,6-F_2-4-HOC_6H_2;[10–11] and the dihydroxyphenylalanine (DOPA) analogue where Ar = 2-F-3,4-$(HO)_2$-C_6H_2.[12]

Normally this route is based on diethyl acetylaminomalonate. However, it is possible to use other *N*-substituted malonates. Thus, condensation of 4-fluorobenzyl chloride with the corresponding phalimidomalonate, followed by hydrolysis in 5 *N* HCl at 100 °C affords 4-fluorophenylalanine in 50% yield (based on the starting benzyl halide).[13] By using the formamidomalonate (IX), removal of the protective group can be achieved under mild conditions so that fluorine-containing aromatic aminoacids with acid-labile substituents (e.g. R_FX = F_2HCO) may be prepared. Thus, treatment of fluorine-containing benzyl bromides with the sodio-derivative of (IX), followed by decarboxylation in aqueous DMSO with NaCl and basic hydrolysis, affords the corresponding polyfluoroalkoxy- and polyfluoromethylthio-phenylalanines (X) in 20–50% yield (based on the benzyl bromide).[4]

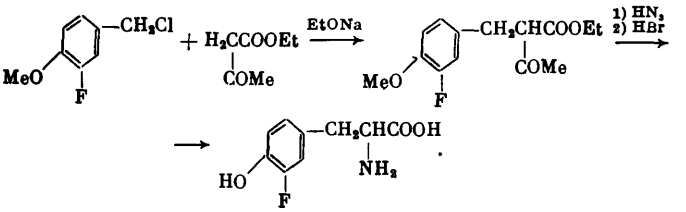


$R_FX = CHF_2O$, CHF_2S, CF_3S, CF_3CH_2O.

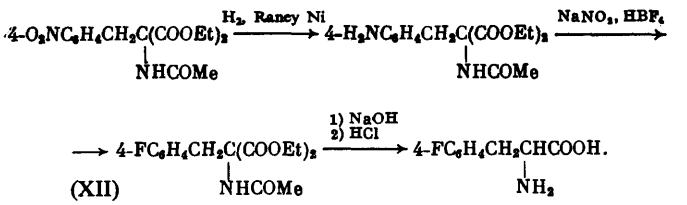
For the synthesis of fluorine-containing aminoacids from the corresponding benzyl halides, it is also possible to use other CH-acidic compounds, such as *n*-acylaminocyanoacetic acid esters,[1] in place of the acylaminomalonates. Thus, 6-fluoro-3,4-dihydroxyphenylalanine has been prepared from the glycinate Schiff base (XI), obtained from ethyl glycinate and benzophenone.[14] Generation of the carbanion in the initial deprotonation requires a strong base, e.g. LDA.



3-Fluorotryosine has been prepared by condensation of 3-fluoro-4-methoxybenzyl chloride with ethyl acetoacetate, followed by replacement of the acetyl group by an amino function with hydrazoic acid. A 63% yield has been recorded for this reaction.[15,16]



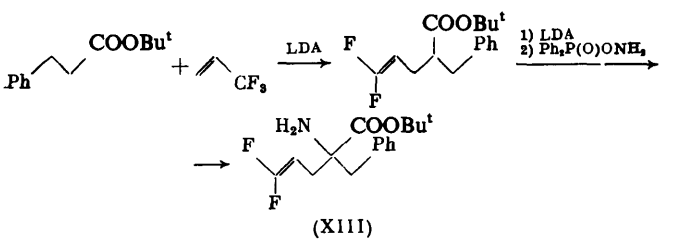
Introduction of the fluorine atom can take place during the course of the malonate-based route. Thus, after condensation of 4-nitrobenzyl chloride with the acetylaminomalonate, the nitro group may be reduced with H_2 over Raney nickel and fluorine introduced by the Schiemann reaction to give (XII).[17]



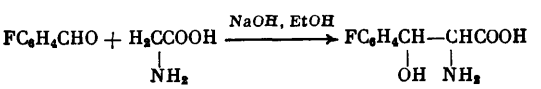
This method of introducing the fluorine atom *en route* is particularly useful for preparing phenylalanine labelled with the short-lived isotope ^{18}F ($\tau_{1/2}$ = 109 min).[18–20]

3. Other methods

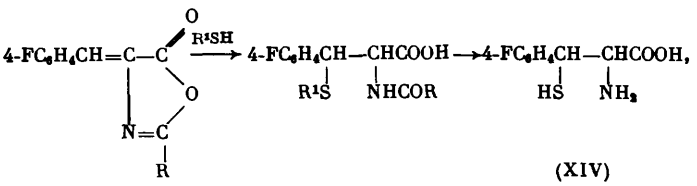
Recently, the phenylalanine derivative (XIII), having a γ,γ-difluoroallyl group in the α-position, was prepared from 3,3,3-trifluoropropylene, as shown below. *O*-Diphenylphosphinylhydroxylamine was used in the last step to introduce the amino group into the α-position relative to the carbonyl group.[21]



Treatment of 2- and 4-fluorobenzaldehyde with glycine in the presence of base affords the corresponding fluorine-containing β-phenylserine.[22,23]



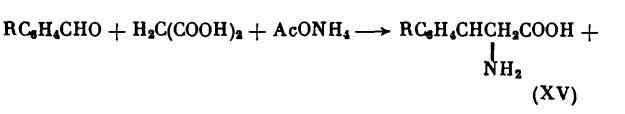
Fluorine-containing β-phenylthioserines have been prepared in the presence of base by reaction of mercaptans with the oxazolones obtained from α-acylamino-4-fluorocinnamic acids.[23] The free aminoacid (XIV) was formed on removal of the protecting groups.



(XIV)

R^1 = Et, $PhCH_2$.

A series of fluorine-containing aromatic aminoacids with an amino group in the β-position was prepared by the Rodionov reaction from benzaldehydes and malonic acid in the presence of ammonia. Thus, 4-fluorobenzaldehyde affords β-(4-fluorophenyl)-β-alanine in high yield.[23,24] Similarly, reaction with 3-fluoro-4-methoxybenzaldehyde, followed by treatment with HBr, affords β-(4-hydroxy-3-fluorophenyl)-β-alanaine.[24] β-[2- and 4-(Difluoromethoxy)phenyl]-β-alanines (XV) have also been prepared from the corresponding difluoromethoxybenzaldehydes.[25] The Rodionov reaction is accompanied by the formation of fluorine-containing cinnamic acids as by-product which may be removed by crystallisation.

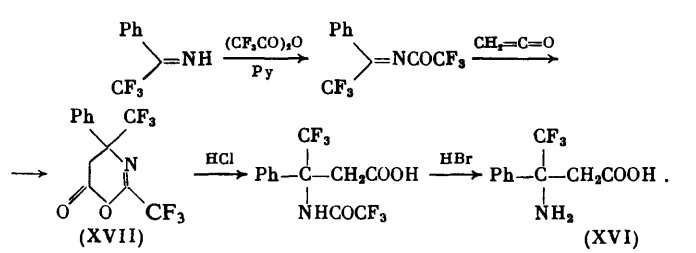


(XV)



R = 4-F, 4-$OCHF_2$, 2-$OCHF_2$.

The Rodionov reaction with ω,ω,ω-trifluoroacetophenone gives 4,4,4-trifluoro-3-phenyl-3-hydroxybutyric acid, rather than the expected β-trifluoromethyl-β-phenyl-β-alanine (XVI).[25] The latter has been obtained, however, by cyclisation of ω,ω,ω-trifluoroacetophenone *N*-trifluoroacetylimine with ketene, followed by hydrolysis of the resulting oxazinone (XVII).[26]



(XVII) (XVI)

Fluorine-containing aminoacids have also been prepared by direct fluorination of the parent aminoacids. A variety of reagents has been used for introducing a fluorine atom into the benzene ring of phenylalanine and tryosine. This route has also been applied to the preparation of homochiral fluorine-containing aminoacids, reaction proceeding as a rule with retention of chirality. The direct fluorination of (*S*)-phenylalanine and (*S*)-tyrosine will be discussed in the next section devoted to the synthesis of optically active aminoacids.

III. Synthesis of optically-active fluorine-containing aromatic aminoacids

Three routes are available for the preparation of optically-active aminoacids substituted by fluorine atoms or fluoroalkyl groups: resolution of racemic compounds into their enantiomers, for which various methods are reported; asymmetric synthesis; and fluorination of homochiral aminoacids with retention of chirality.

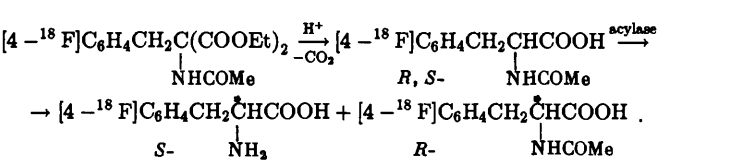
1. Optical resolution of fluorine-containing aromatic aminoacids

(*S*)- and (*R*)-Pentafluorophenylalanine have been isolated via recrystallisation of the diastereoisomeric salts formed on mixing *N*-benzoyl-(*R,S*)-pentafluorophenylalanine with brucine.[27] This method has been applied generally for the resolution of non-fluorinated aminoacids. However, it is laborious and low-yielding.

Chromatographic resolution of racemic aminoacids on chiral stationary phases is of much greater potential in this respect. This is exemplified by the optical resolution of 4-fluorophenylalanine.[28,29]

Enzyme-catalysed resolutions have been generally applied to the preparation of homochiral fluorine-containing derivatives of phenylalanine and tryosine. This route is based on the preferential enzyme-catalysed reaction of the *L*-enantiomer of a racemic mixture of a suitable aminoacid derivative. Thus, as long ago as 1946, the (*R*)- and (*S*)-enantiomers of 3-fluorotyrosine were isolated by papain-catalysed cleavage of racemic 3-fluorotyrosine anilide.[30] Similarly, papain-catalysed cleavage of racemic *N*-acetyl-(2-,3- and 4-fluorophenyl)alanine in the presence of phenylhydrazine afforded the (*S*)- and (*R*)-enantiomers of 2-, 3- and 4-fluorophenylalanine, respectively.[31] Mechanistically, the enzyme catalyses the formation of the corresponding *N*-acetyl-(*S*) fluorophenylalanine phenylhydrazide which is readily separated from the corresponding *N*-acetyl-(*R*)-fluorophenylalanine. The optically pure free aminoacids are obtained by subsequent hydrolysis of the resulting (*R*)- and (*S*)-fluorophenylalanine derivatives.

(*S*)-[4-^{18}F]-Fluorophenylalanine has been obtained by treatment of the racemic *N*-acetyl derivative with aminoacylase.[20] The use of aminoacylase is also recommended for the synthesis of homochiral aminoacids by the malonic ester synthesis, the enzyme substrates (*N*-acetyl derivatives) being formed without the additional requirement of an *N*-acylation step.

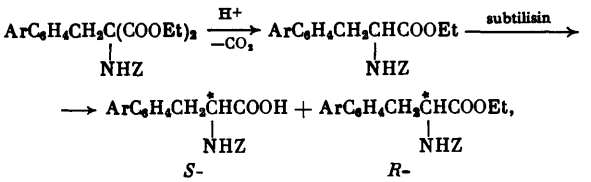


The enantiomers of pentafluorophenylalanine have been isolated via treatment of *N*-trifluoroacetyl-(*R,S*)-pentafluorophenylalanine with an acylase.[32]

α-Chymotrypsin has also been used for the enzymatic resolution of 4-fluorophenylalanine.[33] Thus, racemic 4-fluorophenylalanine is converted to the ethyl ester, which, on incubation with α-chymotrypsin affords (*S*)-4-fluorophenylalanine. The latter is

readily separated from the unreactive ethyl (*R*)-4-fluorophenylalanate. The same enzyme has been used for the resolution of methyl *N*-acetylpentafluorophenylalaninate.[34]

Subtilisin has been used[35] for the resolution of ethyl *N*-benzyloxycarbonyl-(*R,S*)-fluorophenylalaninates, obtained by the malonate route:



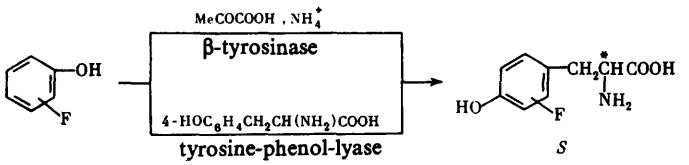
Ar = 3-FC_6H_4, 4-FC_6H_4, C_6F_5; Z = $COOCH_2C_6H_5$.

α-Chymotrypsin has also been used for the resolution of each of the three positional (*o*, *m*- and *p*-) isomers of methyl *N*-acetylfluorophenylalaninate and of *N*-acetyl-4-trifluoromethylphenylalaninate.[36] Carboxypeptidase A, however, is the preferred enzyme for the resolution of the *N*-trifluoroacetyl derivatives of these aminoacids.[36] All three positional isomers of *N*-benzyloxycarbonyl-(*S*)-fluorophenylalanine have been isolated with an enantiomeric excess (e.e.) of 90–97% by treatment of the appropriate racemic trifluoroethyl *N*-benzyloxycarbonylfluorophenylalanates with pig liver lipase.[37]

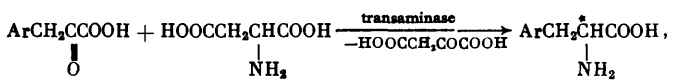
(*R*)-4-Fluorophenylalanine has been isolated by enzymatic resolution of *N*-benzoyl-(*R,S*)-4-fluorophenylalanine with an *Escherichia coli* culture.[38] All three of the positional isomers of fluorophenyl-alanine were resolved with lyophilised yeast, the (*R*)-enantiomers being isolated in 76–86% yield.[39]

2. Asymmetric synthesis

As well as being used for the optical resolution of racemic compounds, enzymes have also been applied to the synthesis of optically active fluorine-containing aminoacids. Thus, 2- and 3-fluoro-(*S*)-tyrosine have been prepared by treatment of the corresponding 3- and 2-fluorophenols with tyrosine-phenol lyase.[40,41]

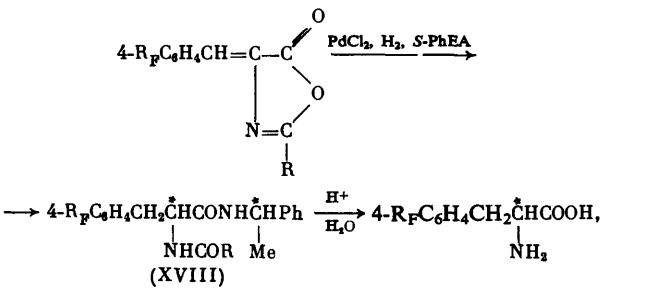


Fluorine-containing (*S*)-phenylalanines have also been synthesised. Thus, trifluoromethyl-, monofluoro-, and pentafluoro-(*S*)-phenylalanines have been prepared by action of transaminase on a mixture of aspartic acid and the appropriate fluorine-containing phenylpyruvic acid.[42]



Ar = FC_6H_4, $CF_3C_6H_4$, C_6F_5.

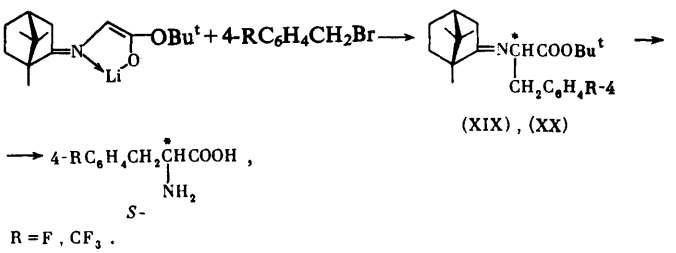
Reductive aminolysis has been used in the preparation of optically active *p*-fluoro- and *p*-difluoromethoxyphenylalanine.[43,44] Thus, reductive aminolysis of fluorine-containing oxazolones by hydrogenation over $PdCl_2$ in a variety of solvents containing (*S*)-(−)-α-phenylethylamine (PhEA) affords the corresponding *N*-acyl-(4-fluoro- or 4-difluoromethoxy-phenyl)alanine α-phenylethylamide (XVIII), predominantly in the (*S,S*)-configuration, with a diastereoisomeric excess (d.e.) up to 47%.



R_F = F, $OCHF_2$; R = Me, Ph.

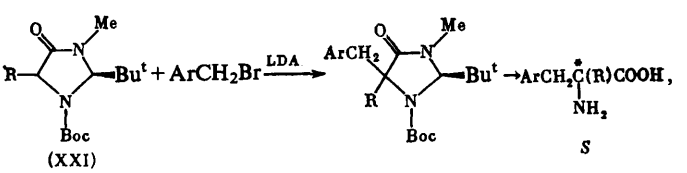
Crystallisation of the *p*-fluorophenylalanine amides affords the optically pure (*S,S*)-diastereoisomers, hydrolysis of which in 6 *N* HCl yields enantiomerically pure 4-fluoro-(*S*)-phenylalanine.[43] Attempts to cleave the amide bond in *p*-difluoromethoxyphenylalanine analogues leads to removal of the difluoromethyl group to give (*S*)-tyrosine.[44]

Fluorine-containing aromatic aminoacids have also been synthesised via alkylation with asymmetric induction. This is exemplified by the alkylation of the Schiff base derived from *tert*-butyl glycinate enolate and (1*R*)-(+)-camphor with fluorine-subtituted benzyl bromides.[45] Reaction proceeds with asymmetric induction to give the corresponding 4-fluoro- and 4-trifluoromethyl-phenylalanate Schiff bases (XIX and XX) with a d.e. of 98 and 76%, respectively. Hydrolysis of (XIX) and (XX) affords the corresponding (*S*)-aminoacid.



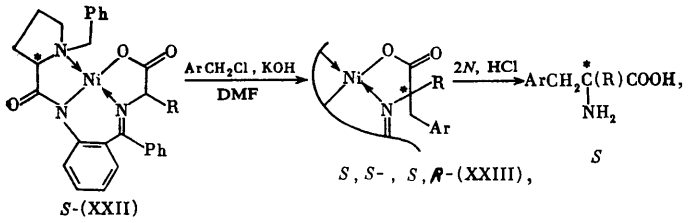
R = F, CF_3.

Stereoselective alkylation of chiral 4-imidazolidones (XXI) with pentafluorobenzyl or *p*-fluorobenzyl bromide also provides fluorine-containing aromatic aminoacids.[46,47] Thus, optically active α-methyl-4-fluorophenylalanine is obtained by alkylation of the diastereoisomeric alanine derivative (XXI), R = Me, with 4-fluoro-benzyl chloride, followed by hydrolysis.[48]



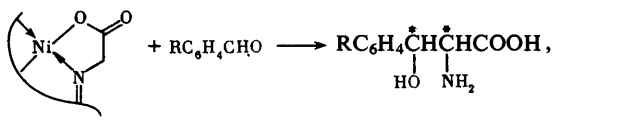
R = H, Me; Ar = 4-FC_6H_4, C_6F_5; Boc = $COOCMe_3$.

Asymmetric synthesis of (*S*)-fluorophenylalanines has been achieved from a homochiral nickel Schiff base complex prepared from (*S*)-2-[*N*-(*N'*-benzylprolyl)-amino]benzophenone and glycine.[49] Thus, complex (XXII) is alkylated with fluorobenzyl chlorides in DMF containing KOH to give a 95:5 mixture of the diastereoisomeric complexes, (*S,S*)- and (*S,R*)-(XXIII). The major isomer, (*S,S*)-(XXIII), may be isolated in optically pure form, and converted to the corresponding (*S*)-fluorophenylalanine (optical purity >99%) by treatment with HCl. The chiral prolyl ligand is also liberated and may be re-used.



R = H, Me; Ar = 2-FC_6H_4, 3-FC_6H_4, 4-FC_6H_4.

A number of diastereoisomeric β-phenylserines may also be prepared by reaction of the chiral complex, (*S*)-(XXII), with fluorine-substituted benzaldehydes.[50]

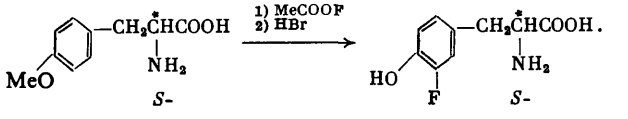


R = 2-F, 4-F 2-$OCHF_2$, 4-$OCHF_2$, 4-OCF_3, 3-CF_3.

3. Direct fluorination of enantiomeric aminoacids

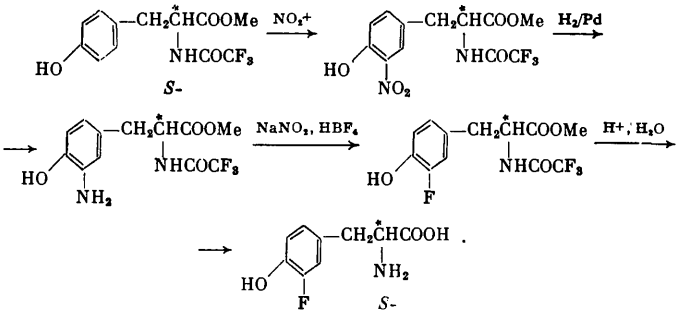
One of the most viable routes to enantiomeric fluorine-containing aminoacids involves introduction of the fluorine atom into the aminoacid molecule with retention of optical activity. Such methodology avoids multistep sequences and is particularly useful for preparing [^{18}F]-fluorinated aminoacids. Elemental fluorine can be the fluorinating agent as well as such auxiliaries as acetyl hypofluorite and XeF_2.

Thus, (*S*)-3-fluorotyrosine has been prepared via fluorination of *O*-methyl-(*S*)-tyrosine with acetyl hypofluorite.[51]



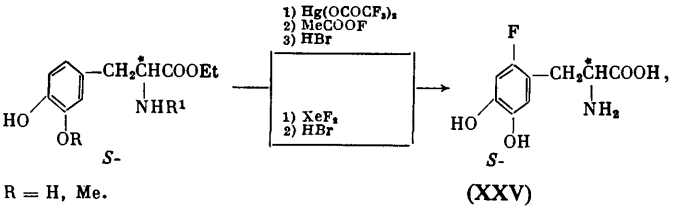
Enantiomeric (*S*)-monofluorophenylalanine and (*S*)-[3-^{18}F]-fluorotyrosine labelled with ^{18}F have also been obtained by this route.[52] Elemental fluorine has also been used for the ring-fluorination of aromatic aminoacids. Thus, treatment of a solution of tyrosine in hydrofluoric acid with N_2-diluted gaseous fluorine affords 3-fluorotyrosine in 46% yield, while fluorination of *O,N*-diacetyltyrosine in trifluoroacetic acid gives a 2:1 mixture of 2- and 3-fluorotyrosine.[53] (*S*)-Fluorophenylalanines with an ^{18}F label in the benzene ring were also prepared by this route;[54] the resulting mixture of labelled (*S*)-2-, (*S*)-3- and (*S*)-4-fluorophenylalanaine was separated by HPLC.

In order to avoid the formation of isomeric fluorine-containing aminoacids, methods have been devised for the regioselective introduction of fluorine atoms into the aromatic nucleus. This is exemplified by the synthesis of 3-fluoro- and 3,5-difluoro-(*S*)-tyrosine.[55]



It is based on the nitration of a protected (*S*)-tyrosine derivative, followed by reduction of the nitro group and introduction of the fluorine atom by the Schiemann reaction. Reaction proceeds with retention of chirality at all stages of the conversion, and provides (*S*)-3-fluorotyrosine in 21% yield.

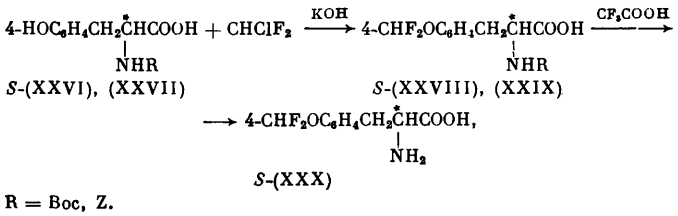
A procedure for introducing a fluorine atom regiospecifically at the 6 position of 3,4-dihydroxyphenylalanine has also been reported.[56] Thus, treatment of protected (*S*)- or (*R*)-3,4-dihydroxyphenylalanine derivatives with mercuric trifluoroacetate affords exclusively the corresponding 6-mercuri-derivatives, which are converted to the respective homochiral 6-fluoro-3,4-dihydroxyphenylalanines (XXV) in 20% yield via fluorination with acetyl hypofluorite. Homochiral (XXV) was also obtained via direct fluorination of a 3-methoxy-4-hydroxyphenylalanine derivative with xenon difluoride;[57] the yield of product after removal of the protective groups, was 25% (based on XeF_2). Both reactions proceed with retention of chirality.



R = H, Me. (XXV)

The procedure for polyfluoroalkylation of phenols[58] has recently been applied to the synthesis of polyfluoroalkylated (*S*)-tyrosine derivatives.[58] Thus, treatment of *N*-Boc-(*S*)-tyrosine (XXVI) or *N*-*Z*-(*S*)-tyrosine (XXVII) with chlorodifluoromethane in the presence of base affords the corresponding optically active *N*-protected *O*-difluoromethyltyrosine derivatives (XXVIII and

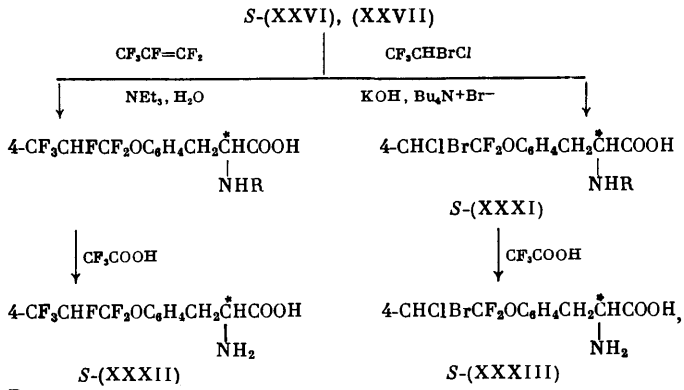
XXIX), which may be used in peptide synthesis as the carboxyl component.



R = Boc, Z.

The free aminoacid (XXX) was isolated by action of trifluoroacetic acid on the Boc-derivative (XXVIII). With the aid of ligand-exchange HPLC on a chiral stationary phase it was shown that the difluoromethylation proceeds without racemisation, and that the optical purity of (*S*)-(XXX) was >99.5%.

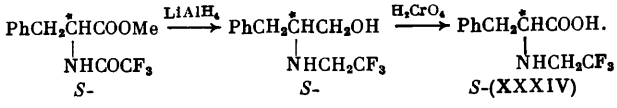
In a similar way,[58] *bis*(difluoromethylation) of *N*-Boc-(*R,S*)-3,4-dihydroxyphenylalanine affords 3,4-*bis*(difluoromethoxy)-(*R,S*)-phenylalanine in 14% yield. The interaction of (*S*)-tyrosine derivatives, (XXVI and XXVII), with hexafluoropropylene in aqueous triethylamine at 70 °C provides the corresponding 1,1,2,3,3,3-hexafluoropropoxy-(*S*)-aminoacids. On the other hand, the 4-polyhalogenoethoxy derivative of *N*-Boc-(*S*)-phenylalanine (XXXI) has been prepared by treatment of *N*-Boc-(*S*)-tyrosine (XXVI) with fluorothane, $CF_3CHBrCl$ (a commercially available inhalant-type anaesthetic), in 50% aqueous KOH containing $Bu_4N^+Br^-$ as phase transfer catalyst.



R = Boc, Z.

The corresponding unprotected polyfluoroalkoxy derivatives of (*S*)-phenylalanine (XXXII and XXXIII) were obtained by cleavage of the *tert*-butoxycarbonyl group in trifluoroacetic acid at 20 °C. The e.e. exceeded 95%, as was demonstrated by ^1H NMR spectroscopy with the aid of the chiral lanthanide shift reagent, Eu(hfc)$_3$. Thus, it has been confirmed that *O*-polyfluoroalkylation of *N*-protected (*S*)-tyrosine derivatives proceeds without racemisation.

Optically active methyl *N*-trifluoroacetyl-(*S*)-phenyalanate has been converted to *N*-trifluoroethyl-(*S*)-phenylalanine (XXXIV) by reduction with $LiAlH_4$, followed by oxidation of the resulting optically active aminoalcohol with Jones' reagent.[59]



IV. Possible fields of application

The replacement of hydrogen by fluorine in the aminoacid molecule does not introduce any steric hindrance since the van der Waal's radius of the atom fluorine is approximately the same as that of hydrogen. As a consequence, living organisms cannot normally distinguish fluorinated aminoacids from natural ones so that the former may be readily incorporated. This phenomenon is called the "masking effect", and is the rationale for using fluorinated aminoacids in biochemical and medical research into the study of metabolic pathways and the mechanism of action of various enzyme systems. In this respect, ^{19}F NMR spectrosocpic analyses and radioactive labelling (notably with the short-lived ^{18}F isotope) have been fruitfully applied in this field of research.

In studying the activity of phenylalanine-ammonia-lyase, it has been shown that deamination of (*S*)-4-fluorophenylalanine proceeds at half the rate of the same reaction with (*S*)-phenylalanine.[60] The substrate specifically of such enzymes as phenylalanine-*t*-RNA-ligase,[61] aspartate-transaminase,[62] chorismate-mutase,[63] lacto-peroxidase,[64] and tyrosine-phenol-lyase[65] has been studied by using 2-fluoro-, 4-fluoro- and 3,4-difluoro-phenylalanine as well as 3-fluorotyrosine. A study has also been made of the effect of molecular geometry and electronic charge distribution on the interaction of aminoacid oxidases with substrates and inhibitors;[6] a determination has been made of the correlation between the rate of degradation of aromatic aminoacids and the Hammett constant for substituents in the aromatic ring. 3-Fluoro- and 4-fluoro-phenylalanine were substrates for this study.

A study of the deactivation of leucocytic elastase by aromatic aminoacid derivatives has shown that deactivation is enhanced if there is a trifluoromethyl group in the *m*-position of the aromatic ring of phenylalanine. This is a consequence of an increase in the hydrophobicity of the molecule.[67]

By applying reverse-phase HPLC, a quantitative assessment has been made of the lipophilicity of phenylalanines containing fluoro-groups in the *p*-position. The change in free energy of sorption was measured as a function of the number of fluorine atoms in the molecule. The increase in hydrophobicity (π_x) for a series of fluorine-containing groups follows the order shown below.[58]

R_F	F	$OCHF_2$	$OCF_2CHClBr$	OCH_2CF_3	$SCHF_2$	OCF_3	SCF_3	OC_2F_5	OCF_2CHFCF_3
π_x	0.14	0.57	0.69	0.93	0.95	1.06	1.43	1.80	1.90

The initial study of 4-fluorophenylalanine metabolism showed that it was converted to tyrosine.[68] However, more recent research has revealed that the formation of tyrosine from 4-fluorophenylalanine proceeds six times more slowly than from phenylalanine.[69] This is explained by the higher C–F bond energy (116 Kcal/mol) relative to the C–H bond (99 Kcal/mol).

4-Fluorophenylalanine is a competitive antagonist of phenyl-alanine.[70] It also possesses fungicidal properties towards a number of pathogenic fungi which infect cucumbers and potatoes.[71]

A study of the physiological activity of 3-fluorotyrosine in mice has shown that this amino-acid, which participates in the normal metabolism of tyrosine, is converted to monofluoroacetic acid. The latter blocks the Krebs cycle, thereby inducing convulsions and death.[72]

A series of fluorinated derivatives of phenylalanine and tyrosine have been found to inhibit the growth of *Neurospora crassa*. 3-Fluorotyrosine is the most active inhibitor in this respect.[73] 2-Flurotyrosine also inhibits the growth of *Escherichia coli*,

Streptococcus faecalis, and other bacteria,[74] while 4-fluorophenylalanine inhibits the development of malignant tumours.[75–78]

In studying the substrate specificity of monoamine oxidase (MAO B)—an enzyme which plays a key role in the formation of neurotransmitters in the central nervous system (CNS)—it has been shown that β-fluoromethylene-*m*-tyrosine (VIII) is an effective irreversible inhibitor of MAO B in the presence of aromatic aminoacid decarboxylase.[79–81] β-Polyfluoromethyl-substituted phenylalanines and tyrosines (VI), which are structurally similar to aminoacid (VIII), have a sedative effect on the CNS.[5]

In studying the effect of introducing fluorine and trifluoromethyl groups at various positions of the phenylalanine and tyrosine ring on the opioid activity of enkephalin, it was demonstrated that substitution of phenylalanine by 4-fluorophenylalanine leads to a significant increase in enkephalin activity; however, introduction of a trifluoromethyl group at the *para*-position of phenylalanine, or substitution of tyrosine by 4-fluorophenylalanine, reduces the activity of the peptide.[82]

The decapeptide, P-Glu-*D*-*p*-F-Phe-Trp-Ser-Tyr-*D*-Ala-Leu-Arg-Pro-Gly-NH_2, having a (*R*)-4-fluorophenylalanine residue in the 2 position displays anti-ovulating activity in mammals,[83] while tripepetides with a (*S*)-4-fluorophenylalanine residue show analgesic activity.[84] Peptides containing fluorinated aromatic aminoacids, especially fluorophenylalanine, possess anti-tumour activity,[85] and have been used as medicaments.[86]

A large number of bradykinin and oxytocin analogues have been synthesised for studies of structure-activity relationships and the mechanism of action of these two peptides. Particular emphasis has been placed on susbtituting phenylalanine by 4-fluorophenylalanine (in oxytocin)[87] and by 3-trifluoromethylphenylalanine (in bradykinin).[88]

As fluorophenylalanine and fluorotyrosine derivatives participate in metabolic processes, they may be incorporated in proteins.[89,90] Thus, on administration of 4-fluorophenylalanine to rabbits, it was shown that this aminoacid is incorporated in the protein of muscles, the liver, and the blood (by replacing phenylalanine). Being incorporated in enzymes, 4-fluorophenylalanine may influence their activity, or have no effect at all, depending on the level of 4-fluorophenylalanine incorporation.[91]

[^{18}F] containing aromatic aminoacids are used for studying the metabolism of fluorinated aminoacids and enzymatic reactions.[92] On studying the distribution of 4-fluorophenylalanine-^{18}F in pig organs, it has been shown that most of the labelled aminoacid is incorporated in the pancreas.[93] Clincially, 4-fluorophenylalanine-^{18}F may be used for scanning this organ.[94,95]

A study of the metabolism of (*S*)-6-[^{18}F]-3,4-dihydroxyphenylalanine has shown that this compound is metabolised more quickly than ^{14}C-labelled 3,4-dihydroxyphenylalanine, which has shed light on the pathways by which this aminoacid is metabolised.[96]

^{19}F NMR spectroscopy has found widespread application in biological studies.[97] This is exemplified by a study of bacteriorodopsin containing 3-fluorotyrosine,[98] of the mechanism of transamination with 4-fluorophenylalanine in the presence of pyridoxal phosphate-dependent enzymes,[99] and of the enzymatic hydrolysis of 3-fluorotyrosine phosphate.[100]

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From this analysis of published data, it is clear that fluorine-containing aromatic aminoacids have a valuable application in the following areas: specific modification of physiologically active peptides; the study of the structure and mechanism of action of complex biologically active molecules with the aid of ^{19}F NMR; and the preparation of effective regulators of bio-systems. Thus, the development of new methods of synthesis of fluorine-containing aromatic aminoacids, especially optically active derivatives, is both timely and potentially fruitful.

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Translated from *Uspekhi Khimii* **60** 2065–2088 (1991) U.D.C. 539.19:541.57

Compounds of the *f*-elements. Chemical bonding and electronic structure

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ABSTRACT. Recent data from experimental and theoretical studies of the nature of the chemical bonding in *f*-element compounds and their electronic structure are reviewed. Implicit and explicit methods of accounting for relativistic effects in quantum-chemical calculations are briefly examined. Results of quantum-chemical calculations of lanthanide trihalides, lanthanide and actinide cyclopentadienides, and other *f*-element compounds are analysed. Questions about the electronic and geometric structure, the nature of the π- and σ-bonding, and the role of *d*- and *f*-orbitals in forming chemical bonds are discussed.

The bibliography includes 95 references.

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I. Introduction

In the lanthanide (Ce → Lu) and actinide (Th → Lr) series, electrons are placed successively in the 4*f*- and 5*f*-orbitals respectively. Therefore, lanthanides (Lns) and actinides (Ans) are frequently classified together as *f*-elements. The varied and ever expanding application of *f*-element compounds in science and technology has in the last decade stimulated interest in the study of their electronic structure and the nature of their chemical bonding.

Crystal field theory[1,2] has been widely used in the majority of earlier theoretical studies for analysing the electronic structure of Lns and Ans. The reason for this is that the *f*-electrons have features different from those for electrons in other subshells. Thus, the energy levles of the 4*f*-orbitals in Lns are rather close to those of the 5*s*-, 5*p*- and 5*d*-orbitals. However, the 4*f*-states extend little into space and the electrons in them are to a large extent localised inside the 5*s*- and 5*p*-subshells.[3] As a result, 4*f*-orbitals poorly overlap with orbitals of neighbouring atoms and the bonding in Lns is mainly due to 5*s*- and 5*p*-electrons, i.e., it is nearly purely ionic. Analogous arguments for the role of the *f*-electrons were made for actinide compounds.

However, the majority of recent studies on the electronic structure of *f*-compounds have utilised molecular-orbital (MO) methods owing to the obvious limitation of crystal field theory for describing *f*-compounds.[3] Such an approach significantly facilitates development of general concepts about the chemical bonding in compounds with *f*-electrons. Previous reports[3–8] are recommended for familiarising oneself with the current state of affairs in this area. Moreover, these references contain numerous citations to earlier reviews and reports on the respective topics.

Hence, the capabilities of quantum-chemical cluster models and methods of describing various characteristics of the electronic structure of solids based on the *f*-elements have been explored.[3,4] In these studies, special attention was paid to the orderly statement of the basic principles of the cluster approach for modelling the electronic structure of solids and the quantum-chemical approaches used in cluster calculations. The nature of interatomic interactions and the role of *f*-subshells in chemical bonding were analysed in detail.

Quantum-chemical calculations of atoms, ions and actinide molecules have been generalised and systematised in a monograph.[5] Features of the electronic structure of 5*f*-elements, the stability of the different An oxidation states, and the analogy between Lns and Ans were analysed. Isomer shifts in Mössbauer spectra were interpreted. The relative role of various mechanisms in forming chemical bonds and the influence of relativistic effects on the properties of Lns and Ans were the subjects of much attention.

The periodic (tetrad) regularity in the change of many properties of the free atoms and ions of the *f*-elements (ionisation potential, electron affinity, redox potentials, etc.) have been analysed.[6]

Relativistic effects in structural chemistry have been reviewed.[7,8] These reviews contain the most detailed information on this subject. A short but rather complete analysis of the relativistic methods of quantum chemistry that are used for calculating the electronic structure of compounds containing heavy elements is also provided.

However, it is noteworthy that few studies analyse the electronic structure of *f*-compounds within the framework of MO methods. Calculations for rather large molecular systems of interest to chemists are just beginning. Consequently, fundamental questions about the features and details of the electronic structure (participation of various groups of electrons in the chemical bonding, specific role of *f*-subshells, relation of the reactivity of *f*-compounds to their electronic structure, etc.) are far from finally resolved.

In the present review, recent results are reviewed and analysed. These have not appeared previously in monographs and reviews and are mainly theoretical studies of the fundamental chemical properties of *f*-element organometallic compounds: their electronic and geometric structure and their reactivity.

Results are also presented for calculations of the electronic and geometric structure of lanthanide trihalides (LnX_3). This material is placed in a separate section since LnX_3 have been a test case of the *f*-block for verifying the capabilities of many quantum-chemical methods.

Methodical problems related to the study of the electronic structure of the *f*-elements should also be noted. As the atomic number of an element increases (nuclear charge Z), the total and

kinetic energy of the electrons increases. For heavy elements, in particular the Lns and even more the Ans, relativistic corrections become important [these are of the order of $(v/c)^2$, where v is the velocity of the electrons and c is the speed of light]. Therefore, the role of relativistic effects and explicit and implicit methods of accounting for them in quantum-chemical calculations must be discussed, although briefly.

II. Relativistic quantum chemistry

The majority of quantum-chemical calculations of interest to chemists are based on the solution of the nonrelativistic Schrödinger equation, the Hamiltonian of which is constructed assuming that the interaction of electrons does not depend on their velocity. The relativistic dependence of the rest mass of particles on velocity is also ignored. These approximations formally correspond to an infinite speed of light. Such calculations are suitable, for example, for approximating the total energy or wave functions of light atoms or molecules consisting of them. The Schrödinger Hamiltonian is unsuitable for describing the finer details of electronic structure. The special structure of a multi-electron atom cannot be even qualitatively described using a nonrelativistic approximation.[9]

The relativistic analogue of the one-electron Schrödinger equation is the Dirac equation. The principal difference between them is that the dependence of the electron mass on its velocity is considered in the relativistic kinetic energy operator. This produces 4 × 4 matrices in the Hamiltonian instead of the usual scalar operators. The solutions of the Dirac equation are four-component wave functions.

Additional difficulties arise on going to multi-electron atoms and molecules. For instance, a complete (conclusive) relativistic theory of electron–electron interaction does not exist. One of the fundamental difficulties is that particles can be generated or absorbed owing to the equivalency of energy and mass. This can occur every time when energy equal to or greater than the rest energy of these particles is transferred during their interaction.[11] The destruction of particles can be systematically accounted for only within the framework of the quantised field concept whereas quantum field theory has its own difficulties and unsolved problems.

Therefore, relativistic effects are accounted for in the majority of cases using approximate Dirac or Dirac–Breit Hamiltonians.[7,8,12] Electron–electron interaction in the first of these is described by the usual nonrelativistic expression. In the second, a relativistic correction (of the order of α^2, where $\alpha = e^2/hc$ is a fine structure constant) to the two electron-interaction, first obtained by Breit, is considered.

Very complicated and long equations must be solved to account for relativistic effects within the framework of the MO LCAO method owing to the appearance of four-component wave functions. Fortunately, only outer valence electrons participate directly in chemical bond formation in the majority of cases. The so-called quasirelativistic approximation is entirely applicable to these. Relativistic effects in this approximation are accounted for to the accuracy given by the $(v/c)^2$ terms.[13]

It is convenient to transform the relativistic Hamiltonian of the multi-electron atom to a form where its nonrelativistic part is clearly separated in order to follow in more detail the relative role and physical meaning of relativistic effects.[14,15] After such a transformation using the Pauli approximation (accounting for terms up to α^2) and in the absence of external magnetic and electric fields, the relativistic Hamiltonian H can be written[8]

$$H = H_0 + H_D + H_{mv} + H_{so},$$

where H_0 is the nonrelativistic Hamiltonian, H_D is the correction for Darwin interaction (the Darwin term has no classical interpretation), H_{mv} is a correction to the kinetic energy accounting for the dependence of particle masses on their velocity, and H_{so} is a correction for spin–orbit coupling.

The correction H_{mv}, which accounts for the dependence of particle masses on their velocity, causes a relativistic contraction of orbitals. This is most noticeable for inner 1*s*- and 2*s*-electrons moving at large velocities.[5,7,8] The inner *p*-orbitals contact to a smaller extent. Owing to the relativistic contraciton of *s*- and *p*-orbitals, electrons in them more effectively screen the nuclear charge. Electrons in *d*- and *f*-orbitals are more weakly attracted to the nucleus. As a result, the *d*- and *f*-orbitals become more diffuse and energetically destabilised (energy levels shift upward relative to their nonrelativistic values).

The correction for spin–orbit coupling H_{so} causes levels to split into sublevels corresponding to different values of total momentum $j = l \pm 1/2$ (l is the orbital moment). Thus, the *p*-level splits into $p_{1/2}$- and $p_{3/2}$-sublevels; the *d*-level, into $d_{3/2}$- and $d_{5/2}$-sublevels, etc.

These relativistic corrections are essential and have a significant influence on the electronic properties of heavy atoms and molecules containing heavy atoms. For example, the lanthanide contraction (decrease of ionic radius on going from La to Lu), which is usually related to incomplete screening of the nuclear charge by 4*f*-electrons, is to a certain degree due to a relativistic effect. A comparison of atomic calculations by Hartree–Fock (nonrelativistic) and Dirac–Fock (relativistic) methods revealed that the lanthanide contraction is 27% due to a relativistic effect.[8,16]

Various quantum-chemical relativistic and quasirelativistic methods for calculating the electronic structure of atomic and molecular systems have been described.[3–5,7,8,16–23] Therefore, we will briefly discuss only those methods that have been used in subsequent studies.

Calculations based on the quasirelativistic or relativistic extended Hückel and *X*α-scattered wave (*X*α-SW) or *X*α-discrete variational (*X*α-DV) methods have been most widely used.

A local approximation for the exchange-correlation potential is used in the *X*α methods. This produces a one-electron Hartree–Fock–Slater equation.[24] There are two methods for solving this equation, which are reflected in their names: *X*α-DV and *X*α-SW.[25,26] Incorporating relativistic corrections does not significantly change the calculation structure of these methods. Relativistic effects have been accounted for within the framework of the *X*α-DV method.[27,28] Relativistic[29,30] and quasirelativistic[31] *X*α-SW methods have been developed. It is noteworthy that *X*α-methods have been successfully employed to interpret photoelectron spectra.

The Hamiltonian is not examined in an explicit form in the relativistically parametrised extended Hückel method,[32–36] like in the nonrelativistic method. The diagonal matrix elements of the effective one-electron Hamiltonian H_{ii} are usually set equal to the orbital energies that are either estimated from experiment or are taken from Dirac–Fock atomic calculations.[37] The off-diagonal elements H_{ij} are estimated using the standard Wolfsberg–Helmholtz formula.

In the quasirelativistic extended Hückel method,[38,39] the usual (quasirelativistic) atomic functions (*p*-, *d*- and *f*-) are used. These are obtained from relativistic ($f_{7/2}$, $f_{5/2}$, $d_{5/2}$, $d_{3/2}$, $p_{3/2}$ and $p_{1/2}$) functions by using the weighted average of each multiplet. This enables such relativistic effects as the relativistic contraction of atomic *s*- and *p*-orbitals and the increased diffuseness of the *d*- and *f*-orbitals in addition to the average shift of the energy levels to be explicitly accounted for. The spin-orbit splitting of the levels and the difference in diffuseness of the two multiplets of the *p*-, *d*- and *f*-orbitals remain unaccounted for. It is proposed that the last two factors have little effect on such properties as the geometry and reactivity.

The principal merit of the extended Hückel method is the complete accounting for overlap intergrals. This enables wave functions with the correct normalisation to be obtained and exchange repulsion effects of filled shells to be qualitatively correctly described. This is very important in describing the structure of complexes. Drawbacks of the extended Hückel method are connected with the lack of accounting for electron-electron interaction, with approximation of the total energy of all orbital energies, and with problems in constructing a satisfactory approximation for the off-diagonal matrix elements H_{ij}. Therefore, this method was very useful for describing conformational effects and other properties that can be interpreted by orbital-energy correlation diagrams. However, it is in general unsuitable for describing the formation and dissociation of chemical bonds and does not treat electrostatic effects.[40]

Naturally, each of the listed methods has its advantages and shortcomings, enables with a different degree of accuracy calculation of the electronic structure, and considers relativistic effects in calculations. Results of various calculations of gaseous LnX_3 are compared in the following section as an illustration of the capabilities of these methods.

III. Lanthanide trihalides

One of the first studies of the nature of the bonding and geometric features of LnX_3 (in the vapour phase) was carried out using the nonrelativistic extended Hückel method (4*f*-orbitals were not included in the valence basis set).[41] The effect of 4*f*-electrons was considered indirectly in the choice of the empirical parameters (the values of the diagonal elements H_{ii}). The most important result of the calculations was the conclusion that a pyramidal structure for these molecules represents the minimum in total energy. An orbital-correlation analysis demonstrated that such a structure enables the optimum interaction between the metal *d*-orbitals (especially d_{z^2}) and the halide *p*-orbitals. The calculated charge on the metal in LaX_3 is much less than +3: +1.10 for LaF_3, +0.66 for $LaCl_3$, +0.54 for $LaBr_3$, and +0.38 for LaI_3. Therefore, these data suggest that the bond in LaX_3 is not purely ionic even for the fluorides and that the covalency increases down the halogen series (F → I).

The structures of LnX_3 have been analysed by the Wolfsberg–Helmholtz method.[42] This is a variation of the extended Hückel method and includes an additional self-consistency procedure for atomic charges. Low-lying excited states of LnX_3 were studied in this work. The transition energies from *f*- to *d*-levels were estimated. A total of 56 molecules were examined. The results obtained (orbital energies, transition energies, atomic charges, etc.) provided a basis for choosing promising molecules for fabrication of new gas lasers.

The electronic structures of MI_3 (M = La, Gd, Lu)[33] have been calculated by the relativistically parametrised extended Hückel method. The experimental data reveal that MI_3 are polar and that a nonplanar structure (pyramidal) represents the minimum in total energy.

The most detailed and thorough of the electronic structures of LnX_3 has been carried out by Ruscic et al.[43] They studied photoelectron spectra (using He I and He II excitation sources) of $LaCl_3$, $LaBr_3$, $CeBr_3$, $NdBr_3$, $LuBr_3$, LaI_3, CeI_3, NdI_3, ErI_3 and LuI_3. The electronic structure of all compounds was calculated by the relativistic $X\alpha$-DV method. An analysis of the results obtained, taking into account literature data for the photoelectron spectra of Ln fluorides and chlorides in addition to mass spectra, demonstrated that the SCF-$X\alpha$ method correctly reproduces the experimental features of the spectra. Regularities found experimentally in the change of the nature of the bonding, the ionisation potentials, and the valence band widths in both the Lns (La → Lu) and the halides (F → I) are discussed.

It has been found[43] that the ionisation energies of the 4*f*-orbitals of light(early) Lns are less than those of the ligand *p*-orbitals. These energies are comparable for the middle Lns. For the heavy (late) Lns, the energies of the 4*f*-electrons decrease so much that they act like core electrons. Although the ionisation energies of the Ln 4*f*-orbitals for the majority of LnX_3 are very close to those of the halide valence orbitals, nevertheless, the 4*f*-orbitals interact very weakly with the halide orbitals. The reason for this is that the 4*f*-electons of the Lns and the valence electrons of the halides are localised in physically separated regions of the molecule. Therefore, the overlap of the respective orbitals is very poor. The corresponding radii of maximal electron density can be used as a measure of the localisation of the Ln orbitals. For the principal component of the $4f_{7/2}$-orbital, the radial electron density is maximal at $r \sim 0.4$ Å for $La^{+1.5}$ and $r \sim 0.3$ Å for $Lu^{+1.01}$ (r is the distance from the nucleus) whereas the maxima for the $5d_{5/2}$-, $6p_{3/2}$-, and 6*s*-orbitals are reached at r = 1.22, 2.27 and 1.89 Å, respectively. Moreover, the electron density in the 4*f*-states is mainly concentrated in the narrow region between 0.2 and 0.7 Å. Such localisation ensures that the 4*f*-orbitals will have a very low chemical activity.

Theoretical and experimental data indicate that the bonding in LnF_3 is primarily ionic ($Ln^{+2.2}$). A more covalent nature is acquired on going to the chlorides ($Ln^{+1.6}$), bromides ($Ln^{+1.3}$) and iodides ($Ln^{+1.01}$). As already demonstrated above, the reason for the highly ionic bonds in the fluorides is the poor overlap between the halide and metal orbitals. The covalency increases primarily as a result of the involvement of 5*d*-, 6*p*- and 6*s*-orbitals. This is confirmed by an analysis of the corresponding overlap integrals between the orbitals and the outer *p*-orbitals of the halides.

The ground state, only La, Ce, Gd and Lu atoms have the electronic configuration $4f^n5d6s^2$. This corresponds to trivalent Lns in organometallic compounds where on 5*d*- and two 6*s*-electrons participate in the bonding. The electronic configuration of other Ln atoms in the ground state does not include the *d*-level. The energy ΔE must be lost in promoting an electron from the 4*f*- to the 5*d*-level (the $4f^n6s^2 \rightarrow 4f^{n-1}5d6s^2$ transition) and convering these Lns to the trivalent state. Naturally, it is expected (under otherwise equal conditions) that as the energy ΔE that must be lost increases, the energy subsequently gained in bond formation decreases. This is confirmed by the fact that the enthalpy change for atomisation of

LnX_3 and lanthanide monoxides correlates with the energy change of the $4f^n6s^2 \rightarrow 4f^{n-1}5d6s^2$ transition in the Ln series.[43,44]

It has been found[43] that the dissociation energy of La, Ce, Gd and Lu monoxides (i.e., Lns that have a populated *d*-level in the atomic ground state) into the atoms (E_d^*, kcal mole^{-1}) decreases smoothly with increasing atomic number according to the law $E_d^* = 190.6 - 3.75N + 0.094N^2$, where $N = Z$(atomic number) $- 57$. In this instance, the change in lanthanide monoxide dissociation energies along the whole series La → Lu should be described by the equation $E_d(N) = E_d^*(N) - \Delta E(N)$, where $\Delta E(N)$ is the energy of the $4f^n6s^2 \rightarrow 4f^{n-1}5d6s^2$ transition for Ln atoms that do not have a populated 5*d*-level in the ground state. The E_d values calculated in this manner[44] correctly describe the experimentally observed double periodicity in the change of dissociation energy of lanthanide monoxides (Fig. 1).

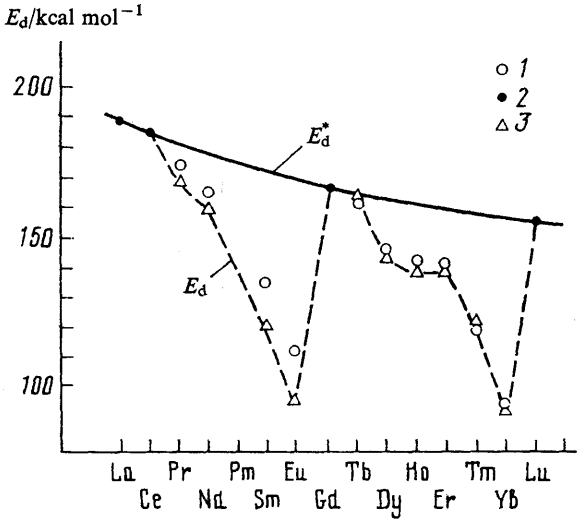


Figure 1. Change of lanthanide monoxide dissociation energy as a function of atomic number.[44] Experimental data (*1*), experimental data used to construct the dependence of E_d^* on N (*2*), calculated E_d (*3*).

The data plotted in Fig. 2 [43] demonstrate an analogous periodicity in the change of enthalpy of atomisation for LnX_3.

It is noteworthy that the average bond energy Ln–X (X is a halide) decreases on going from F to I. Hence, the average enthalpy of atomisation of LnF_3, $LnF_3(g) \rightarrow Ln(g) + 3F(g)$, is about 420 kcal mol^{-1}. Consequently, the Ln–F bond energy is 140 kcal mol^{-1}.[43] The corresponding values for $LnCl_3$ are 325 and 108 kcal mol^{-1}; for $LnBr_3$, 290 and 97 kcal mol^{-1}; and for LnI_3, 228 and 76 kcal mol^{-1}.[43] The conclusion is also reached that electrostatic forces provide the principal contributions to the bonding although the positive charges on the Ln ions is always much less than three. This occurs since the overlap integrals between the atomic orbitals of the Lns and halides (which can be viewed as a measure of the covalency) are very small.

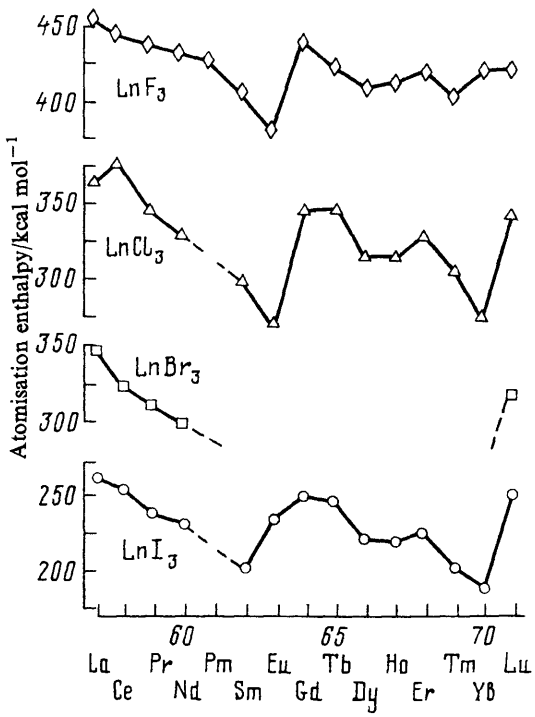


Figure 2. Dissociation enthalpy of LnX_3 into free atoms as a function of Ln atomic number.[43]

Spin-orbit splitting of filled valence and core levels in LnX_3 has been studied.[45] Calculations were made using the relativistically parametrised extended Hückel method. A total of 60 LnX_3 molecules were examined, where X = F → I and Ln = La → Lu. The geometric structure was selected to be the same as in previous studies[43] in order to facilitate comparison with results obtained by the $X\alpha$-DV method. The following basic principles were found. On going from F to I, the positions of the *p*-orbital energy levels of the halides X(*np*) are raised and the width of the valence band (the difference between the highest and lowest energy levels of these orbitals) increases from 1.2 to 2.8 eV. The latter agrees well with photoelectron spectra for La, Gd and Lu trihalides. The width of the X(*ns*)-level band changes from 0.25 to 1.0 eV. The ligand-field splitting of the Ln($5p_{3/2}$)-levels is small [from 0.25 (La) to 0.75 eV (Lu)] compared with the spin-orbit splitting $p_{3/2} - p_{1/2}$, which increases on going from La to Lu from 2.73 to 7.29 eV. On going from F to I and from La to Lu, the splitting of the $5p_{3/2}$-levels decreases. The spin-orbit splitting of the $4f_{7/2}$- and $4f_{5/2}$-levels agrees well with the experimental values obtained for GdX_3 and LuX_3. The charges on the Ln atoms (calculated according to Mulliken) in LnX_3 decrease on going from F to I. The values for LuX_3 are 2.82 (F), 2.37 (Cl), 2.31 (Br) and 2.01 (I). These changes in the charges occur in concert with the decrease of ionisation energy of the 4*f*-electrons and reflect the increasing population of the 6*s*- and 5*d*-orbitals of the Ln. Thus, the orbital charges for LuX_3, where X = F, Cl, Br, and I, are 0.029, 0.156, 0.168 and 0.245 for 6*s*; 0.070, 0.196, 0.220 and 0.326 for $5d_{3/2}$; and 0.090, 0.284, 0.307 and 0.424 for $5d_{5/2}$-orbitals, respectively.

Nonrelativistic nonempirical *ab initio* calculations on LaH_3, LaF_3 and $LaCl_3$ using the program GAUSSIAN-82[45] were also carried out in order to refine further the geometric structures of LnX_3. It was found that the pyramidal C_{3v}-structure is energetically favorable for LaH_3 and LaF_3 whereas the total energy minimum for $LaCl_3$ corresponds to the planar D_{3h}-structure (Table 1).

Table 1. Equilibrium geometric structure parameters of planar (D_{3h}) and pyramidal (C_{3v}) LaX_3.[45]

Molecule	Symmetry	La–X bond length, Å	X–La–X angle, deg	ΔE^*, cm^{-1}
LaH_3	C_{3v}	2.129	114.7	239
	D_{3h}	2.137	120.0	
LaF_3	C_{3v}	2.080	112.0	921
	D_{3h}	2.089	120.0	
$LaCl_3$	C_{3v}	2.613	112.0	−381
	D_{3h}	2.623	120.0	

*$\Delta E = E(D_{3h}) - E(C_{3v})$ is the difference of total energies.

Table 2. Geometric structure and ionisation potential of $LnCl_3$.[47]

Lanthanide (Ln)	Ln–Cl bond length, Å		Cl–Ln–Cl angle, deg		Ionisation potential, eV	
	theory	experiment	theory	experiment	theory	experiment
Ce	2.570	2.569	115.6	111.6	10.0	9.8
Pr	2.566	2.553	108.5	110.8	11.8	10.9–11.2
Nd	2.563	2.545	112.7	–	13.3	12.0
Pm	2.556	–	112.7	–	14.4	–
Sm	2.544	–	113.0	–	15.3	13.7–17.0
Eu	2.532	–	113.2	–	16.4	–
Gd	2.514	2.489	110.0	113.0	17.7	15.5–16.5
Tb	2.496	2.478	109.8	109.9	13.0	13.0–20.5
Dy	2.479	–	110.1	–	14.3	14.0–20.0
Ho	2.464	2.459	112.0	111.2	15.0	15.5–20.0
Er	2.448	–	110.9	–	15.6	11.5–16.0
Tm	2.430	–	108.5	–	15.9	15.3–21.0
Yb	2.421	–	109.6	–	15.9	15.5–21.0
Lu	2.415	2.417	108.2	111.5	18.6	17.4–18.7

The structures of LnX_3 have also been analysed by the INDO method. The electronic structure of LnF_3 has been studied.[46] It was found that the 4*f*-orbitals of Ln atoms have almost no contribution to bond formation. The covalent bonding between Ln and F is mainly due to the Ln 5*d*-, and to a lesser extent, the 6*s*- and 6*p*-orbitals.

Other results[47] demonstrate that the INDO calculations reproduce well the geometric structure and ionisation potentials of LnX_3 (Table 2). The pyramidal structure is energetically favourable (i.e., corresponds to the total energy minimum). It was demonstrated that the *f*-orbitals contribute little to the bonding. Nevertheless, the calculated Ln–Cl bond lengths agree better with the experimental values if the *f*-orbitals are included in the calculations.

Therefore, results of quantum-chemical calculations using various methods suggests, firstly, that the bonding in LnX_3 is purely ionic even for such molecules as LnF_3. The covalency of the Ln–X bond increases in the order F → I. The principal contribution to the covalency comes from the Ln 5*d*-, and to a lesser extent, the 6*s*- and 6*p*-orbitals.

Secondly, the majority of LnX_3 in the vapour phase have a pyramidal structure. It is possible that this is a consequence of the participation of 5*d*-orbitals in the chemical bonding. However, a clear link between the pyramidal structure of LnX_3 and the degree of covalency of the Ln–X bond in them has not been established. It is noteworthy that spectral and electron-diffraction investigations are also consistent with a pyramidal structure for LnX_3.[48]

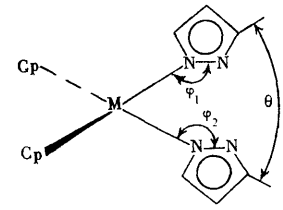
Thirdly, the change of Ln–X bond dissociation energy in LnX_3 correlates with the change of $4f^n6s^2 \rightarrow 4f^{n-1}5d6s^2$ transition energy in the Ln series. This means that the mutual position of the 4*f*- and 5*d*-levels can significantly affect the reactivity of the nascent bond although the 4*f*-orbitals themselves participate little in the bonding.

Fourthly, it is interesting that all calculational methods give results that mainly agree with each other and experiment.

IV. Cyclopentadienyl derivatives of lanthanides and actinides

The most intriguing structural feature of An biscyclopentadienides is that certain $Cp^*_2AnL_2$ [Cp* = pentamethylcyclopentadiene, L = η^2-pyrazolyl (pz), η^2-acyl, etc.] have a 20-electron configuration (considering the total number of valency electrons that is obtained by adding the number of electrons donated by the ligands to the formal number of metals *d*-electrons). However, the majority of transition metal complexes obey the 18-electron rule.[39] Examples of the 20-electron compounds are $Cp^*_2U(\eta^2\text{-pz})_2$,[49] $Cp_2U(acac)_2$,[50] $Cp_2U[O_2C_2CHPMePh_2Fe_2Cp_2(CO)_2]_2$,[51] $Cp^*_2An(\eta^2\text{-COR})_2$ and $Cp^*_2An(\eta^2\text{-CONR}_2)_2$.[52] In particular, the ligands pz^-, COR^- and $CONR_2^-$ can coordinate using one atom (η^1-coordination) or two (η^2-coordination). In the first instance, they act as 2-electron donors; in the second, as 4-electron. The reasons causing such behaviour of the ligands have been analysed in a series of studies.[38,39,53–59] using the quasirelativistic extended Hückel method. In addition, other structural featurs of Th and U biscyclopentadienides were studied.

Three compounds, $Cp_2Mo(pz)_2$, $Cp_2Mo(pz)_2^{2+}$ and $Cp_2U(pz)_2$ (the metal atom in the first molecule has the d^2-electron configuration; in the second d^0), have been examined in order to study the differences in the electronic structure of complexes of *d*-transition metals and Ans.[39] The potential energy surface for these model complexes was calculated as a function of the angles M–N–N and pz–M–pz (angles φ_1, φ_2, and θ).



(I)

The total energy minimum for $Cp_2Mo(pz)_2$ corresponds to the structure with $\eta^1-\eta^1$-coordination of the pyrazoles ($\varphi_1 = \varphi_2 = 128°$, $\theta = 52.5°$). Such structure conforms to the 18-electron rule. The structures with $\eta^1-\eta^2$- and $\eta^2-\eta^2$-coordination of 20- and 22-electron configuration were found to be less stable. On going from the d^2- to the d^0-configuration [i.e., to $Cp_2Mo(pz)_2^{2+}$], the complex with $\eta^1-\eta^2$-coordination becomes more stable. The deficiency of electrons owing to the decreased number of *d*-electrons is reasonably compensated for by η^2-coordination of one of the pz ligands. Thus, the 18-electron rule is again obeyed.

The U complex (in addition to the Th) $Cp_2U(pz)_2$ is ostensibly an analogue of $Cp_2Mo(pz)_2^{2+}$ in the sense that both formally have the d^0-configuration. Nevertheless, the optimal coordination of the pz ligands for them is complete different. Calculations demonstrated that the total energy minimum corresponds to the complex with $\eta^2-\eta^2$-coordination ($\varphi_1 = \varphi_2 = 73°$, $\theta = 113°$). The surprising agreement of these results with the X-ray structure ($\varphi_1 = 75.4°$, $\varphi_2 = 75.1°$ and $\theta = 112.2°$) should be noted.

The geometric structure of these complexes can be understood by analysing the interaction of the frontier orbitals of the fragments. There are three low-energy *d*- and *sp*-hybrid orbitals in the Cp_2Mo^{2+} fragment (Fig. 3*a*). These are the $2a_1$, b_2, and $1a_1$ orbitals. Each pz^- ligand has two orbitals occupied by unshared electron pairs of the N atoms (Fig. 3*b*).

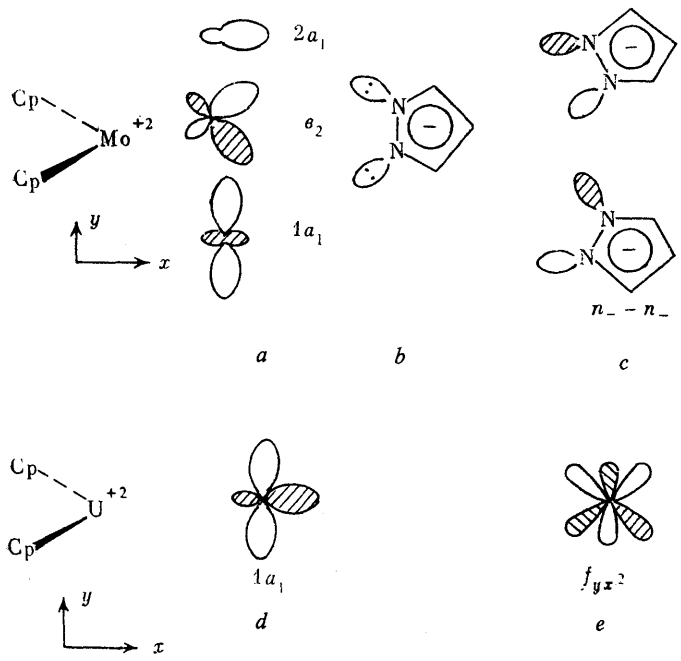


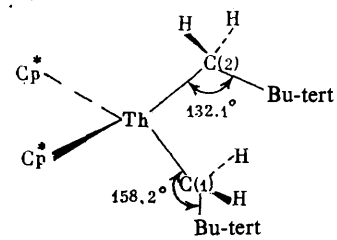
Figure 3. Structure of frontier orbitals of fragments in $cp_2M(pz)_2$ (M = Mo, U). For explanation, see the text.

For the d^2-configuration of Mo, the vacant $2a_1$- and b_2-orbitals of the Cp_2Mo^{2+} fragment interact with one orbital of each pz^- ligand forming the $\eta^1-\eta^1$-coordination. The filled $1a_1$ orbital does not participate in the bonding. For the d^0-configuration, the $1a_1$-orbital can also participate in the bonding. As a result, the structure with $\eta^1-\eta^2$-coordination becomes energetically favorable. The structure with $\eta^2-\eta^2$-coordination always remains energetically unfavorable since the orbitals of the Cp_2Mo^{2+} fragment interact (overlap) poorly with the $(n_- - n_-)$-orbital (Fig. 3*c*), which forms if two pz^- ligands are simulaneously η^2-coordinated.

The Cp_2U^{2+} fragment also has vacant $2a_1$-, b_2- and $1a_1$-orbitals. However, they lie at much higher energy and are more diffuse than the frontier orbitals of Cp_2Mo^{2+}. The shape of the $1a_1$-orbital of Cp_2U^{2+} is different (Fig. 3*d*) from that of Cp_2Mo^{2+}. The components of this orbital for Cp_2U^{2+} along the *x* and *y* axes are about equal whereas the $1a_1$-orbital in Cp_2Mo^{2+} has a shape very close to the pure d_{z^2}-atomic orbital. Another feature is the presence of a vacant f_{yx^2}-orbital for U (Fig. 3*e*) that has the proper symmetry for good overlap with the $(n_- - n_-)$-orbital of two pz^- ligands. Taken together, these features cause the total energy minimum to correspond (i.e., to be energetically favorable) to the $Cp_2U(pz)_2$ complex with $\eta^2-\eta^2$-coordination.

It was also found that these differences in the frontier orbitals affect the structure of $Cp_2M(COR)_2$ and $Cp_2M(CONR_2)_2$, where M = Ti and U.[39,54,56–58] A search for the total energy minimum demonstrated that $\eta^2-\eta^2$-coordination is energetically favorable for M = U whereas $\eta^1-\eta^2$-coordination occurs for M = Ti. In this instance, interaction between donor orbitals of the acyl groups (RC=O) and *f*-orbitals of the An significantly stabilise $\eta^2-\eta^2$-coordination. It is noteworthy that these conditions were also fruitful in understanding the unique reactivity of η^2-coordinated acyl ligands in biscyclopentadienides that is due to the presence of low-lying (in energy) carbene-like acceptor orbitals.[39,57]

The effect of Cp_2An^{2+} (where An = Th) frontier orbitals is evident in the unusual structure of $Cp_2Th(CH_2Bu\text{-}tert)_2$ (II). According to neutron-diffraction data, the angle Th–C(1)–C(alkyl) is 158.2° whereas the other analogous angle Th–C(2)–C is 132.1°.[39,60]



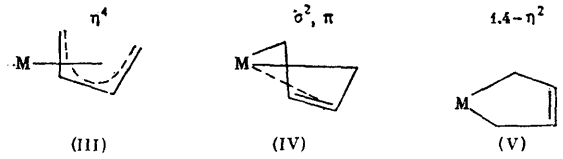
(II)

The quasirelativistic extended Hückel method has been used[39,59] to calculate the potential energy curve for rotation of the ethyl group in Cp_2ThEt_2. The curve was found to be very gently sloped with a shallow minimum at $\alpha = 160°$. An analysis demonstrated that the ethyl group remains strongly bound to the Th in spite of the large deformation (large α). The calculated populations of the overlapping orbitals of the perturbed ethyl group forming the Th–C bond are even slightly greater than those of the unperturbed one. This agrees with the experimentally observed geometric structure of $Cp_2Th(CH_2\text{-}tert)_2$.

Other interesting examples demonstrating the influence of electronic structure on geometric structure are the 1,3-diene complexes $Cp_2M(C_4H_6)$ (where M = Zr and Th). The diene $Cp_2Zr(C_4H_6)$ is known to be able to adopt both the *s-cis*- and *s-trans*-configurations. For example, two geometric isomers of $Cp_2Zr(C_4H_6)$ coexist in solution at 25 °C in the ratio *s-cis*/*s-trans* = 55/45.[61] The *trans* structure becomes more preferred if the terminal

H atoms are replaced by Me- or Ph-groups. The dienes in the isolated An complexes $Cp^*_2Th(C_4H_6)$, $Cp^*_2U(C_4H_6)$, $Cp^*_2Th(CH_2.CMeCMeCH_2)$ and $Cp^*_2Th(CPhHCHCHCPhH)$ have exclusively the *s-cis*-configuration.[38,62,63] Furthermore, whereas low-temperature irradiation of $Cp_2M(s\text{-}cis\text{-}C_4H_6)$ (M = Zr and Hf) leads to formation of the *trans* complexes, such *cis*–*trans* isomerisation is not observed for the analogous Th complex.

The ligand *cis*-butadiene can in principle be bonded to the metal in various ways: by η^4- (III); σ^2,π- (IV); and 1,4-η^2-coordination (V).



(III) (IV) (V)

For example, η^4-coordination is found in $Fe(CO)_3(C_4H_6)$ whereas σ^2,π-coordination (IV) is dominant in complexes of Group IV and V metals. According to X-ray structure analysis, σ^2,π-coordination occurs in Th complexes of butadiene.

Factors determining the preference of butadiene for *s-cis*-coordination in $Cp_2An(C_4H_6)$ (An = U and Th) have been investigated.[38] The total energies of the isomeric forms of the model An complexes $Cp_2An(s\text{-}cis\text{-}C_4H_6)$ (Fig. 4*a*) and $Cp_2An(s\text{-}trans\text{-}C_4H_6)$ (Fig. 4*b*) as functions of the variables L, θ and φ were calculated by the quasirelativistic extended Hückel method.

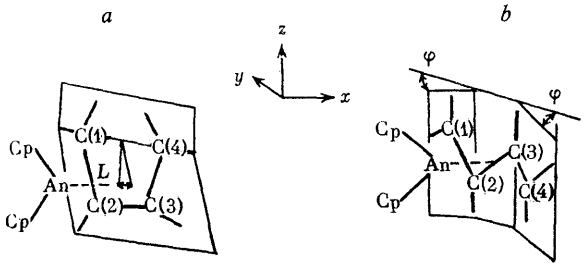


Figure 4. Structure of two isomeric $Cp_2An(C_4H_6)$: *s-cis* (*a*) and *s-trans* (*b*).[38] The variable describes the movement of butadiene as a whole along the *x* axis. The angle θ describes rotation of the molecule around the axis passing through atoms C(1) and C(4). The variable φ (only for the *trans* isomer) characterises the synchronous movement of the two terminal methyl groups toward the metal.

It was found that *s-cis*-coordination is in fact energetically more favourable in the An complex. The corresponding ΔE is 0.74 eV for $Cp_2Th(C_4H_6)$ and 0.42 V for $Cp_2U(C_4H_6)$. The values L and θ for the equilibrium structure are consistent with σ^2,π-coordination of *cis*-butadiene to the An. The experimental data are also consistent with this structure. Calculations for the Zr complexes[38,64] indicate that the total energy for $Cp_2Zr(s\text{-}cis\text{-}C_4H_6)$ is more favourable by 0.07 eV than that for $Cp_2Zr(s\text{-}trans\text{-}C_4H_6)$. As in the examples examined above, such a difference between the An and Zr complexes is due to the difference in the structure of the frontier $1a_1$-orbital of Cp_2M^{2+} (M = Zr, U and Th) in addition to the participation of U and Th 5*f*-orbitals in the bonding.

The butadiene molecule has four π-orbitals (π_1, π_2, π^*_3, π^*_4). It has been demonstrated[38] that the bonding Th–π^*_3MO in $Cp_2Th(s\text{-}cis\text{-}C_4H_6)$ contains contributions from the *d*- (16%) and *f*-orbitals (17%) of Th. These orbitals also contribute to the Th–π_2MO at 13 and 2% respectively. Uranium bonds to butadiene in an analogous manner, but there is a slight difference. In the U complex, the 5*f*-orbitals are more involved in the bonding whereas the contribution from the *d*-orbitals decreases. Thus, the bonding U–π^*_3MO is composed of 6 and 48% of U *d*- and *f*-orbitals, respectively.[38]

An important feature of the electronic structure of $Cp_2Th(s\text{-}cis\text{-}C_4H_6)$ is the greater overlap between Th and the terminal C(1) compared with that of the Th–C(2) bond (Table 3). This population difference (ΔP) can serve as an index indicating the preference for one mode of diene coordination or another. The data of Table 3 clearly show that the diene has σ^2,π-coordination in $Cp_2Th(s\text{-}cis\text{-}C_4H_6)$. The value ΔP decreases little on going from Zr to Th. However, it remains larger in both cases than in $Fe(CO)_3(C_4H_6)$. This agrees with experimental data indicating that η^4-coordination occurs in $Fe(CO)_3(C_4H_6)$.

For *s-trans*-coordination, the interaction Th–π^*_3 is weaker and the energy level of this orbital is 0.23 eV higher than for $Cp_2Th(s\text{-}cis\text{-}C_4H_6)$. This is the reason for the relative instability of $Cp_2Th(s\text{-}trans\text{-}C_4H_6)$.

In contrast with the An complexes, the interactions Zr–π^*_3 in $Cp_2Zr(s\text{-}cis\text{-}C_4H_6)$ and $Cp_2Zr(s\text{-}trans\text{-}C_4H_6)$ are approximately equal. This determines the approximate equal total energies of these complexes.

The electronic structure of U biscyclopentadienides with other ligands is also interesting. Calculations for Cp_2UMe_2 and Cp_2UCl_2 by the $X\alpha$-SW method with relatistic corrections[65] demonstrated that the U 5*f*- and 6*d*-orbitals contribute noticeably to the U–Cp bonds. It was found that the highest occupied molecular orbital in both complexes has almost pure 5*f*-character. The ionisation potentials calculated using the transition-state formalism agree well with expermental data even when spin–orbit coupling is ignored.

Photoelectron spectra of gaseous complexes Cp_2UL_2 (L = BH_4, NEt_2, OCBu-tert, S_2CNEt_2) have been investigated.[66] It was found that the first ionisation potential always correspond to removal of *f*-electrons. For L = NEt_2, the next occupied (after the 5*f*-orbitals) MO is almost purely the atomic 2*p*-orbital of N (with an unshared electron pair). For the other compounds, the next occupied MO is the π-orbital of the Cp ligands. Such a result is consistent with the high reactivity of amidocomplexes relative, for example, to molecules containing polar double bonds and with the smaller lability of the U–Cp bonds in this complex compared with other Cp_2UL_2 complexes.

Data also exist for the electronic structure of Ln biscyclopentadienides. The electronic structure and the nature of the chemical bonding in $Cp_2LuCl.OC_4H_8$ have been studied by the INDO method.[67] The bonds in this complex were found to be covalent. Thus, the bond order (according to Mulliken) Lu–Cl, Lu–O and Lu–C are 0.656, 0.314 and 0.254, respectively (Table 4). The charge on Lu is +0.542. This is far from the +3 predicted by the ionic model. The overlap between the 4*f*- and other orbitals is zero. This means that the 4*f*-orbitals in the complex remain essentially atomic. The overlap data for various orbitals (Table 4) confirm that the 5*d*-orbitals of Lu play a dominant role in the bonding.

Table 3. Electronic population of bonds (P) and atomic charges (Q) in $Cp_2M(s\text{-}cis\text{-}C_4H_6)$, $Cp_2M(s\text{-}trans\text{-}C_4H_6)$ (M = Zr, Th, U) and $Fe(CO)_3(C_4H_6)$.[38]

Compound	P(M—C(1))	P(M—C(2))	ΔP*	Q(C(1))	Q(C(2))
			s-cis		
$Cp_2Zr(C_4H_6)$	0.338	0.060	0.278	−0.100	0.120
$Cp_2Th(C_4H_6)$	0.318	0.049	0.269	−0.398	−0.087
$Cp_2U(C_4H_6)$	0.262	0.029	0.239	−0.282	−0.039
$Fe(CO)_3(C_4H_6)$	0.202	0.184	0.018	−0.220	0.018
			s-trans		
$Cp_2Zr(C_4H_6)$	0.204	0.164	0.040	−0.029	0.072
$Cp_2Th(C_4H_6)$	0.184	0.095	0.089	−0.443	−0.080
$Cp_2U(C_4H_6)$	0.128	0.078	0.050	−0.293	0.072

* ΔP=P(M—C(1)) − P(M—C(2)).

Table 4. Electronic population of orbitals and bonds in $Cp_2LuCl.OC_4H_8$.[67]

Ligand	Orbital	Lu electronic population 6s	6p	5d	4f	Lu–L Bond order
				Orbital population		
–	–	0.377	0.629	1.452	14.000	
				Overlap population		
Cl	3s	0.099	0.207	0.058	0.000	0.656 (Lu–Cl)
	3p	0.036	0.059	0.098	0.000	
O	2s	0.048	0.066	0.064	0.000	0.314 (Lu–O)
	2p	0.011	0.012	0.113	0.000	
C	2s	0.037	0.079	0.020	0.000	0.254 (Lu–C)
	2p	0.018	0.021	0.079	0.000	

The nature of the bonding in Cp_2Ln (Ln = Sm, Eu, Yb) has been studied by comparing photoelectron spectra and quasirelativistic calculations by the $X\alpha$-SW method.[68] An analysis of the MOs revealed that the metal–ring bond is slightly covalent. The small ligand splitting of the 4f-orbitals and their strict localisation are evidence of the ionic interaction. The MOs in Cp_2Eu are ordered the same as in Cp_2Yb. This means that the 4f-levels of divalent Lns do not change their position relative to the energy levels of ligand valence orbitals. This is in contrast with results for LnX_3, where the position of the 4f-orbital energy levels (relative to those of the ligand valence orbitals) depends significantly on the nature of the ligand. The calculated ionisation potentials agree well with the experimental values.

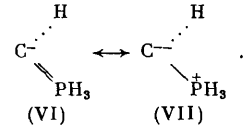
The nature of the bonding of two $LnCp_2$ fragments through H bridges has been studied by the quasirelativistic extended Hückel method.[69] The Ln d-orbitals (in the electronic configuration d^0f^n) apparently stabilise the bridging H atoms. Bonding through symmetric H bridges is energetically more favorable compared with asymmetric bridges.

Besides An biscyclopentadienides, complexes with three cyclopentadienide ligands Cp_3AnL frequently form (in contrast with d-transition metals). The majority of known complexes contain a monodentate anionic ligand (L) such as halide or alkyl and have a trigonal-pyramidal or pseudotetragonal structure. An interesting feature of the Cp_3U fragments is the fact that they can be bonded to η^2-acyl, η^2-pyrazolyl and even η^5-cyclopentadienide ligands in spite of seemingly large steric hindrances to coordination of the last.

The electronic structure of tris(η^5-cyclopentadienyl)An complexes has been studied by the quasirelativistic extended Hückel method.[70,71] Two ligand orbitals in the Cp_3U fragment (C_{3v} symmetry) have a_2 symmetry and can interact only with U $f_{y(3x^2-y^2)}$-orbitals. This means that the f-orbitals can play a significant role in stabilising the An–Cp bond in Cp_3An complexes. Nevertheless, the calculations suggest that the contribution of the $f_{y(3x^2-y^2)}$-orbital to the bonding MO a_2 is amll and reaches only 5–8%. The remaining f-orbitals are essentially nonbonding. The U 6d-, 7s- and 7p-orbitals also participate very little in the bonding. As a result, the population (according to Mulliken) of the U–C(Cp) bonds is very small and reaches only 0.05. Taking into account contributions from H atoms of the C_5H_5 groups, the total overlap U–Cp decreases to 0.01. This contrasts with the high population of M–Cp bonds in transition metal complexes. For example, this value for $CpFeMe(CO)_2$ is 0.57. The small population of the U–Cp bonds indicates that this bond is very weakly covalent and much weaker than the Fe–Cp bond.

Examination of the model complex Cp_3UMe enabled the nature of the σ-bond in An complexes to be analysed. The methyl σ-orbital overlaps mainly with the $6a_1$-orbital (consisting primarily of the U $6d_{z^2}$-orbital) of the CpU fragment. Two other orbitals of the fragment, $3a_1$ and $4a_1$, make a smaller contribution to the bonding interaction. The last two orbitals are primarily f_{z^3} in character. A strong covalent bond between U and Me forms owing to such interactions. The covalent nature of the bonding is consistent with the large overlap of 0.40 in the U–C(Me) bond. It is noteworthy that the corresponding value is 0.44 for the Fe–C(Me) bond in $CpFe(Me)(CO)_2$. The U 7s- (2%), 7p_z- (6%), 6d_{z^2}- (4%) and 5f_{z^3}-orbitals (4%) participate in forming the strong U–C(Me) σ-bond. The contribution of each orbital is small but the sum is 16%.

The nature of the bonding in $Cp_3UCHPPhMe_2$ is of great interest. The anionic ylide ligand can be assigned two resonance forms

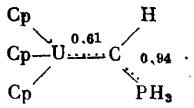


(VI) (VII)

Structure (VII) is formally a dianionic ligand, analogous to a carbene. Hence, U–C double bond can form on coordination of the ylide to U. Quantum-chemical calculations (quasirelativistic extended Hückel method) of the simplified model Cp_3UCHPH_3 demonstrated that the ligand $CHPH_3^-$ has two occupied frontier orbitals. These are a π-orbital with energy −11.3 eV and a σ-orbital with energy −11.9 eV.



Interaction of the σ-orbital with vacant $6a_1$-, $4a_1$-, and $3a_1$-orbitals of Cp_3U^+ forms σ-bonding MO. Furthermore, interaction of the π-orbital with the 8*e*-, 5*e*- and 4*e*-orbitals of Cp_3U^+ forms a π-bonding MO. It should be noted that the 5*e*- and 4*e*-orbitals have primarily f_{yz^2} character. The double bond formed is not localised but has a π-delocalised character U ⋯ C ⋯ P:



Nevertheless, the population of the U–C bond is 0.61 (the contribution from the π-component is 0.19). This surpasses the population in other complexes. In general, the calculations demonstrated that the population of the U–C bond in various complexes decreases in the order $Cp_3UCHPH_3 \simeq Cp_3U(C{\equiv}CH) > Cp_3UCH_3 > CpU[CH_2CH_2PH_2]_3$. This correlates with the increasing U–C bond length in this order.

Additional and more accurate data on the electronic structure of tris(cyclopentadienyl)An complexes have been obtained using quasirelativistic *X*α-SW calculations.[72–76] The complexes Cp_3U and Cp_3Th were examined. It was confirmed that the U *f*-orbitals can play an important role in the bonding. It was demonstrated that the U–Cp bond forms through donation of electron density from the π_2-orbital of the Cp ligand into the U 6*d*- and $5f_{y(3x^2-y^2)}$-orbitals. It was found that the highest occupied orbital in Cp_3Th has primarily $6d_{z^2}$ character (89%) and is located 1 eV below the 5*f*-orbitals. The energy level of the 5*f*-orbitals decreases along the series Th → Pu. At the end of the series, it is below the level of the 6*d*-orbitals.

Analysis of the electronic structure of Cp_3UL (where L = H, CO, NO, OH) demonstrated that mainly the U $6d_{z^2}$-orbital participates in bonding to the σ-ligands. The 5*f*-orbitals are not additionally split (compared with Cp_3U). Thus, the bonding orbital for Cp_3UH is 56% hydride in character with the principal contribution coming from the U $6d_{z^2}$-orbital (24%) and small contributions from the $5f_{z^3}$- (1%), 7*s*- (3%) and $7p_z$-orbitals (3%). It must be noted that the relative contribution of the 5*f*-orbitals is greater than the shorter the U–H bond. However, the role of the 6*d*-orbitals in chemical bond formation remains dominant.[74] The contribution of the σ-component remains substantial for Cp_3U complexes with both π-acids (CO, NO) and π-bases (OH). Besides the σ-bonding, π-backbonding occurs in which electrons are donated from the U *f*π-levels into the CO and NO π*-orbitals. Thus, interaction of the CO 2*p*-orbitals with U 5*f*-orbitals in Cp_3UCO forms a bonding orbital consisting of 14% CO orbitals and 84% U orbitals. Such an interaction stabilises the U 5*f*-levels. As with carbonyl complexes of *d*-transition metals, backbonding into a CO antibonding orbital decreases the vibrational frequency of the CO double bond compared with ν_{CO} of the free molecule.

The electronic structure of Cp_3UX (X = F, Cl, Br) has been investigated theoretically (nonrelatistivic *X*α-DV calculations) and experimentally (photoelectron spectra using He I and He II excitation sources).[77] The calculated ionisation potentials for the high (in energy) MOs of Cp_3UCl agree with the experimental values. The conclusion was made that the nonrelativistic calculation can give a good analysis of the photoelectron spectra and an adequate description of the nature of the bonding in An complexes. Nevertheless, the nonrelativistic approach underestimates the contribution of the 6*d*-orbitals (relative to the 5*f*) in forming the metal–ligand bonds. Therefore, a relativistic calculation is required for more accurate information.

Therefore, the following conclusions can be made in finishing this section. Firstly, many of the structural features of An (Th and U) cyclopentadienides, for example, the stability of complexes with a 20-electron configuration, the highly favourable energy of $Cp_2An(s\text{-}cis\text{-}C_4H_6)$ compared with its *trans* isomer, and the unusual geometry of the $Cp_2Th(CH_2Bu\text{-}tert)_2$ structure, are due to participation of both An 6*d*- and 5*f*-orbitals in the chemical bonding.

Secondly, the Ln 4*f*-orbitals in the cyclopentadienides remain essentially atomic. The 5*d*-orbitals play the dominant role in bond formation.

Thirdly, the metal–ligand bonds in Ln and especially in An complexes are not purely ionic but have a significant covalent character.

Application of the quasirelativistic extended Hückel method enables many features of the electronic and geometric structure of cyclopentadienides to be understood qualitatively (and sometimes quantitatively). However, more complicated calculations must be used to obtain more accurate and reliable information on the details of the electronic structure.

Table 5. Electronic population of orbitals and charges on atoms in $M(BH_4)_4$ (M = Zr, U).[85]

A. $Zr(BH_4)_4$

Atom	Charge	Orbital	Population
Zr	+2.02	4*d*	1.95
		4*f*	0.00
		5*s*	0.04
B	−0.50	2*s*	0.89
		2*p*	2.61
H_t	+0.08	1*s*	0.92
H_b	−0.03	1*s*	1.03

B. $U(BH_4)_4$

Atom	Charge	Orbital	Population
Nonrelativistic approximation			
U	+1.93	6*d*	1.11
		5*f*	3.27
		7*s*	−0.11
		7*p*	−0.18
B	−0.42	2*s*	0.88
		2*p*	2.55
H_t	+0.05	1*s*	0.95
H_b	−0.04	1*s*	1.04
Relativistic approximation*			
U	+2.25	6*d*	1.30 (0.56 for $j=3/2$ and 0.74 for $j=5/2$)
		5*f*	2.43 (1.83 for $j=5/2$ and 0.60 for $j=7/2$)
		7*s*	0.11
		7*p*	−0.12 (−0.01 for $j=1/2$ and 0.11 for $j=3/2$)
B	−0.58	2*s*	0.98
		2*p*	2.60 (0.88 for $j=1/2$ and 1.72 for $j=3/2$)
H_t	+0.09	1*s*	0.91
H_b	−0.02	1*s*	1.02

* $j=l+1/2$.

V. Other *f*-element compounds

The electronic structure of uranocene $U(C_8H_8)_2$, which has been investigated in sufficient detail, should be discussed. Calculations have been performed for this molecule using the relatistically parametrised Hückel method,[32] $X\alpha$ (nonrelativistic and relativistic) method.[78–81] and the nonempirical SCF MO method including spin–orbit coupling and a relativistic core potential. In general, results of all these studies agree. It has been found[78–80] that both 5*f*- and 6*d*-orbitals of the metal participate in bonding to the ring. Chang and Pitzer[82] emphasise that the 6*d*-orbitals play the principal role in the covalent bonding; the 5*f*-orbitals, a secondary role. It was also demonstrated that the electronic ground state of uranocene is E_{3g} and the characteristic green colour of uranocene is due to transitions to E_{2u} and E_{3u} excited states. In agreement with the compositions of the MOs, these transitions are qualitatively described as $5f \rightarrow 6d$-transitions.

Of other metallocenes, $Th(C_8H_8)_2$ and $Ce(C_8H_8)_2$ have been investigated.[78,79] The bonding in cerocene was found to be less covalent (more ionic) than in uranocene and thorocene. A study of the photoelectron spectrum also confirms the high covalency of thorocene.[83]

Relativistic and nonrelativistic $X\alpha$-DV methods have been used to study the electronic structure of the borohydrides $M(BH_4)_4$ (M = Zr, U). The results obtained agree with calculations by the $X\alpha$-method.[85] The calculated and experimental ionisation potentials were in good agreement. The relativistic solution better describes the metal–ligand bonding in the U complex. It was demonstrated that the contribution from U 5*f*-orbitals is overestimated and that of the 6*d*-orbitals underestimated in the nonrelativistic approach (Table 5).

Structures of the two η^6-arene complexes $Sm(C_6Me_6)(AlCl_4)_3$ and $U(C_6Me_6)(AlCl_4)_3$ have been compared.[86] The differences in metal–ligand bond lengths was found to be determined by the difference in the U and Sm ionic radii. According to the authors, this means that the acceptor orbitals in the An and Ln complexes are comparable and, therefore, the *f*-orbitals are not involved in bonding to the arene.

Calculations have been performed using the $X\alpha$-SW method for $Eu(C_2H_4)_2$ assuming C_{2v} symmetry.[87] The calculations demonstrated that the complex is weakly bonding owing to donation of charge density from the doubly occupied $f_{z(x^2-y^2)}$-orbital of Eu into the π^*-orbitals of ethylene. However, little density is directly donated from filled ethylene orbitals onto the metal.

A rather large number of molecules and clusters containing 4*f*- and 5*f*-elements has been calculated by the relativistically parametrised extended Hückel method. Reviews of the results have been published.[7,32–35,88] It was demonstrated that this method qualitatively correctly estimates the spin–orbit splitting energies of the valence levels and the role of relativistic effects in the chemical bonding. In particular, it is emphasised[88] that the early 5*f*-elements can be treated as 6*p*-elements in the sense that the 6*p* atomic orbitals of these elements are mixed with ligand orbitals.[7,89] This mixing is especially large in uranyl and other actinyls. Direct experimental proof of the mixing of U 6*p*-orbitals with O 2*p*-orbitals in uranyl and other compounds has been given.[90,91] The contribution of 6*p*-orbitals to nuclear quadrupole coupling has been interpreted on the basis of these results.[35,88]

The electronic structures (quasirelativistic extended Hückel method) of $C_4H_7NdCl_2$. $C_4H_7NdCl_2.3THF$ (THF = tetrahydrofuran) and $C_4H_7Nd(AlCl_4)_2$ (Fig. 5) have been analysed.[92–94] These compounds model the active polymerisation centres of butadiene in the Nd–Al catalytic system. Data for the electronic structure of the *anti*- and *syn*-forms of $C_4H_7NdCl_2$ are presented in Table 6. It was found that the contribution of Nd 4*f*-orbitals to the covalent bonding is insignificant. The partial covalency of the Nd–C bond is due mainly to participation of Nd 5*d*-orbitals in the bonding.

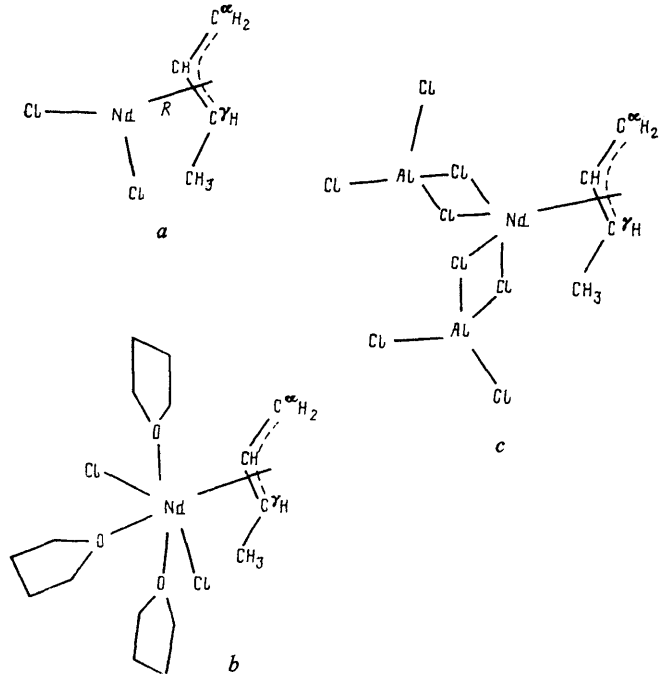


Figure 5. Diagram of active center models, *syn*-$C_4H_7NdCl_2$ (*a*) (*R* is the distance from Nd to the plane of the crotyl group), *syn*-$C_4H_7NdCl_2.3THF$ (*b*), *syn*-$C_4H_7Nd(AlCl_4)_2$ (*c*).

Table 6. Electronic structure of $C_4H_7NdCl_2$ isomers.[93]

$H_{ii}(4f)$, eV	$H_{ii}(5d)$, eV	Isomeric form	ΔE *1	q_i *2				
				$q_{C^{\alpha}}$	$q_{C^{\gamma}}$	q_{Nd}	P (Nd–C^{α}) *3	P (Nd–C^{γ}) *3
−9.82	−8.82	*anti*	10.6	−0.48	−0.33	1.95	0.07(5)	0.08(3)
		syn		−0.45	−0.34	1.93	0.06(5)	0.09(3)
−11.0	−10.8	*anti*	15.5	−0.25	−0.10	0.93	0.12(5)	0.14(4)
		syn		−0.23	−0.11	0.91	0.12(3)	0.16(3)

*$\Delta E = E_{syn} - E_{anti}$, where $E_{syn}(E_{anti})$ is the total energy (kJ mol^{-1}) of the *syn* (*anti*) form; *^2q_i is the excess of electronic charge on the *i*-th atom; *^3P(Nd–C_i) is the electronic population of the Nd–C_i bond. Contributions (%) of partial populations Nd(4*f*)–C_i(2*p*) to the corresponding total populations are given in parentheses.

It was demonstrated that the *syn*-form of the active centres is energetically more favorable than the *anti*-form with respect to the total energy. It was proposed on the basis of the results that kinetic and steric control of the microstructure of polybutadiene is possible in Ln catalytic systems. This validity of this conclusion has been confirmed experimentally.[93,95]

Therefore, existing quantum-chemical methods enable useful information about the electronic and geometric structure of large chemical containing *f*-elements to be obtained. Metal–halide and M–C bonds in these compounds are not purely ionic. The degree of covalency increases on going from Ln to An compounds. The *d*-orbitals of the Lns and Ans make the principal contribution to the chemical bonding. For the latter, the 5*f*-orbitals noticeably participate in forming chemical bonds. This is responsible for many of the strucural features of An compounds. The Ln 4*f*-orbitals interact very weakly with ligand valence orbitals. Their direct contribution to forming chemical bonds is insignificant.

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Translated from *Uspekhi Khimii* **60** 2089–2112 (1991) U.D.C. 541.127+833.220

The verdazyl method for the study of the kinetics and mechanisms of the unimolecular heterolysis reactions of organic compounds

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ABSTRACT. **Data concerning the use of triphenylverdazyl radicals as internal indicators to study of the kinetics and mechanisms of the heterolysis of organic substrates in various protic and aprotic solvents are surveyed. The application of the verdazyl method made it possible to put forward a new mechanism of the heterolysis of a covalent bond—the reaction proceeds via the consecutive formation of contact, spatially separated, and solvent-separated ion pairs.**

The bibliography includes 135 references.

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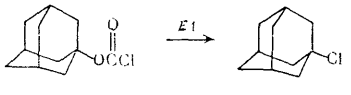
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I. Introduction

The unimolecular heterolysis reactions of organic compounds (S_N1, $E1$, $F1$, solvolysis) are widely used in laboratory and industrial synthesis.[1–3] Depending on the conditions in the heterolysis of, for example, 1-halo-1-phenylethane, one of three reactions can take place:[4,5]

$$\mathrm{PhCHXMe}\left\{\begin{array}{ll}\xrightarrow[S_N1]{Y^-} & \mathrm{PhCHYMe}+X^-,\\ \xrightarrow[E1]{} & \mathrm{PhCH{=}CH_2}+\mathrm{HX},\\ \xrightarrow[\text{solvolysis}]{ROH} & \mathrm{PhCH(OR)CH_3}+\mathrm{HX}.\end{array}\right. \qquad (1)$$

The decomposition of 1-adamantyl chloroformate may serve as an example of the fragmentation reaction:[6]



(2)

The study of the mechanism of unimolecular heterolysis reactions is in the vanguard of the mechanistic research in organic chemistry.[1,2,7,8] The mechanism of these reactions is interpreted on the basis of Winstein's ionisation-dissociation scheme (see, for example, Refs. 7–10):

$$\mathrm{RX} \rightleftharpoons \underset{\text{CIP}}{\mathrm{R^+X^-}} \rightleftharpoons \underset{\text{SSIP}}{\mathrm{R^+\,|\,Solv\,|\,X^-}} \rightleftharpoons \mathrm{R^+}+\mathrm{X^-}. \qquad (3)$$

It has been suggested that the reaction begins with the formation of a contact ion pair (CIP), which is then slowly converted into a solvent-separated ion pair (SSIP) and the latter rapidly decomposes, affording the free carbonium ion. The reaction products are formed from the last two intermediates. They in fact determine the type of reaction occurring. The rate of reaction is described by a first-order kinetic equation:

$$v=k[\mathrm{RX}]. \qquad (4)$$

The rate increases sharply with increase in the polarity of the medium.[10–13]

The rate of the $E1$ and solvolysis reactions can be conveniently followed from the acid evolved.[14,15] The reaction is usually performed in the presence of an amine, which binds the acid and thus suppresses the reverse reaction and eliminates the possible catalytic effects of the acid. However, in an aprotic medium, the salt formed can lead to appreciable errors in the determination of the reaction rate.[16,17] The rate of the solvolysis reaction is relatively insensitive to the action of salts.[7] In a number of instances, this is true also of the $E1$ reactions.[7,11] The above method for the study of the kinetics of such reactions therefore generally yields satisfactory results.

The rates of S_N1 reactions in an aprotic medium depend greatly on the added salts,[18] which makes it difficult to obtain reliable results. The kinetics of these reactions are usually investigated by measuring the rate of the radioactive exchange of the nucleofugal species in the substrate[19] or by carrying out the reaction in the presence of strong nucleophiles (PhONa [20]). However, these methods are complex to carry out and are insufficiently correct owing to the influence of the salts present in the solution. The latter complicates the interpretation of the experiment and sometimes leads to gross errors.[20,21]

Before the appearance of the verdazyl method for the study of the unimolecular heterolysis reactions,[18,22] there was no effective method available in the literature for the study of the kinetics of S_N1 reactions in an aprotic medium. In certain cases (in polar aprotic solvents), the problem was solved by determining the rate of reaction in the presence of small amounts of water,[23,24] i.e. in a sense the rate of solvolysis was determined. However, it is noteworthy that, in order to obtain reliable results, it is necessary in this instance to carry out special investigations of the influence of water on the rate of reaction.

The interpretation of the mechanism of the *Fl* reactions occurring via an ionisation-fragmentation pathway frequently gives rise to difficulties[25,26] owing to the presence in this instance of not only consecutive but also of parallel stages.[27]

The study of the kinetics of the heterolysis of organic substrates in aprotic solvents is significantly hindered also by the fact that such reactions are very slow. Thus the half-reaction time for t-BuCl in hexane at 25 °C is $\sim 1 \times 10^9$ years[17] and the rate of heterolysis of certain skeletal compounds is even lower, by several orders of magnitude.[7,10] The accumulation of kinetic data has therefore been slow and difficult. The detailed specification of the mechanism stopped at the level of Winstein's scheme, which was proposed as early as the middle 1950s.[9,28] Attention was concentrated on the study of the solvolysis reactions, which, however, yield inadequate information since the kinetic relations for them are indefinite, the solvation effects are uniform, and the salt effects are indistinct.

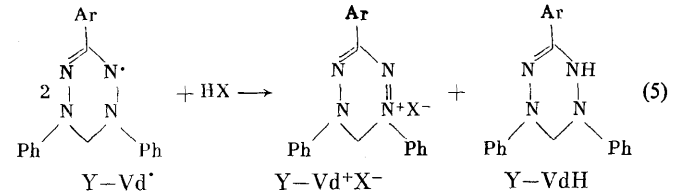
Considerable progress in the study of the kinetics and mechanism of the unimolecular heterolysis reactions was achieved by virtue of the development and wide scale application of the verdazyl method,[18,21,22,27,29–80] which uses triphenylverdazyl radicals as internal indicators. The indicator methods had been used earlier only for the study of solvolysis reactions,[81,82] but since they had no significant advantages they were not applied on a wide scale.

II. The verdazyl method for the study of the kinetics of the heterolysis of organic compounds

The application of triphenylverdazyl radicals as internal indicators in the determination of the rate of heterolysis of organic compounds is based on the fact that they react rapidly and quantitatively with the reaction products (acids[83]) or the cationoid intermediate derived from the substrate, formed after the rate-limiting stage, which makes it possible to follow the rate of reaction from the consumption of triphenylverdazyl (Y—Vd$^{\cdot}$) and/or from the formation of the verdazyl salt (Y—Vd$^+$X$^-$).

Triphenylverdazyl radicals are some of the most stable free radicals.[84] They can be readily synthesised and purified. They can be stored in air in the crystalline state for more than 10 years without appreciable changes. A solution of Y—Vd$^{\cdot}$ in non-polar solvents is stable for several days and in polar solvents for ~ 10 h.

Triphenylverdazyls react rapidly and quantitatively with hydrogen halides and the halogens:[84,85]



(5)

$$2Y\text{—}Vd^{\cdot} + X_2 \rightarrow 2Y\text{—}Vd^+X^- . \qquad (6)$$

The reaction can be readily followed spectrophotometrically from the consumption of Y—Vd$^{\cdot}$ and the formation of Y—Vd$^+$X$^-$. By virtue of the different stoichiometries of reactions (5) and (6), it is possible to determine quantitatively the content of the halogen and the hydrogen halide when they are present jointly in the solution.

The reaction of Y—Vd$^{\cdot}$ with carboxylic acids is reversible.[86–88] In an aprotic medium, the rate of reaction is described by a third-order kinetic equation:[87]

$$v = k[Y\text{—}Vd^{\cdot}]^2[RCO_2H].$$

In aprotic solvents of low polarity, I_2 reacts with Y—Vd$^{\cdot}$ also reversibly,[89] the rate of reaction being described by a fourth-order kinetic equation:[90]

$$v = k[Y\text{—}Vd^{\cdot}]^2[I_2]^2.$$

It is necessary to take this into account in the study of the heterolysis of organoiodine compounds in a non-polar medium[89] and in the study of the influence of salts of hydriodic acid on the rate of heterolysis of organic substates.[40,49] In the reaction of Y—Vd$^{\cdot}$ with Cl_2, Br_2, hydrogen halides, and other strong acids, the reaction equilibrium is almost wholly displaced towards the products.[46]

Triphenylverdazyls are powerful electron donors,[91,92] reacting readily with Lewis acids,[93–95] tetranitromethane,[98] tetracyanoethylene,[97] iminoxyls and phenoxyls,[98] the tropylium cation,[99] and the ion pair $PhN_2^+BF_4^-$.[100] These reactions proceed via electron transfer from the radical to the electrophile and the rate of reaction is described by a second-order kinetic equation, i.e.

$$v = k[\text{electrophile}][Y\text{—}Vd],$$

and increases with the enhancement of the electron-donating properties of the substituent in the radical. Clearly the Y—Vd$^{\cdot}$ radical should also react readily with the intermediate cationoids formed in the heterolysis of an organic substrate, for example with a solvent-separated ion pair.

In the heterolysis of organic substrates in the presence of Y—Vd$^{\cdot}$, identical stoichiometric ratios are usually observed regardless of the type of reaction: 2 moles of the verdazyl radical are consumed per mole of the substrate and one mole of the verdazyl salt is formed:

$$RX + 2Y\text{—}Vd^{\cdot} \begin{cases} \xrightarrow{\text{solvolysis}} Y\text{—}Vd^+X^- + Y\text{—}VdH + ROS, \\ \xrightarrow{S_N1} Y\text{—}Vd^+X^- + Y\text{—}VdR, \\ \xrightarrow{E1} Y\text{—}Vd^+X^- + Y\text{—}VdH + \text{olefin}. \end{cases} \qquad (7)$$

Verdazyls were used for the first time to study the kinetics of the dehydrohalogenation of t-butyl halides.[22,29–36,38] Apart from 1,3,5-triphenylverdazyl (Vd$^{\cdot}$), the following radicals were also used: 3-(4-methoxyphenyl)-1,5-diphenylverdazyl (MeOVd$^{\cdot}$), 3-(4-methylphenyl-1,5-diphenylverdazyl (MeVd$^{\cdot}$), 3,5-di(4-methoxyphenyl)-1-phenylverdazyl [$(MeO)_2$Vd$^{\cdot}$], 3-(4-chlorophenyl)-1,5-diphenylverdazyl (ClVd$^{\cdot}$), and 3-(4-nitrophenyl)-1,5-diphenylverdazyl (NO_2Vd$^{\cdot}$). It was postulated that Y—Vd$^{\cdot}$ reacts with the hydrogen halide split off.[22,30–32] Leucoverdazyl, which is comparatively readily oxidised by atmospheric oxygen to verdazyl, is formed in the course of E1 and solvolysis reactions. Under the conditions of the kinetic experiment, leucoverdazyl is preserved without change over a period of ~ 8 h.

In the kinetic experiment, a solution of the verdazyl at a concentration suitable for spectrophotometric determinations ($\sim 10^{-4}$ M) is mixed with a solution of the substrate at a concentration ensuring an acceptable reaction rate (from 10^{-5} to 1 M depending on the reactivity of the substrate). The solution obtained

is placed in the thermostatted cell of the spectrophotometer and the absorption strength is measured at 720 and 540 nm. Although the values of λ_{max} for Y—Vd$^{\cdot}$ and Y—Vd^{+}X^{-} and their extinction coefficients depend comparatively little on the nature of the substituent and the solvent,[53,56,64,66,76] the values of λ_{max} corresponding to the given verdazyl must be used in order to obtain valid data.

In the study of the kinetics of rapid reactions, the substrate concentration during the experiment may be comparable to the concentration of Y—Vd$^{\cdot}$ [29] or may slightly exceed it.[66] In this case, the "Y—Vd$^{\cdot}$ (Y—Vd^{+}X^{-}) concentration—time" relation is curved and the rate of reaction in each individual experiment is calculated from the kinetic equation (4). In such experiments, the degree of conversion of the substrate can reach 100%. Cases of this kind are observed rarely because the heterolysis of organic compounds is comparatively slow. The concentration of Y—Vd$^{\cdot}$ is usually appreciably lower than the substrate concentration (by a factor of $5-10^5$), which makes it possible to carry out reliable determinations of the rates of reaction for low and very low degrees of conversion of the substrate (0.001—5%) and thus in the course of several hours one can determine the rate of a reaction with a half period reaching 1000 years. In these experiments, the substrate concentration hardly changes during the kinetic experiment, so that in each individual experiment the rate of reaction is described by the pseudo-zero-order kinetic equation $v = k_0$, the Y—Vd$^{\cdot}$ and Y—Vd^{+}X^{-} concentrations varying linearly as a function of time. The first-order rate constant is calculated from the equation $k = k_0[RX]$. Thus the verdazyl method is in this case based on the determination of the initial rates of reaction.

The determination of the rate of heterolysis from the consumption of Y—Vd$^{\cdot}$ and the formation of Y—Vd^{+}X^{-} leads to satisfactorily concordant results, the rate of reaction being independent of the concentration of Y—Vd$^{\cdot}$ and of the nature of the substituent in the latter. Consequently the verdazyl enters into the reaction after the rate-limiting stage.

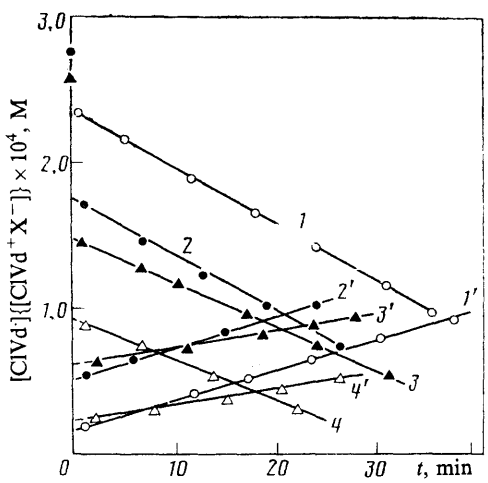


Figure 1. Kinetics of the heterolysis of t-BuBr in propylene carbonate in the presence of ClVd$^{\cdot}$: *1*, *1'*, *2*, and *2'*, [t-BuBr] = 0.0105 M, [ClVd$^{\cdot}$] = 2.75 × 10^{-4} M, 25 °C, k = 3.20 (3.16) × 10^{-6} s^{-1}; *3* and *3'*, [t-BuBr] = 0.025 M, [ClVd$^{\cdot}$] = 2.60 × 10^{-4} M, 32.5 °C, k = 8.48 × 10^{-6} s^{-1}; *4* and *4'*, [t-BuBr] = 0.025 M, [ClVd$^{\cdot}$] = 1.3 × 10^{-4} M, 32.5 °C, k = 8.67 × 10^{-6} s^{-1}.

Fig. 1 presents a series of characteristic curves for the heterolysis of t-BuBr in propylene carbonate in the presence of ClVd$^{\cdot}$ under conditions such that [t-BuBr] ≫ [ClVd$^{\cdot}$].[29] The ClVd$^{\cdot}$ (straight lines *1—4*) and ClVd^{+}Br^{-} (straight lines *1'—4'*) concentrations vary linearly with time beause the t-BuBr concentration is constant during the experiment. According to the stoichiometric Eqn. (7), the rate of reaction in each individual experiment is described by a pseudo-zero-order kinetic equation:

$$-d[Y-Vd^{\cdot}]/2dt = d[Y-Vd^{+}X^{-}]/dt = k_0. \quad (8)$$

The abrupt change in the concentrations of the radical and the salt over the initial section of the kinetic curve is caused by the rapid reaction of the radical with the hydrogen halide formed as a result of the decomposition of t-BuBr before the start of the measurements. The size of the jump increases with increase in the time interval between the preparation of the substrate solution and its mixing with the verdazyl solution. In conformity with the stoichiometry of reaction (7), on decomposition of t-BuCl the abrupt changes in the concentrations of the radical and the salt are in the ratio 2 : 1. In the case of t-BuBr and especially t-BuI, the changes in the concentrations of Y—Vd$^{\cdot}$ and Y—Vd^{+}X^{-} in the initial period usually differ by a factor less than 2 and in certain cases (t-BuI) the ratio is 1 : 1. This is associated with the fact that the HBr(HI) formed before the start of the measurements is fully or partly oxidised by atmospheric oxygen to the halogen.

Apart from t-butyl halides,[27,29—36,38,50,51,68,71,73] the verdazyl method has been applied to the study of *E*1 reactions involving 7α-bromocholesteryl benzoate,[59,63,64,70,74,75] 1-chloro-1-phenylethane,[60,65,69] 2-bromo-2-methyladamantane,[50,55,57,68] 2-chloro-2-methyladamantane,[71] and cumenyl chloride.[79] Similar kinetic relations were observed in all cases.

It has been shown in relation to 7α-bromocholesteryl benzoate,[70] t-BuBr,[50,68,73] t-BuCl,[68,71] cumenyl chloride,[79] 2-bromo-methyl-adamantane,[68] and 2-chloro-2-methyladamantane[68,71] that, in the course of the *E*1 reaction, the Y—Vd$^{\cdot}$ radical reacts not with the hydrogen halide, as postulated initially, but with the solvent-separated ion pair comprising the substrate:

$$R^{+}|Solv|X^{-} + 2Y-Vd^{\cdot} \longrightarrow Y-Vd^{+}X^{-} + [Y-Vd-R] \xrightarrow{(I)} Y-VdH + \text{olefin}. \quad (9)$$

This reaction apparently results in the initial formation of the product of the alkylation of the verdazyl (I), which then decomposes comparatively rapidly into an olefin and leucoverdazyl, which agrees with the stoichiometric Eqn. (7). This conclusion was reached in the study of salt effects, which demonstrated that Y—Vd$^{\cdot}$ and the salt act on the same cationoid intermediate.

The quantitative formation of leucoverdazyl in solution can be readily followed with the aid of the disproportionation reaction[101]

$$Y-VdH + Y-Vd^{+}X^{-} + NaOH \rightarrow 2Y-Vd^{\cdot} + NaX + H_2O. \quad (10)$$

After the addition of one drop of a 1 M aqueous NaOH solution to the reaction mixture at the end of the kinetic experiment, the initial verdazyl concentration is restored in the solution.

In contrast to t-butyl halides, 2-bromo-2-methyladamantane, and cumenyl chloride, the rate of heterolysis of 1-chloro-1-phenylethane[65,69] and especially 7α-bromocholesteryl benzoate[70,75] depends comparatively strongly on the verdazylium salt formed during the reaction, which leads to an appreciable distortion of the "$Y-Vd^{\cdot}$ ($Y-Vd^{+}X^{-}$) concentration–time" relation. The rate of reaction was calculated in this case from the initial linear section of the kinetic curve.

It has been shown in relation to the heterolysis of t-BuBr and t-BuCl in acetonitrile[22] and acetone,[30] of t-BuCl in isopropyl alcohol and t-butyl alcohol,[38] of PhCHClMe in ethanol,[65] and of $PhCMe_2Cl$ in acetonitrile[79] that the data obtained by the verdazyl method agree satisfactorily with the results obtained by other methods.[102–108] The gross errors made in the determination of the rate constants for the solvolysis of t-BuCl in isopropyl alcohol and t-butyl alcohol and of t-BuBr in t-butyl alcohol were detected by means of the verdazyl method. The rate constants quoted by Viana and coworkers[109,110] differ by 1–3 orders of magnitude from the values found by the verdazyl method[38] and also those quoted by Rudakov.[107]

The application of the verdazyl method proved to be particularly effective in the study of S_N1 reactions. There exist data at present on the heterolysis of Ph_2CHBr,[34,35,38–45,72] Ph_2CHCl,[21,38] 1-adamantyl iodide (1-AdI),[47,49,51] 1-AdBr,[36,48] 1-adamantyltoluene-*p*-sulphonate (1-AdOTs),[46,48,54,80] 1-adamantyl picrate (1-AdOPic),[52,53,56,80] 3-bromohomoadamantane,[58] $PhCCl_3$,[61,67,76] *p*-methoxy(trichloromethyl)benzene,[62,66] Ph_2CCl_2,[69,77] *p*-methoxybenzylidene chloride,[77,78] and di(*p*-chlorophenyl)dichloromethane.[69]

In these cases, the rate of reaction is also described by the kinetic Eqn. (4) and is as a rule independent of the concentration and nature of $Y-Vd^{\cdot}$. Consequently verdazyl enters into the reaction after the rate-limiting stage, which in fact makes it possible to use it as an internal indicator.

The rates of S_N1 reactions in an aprotic medium are very sensitive to the influence of salts, including those which are formed during the reaction. In certain cases,[40,62,68,69] the salt effect is so great that, when $[Y-Vd^{+}X^{-}] \simeq 10^{-4}-10^{-5}$ M, the "$Y-Vd^{\cdot}$ concentration–time" relation is greatly distorted. The rate constant for the pseudo-zero-order reaction was calculated in this case either from the initial linear section of the kinetic curve, if it can be identified, or was found by extrapolating the values of k_0 or k to the $[Y-Vd^{+}X^{-}] = 0$ zero straight line.[62]

It has been shown in relation to the heterolysis reactions of Ph_2CHCl in methanol,[21] 1-AdOTs in isopropyl alcohol,[46] 1-AdOPic in sulpholan, methanol, and ethanol,[52,56] $PhCCl_2$ in aqueous ethanol,[76] Ph_2CCl_2 in ethanol and aqueous dioxane,[69,77] and *p*-$MeOC_6H_4CHCl_2$ in aqueous dioxane[77,78] that the rate constants found by the verdazyl method agree satisfactorily with those determined by other procedures.[24,111–117] The rate constant for the heterolysis of Ph_2CHCl in acetonitrile, found by the verdazyl method,[21] proved to be ~3 orders of magnitude lower than the value obtained in the presence of PhONa.[118] The presence of a gross error in the study of Okamoto et al.[118] has been demonstrated.[21] An even greater error was made in an investigation[119] where the rate constant for the hydrolysis of $(p\text{-}ClC_6H_4)_2CCl_2$ at 25 °C, calculated from the results of this study, proved to be ~5 orders of magnitude lower than the value found by the verdazyl method.[69]

Fig. 2 presents the temperature dependences of the logarithms of the rate constants for the heterolysis of t-BuBr in acetone[30,104] ($E1$ reaction) and of 1-AdOPic in sulpholan[52,112] (S_N1 reaction), obtained by the verdazyl method and other independent methods. In both cases, all the points lie on a single straight line, which illustrates the validity of the verdazyl method. The most convincing evidence for the validity of the method is that the enormous amount of experimental data obtained by this procedure for 21 substrates (each in 10–40 solvents) is fully consistent with the available literature data for the unimolecular heterolysis of organic compounds.

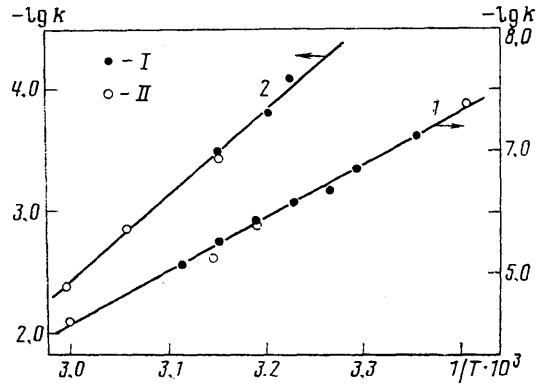


Figure 2. Temperature variation of the rate of heterolysis of t-BuBr in acetone (line *1*) and of 1-AdOPic in sulpholan (line *2*); *I*, verdazyl method; *II*, other methods.[24,104,112]

Valuable information about the mechanism of S_N1 reactions is provided by the reaction products formed with participation of verdazyl. Depending on the nature of the substrate and the reaction conditions, they can be various, different stoichiometric $[RX]:[Y-Vd^{\cdot}]:[Y-Vd^{+}X^{-}]$ ratios and different forms of the kinetic pseudo-zero-order equations being observed. The verdazyl alkylation products are usually formed in the course of the reaction:[39,49,51,54]

$$RX+2Vd^{\cdot} \rightarrow Vd-R+Vd^{+}X^{-}, \quad R=Ph_2CH,\ 1\text{-Ad}. \tag{11}$$

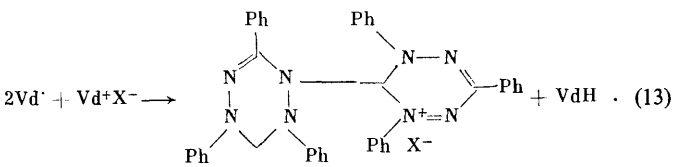
The rate of reaction is in this case described by the kinetic Eqn. (8) subject to the condition $[RX] \gg [Y-Vd^{\cdot}]$.

The solvent molecule, for example that of acetonitrile, can participate in the formation of the reaction product:[46,47,52]

$$1\text{-AdX} + 2Vd^{\cdot} \xrightarrow{MeCN} 1\text{-Ad}-N=\overset{\displaystyle Me}{\overset{|}{C}}-Vd + Vd^{+}X^{-}. \tag{12}$$

Reaction (12) indicates the intermediate formation of the ion pair $1\text{-Ad}-N=C(Me)^{+}X^{-}$, apparently via the addition of 1-AdX to the triple bond of acetonitrile located in the interionic space of the solvent-separated ion pair $1\text{-Ad}^{+}|MeCn|X^{-}$. The new ion pair formed subsequent reacts rapidly with the indicator. In this case, the kinetic relatins remain the same as in reaction (11).

The isolation of the reaction products is hindered by the occurrence of the side reaction of $Y-Vd^{\cdot}$ with $Y-Vd^{+}X^{-}$, which leads to the formation of the sparingly soluble verdazylium salt (II) and of leucoverdazyl:[26,46,47,49,52,62,120]



(II)

This rection proceeds only at comparatively high concentrations of the reactants (~0.1 M). Under the conditions of the kinetic experiment at low $Y-Vd^{\cdot}$ and $Y-Vd^{+}X^{-}$ concentrations ($\sim 1 \times 10^{4}$ M), it does not take place.[120]

In the heterolysis of polychlorinated organic compounds ($ArCCl_3$, Ph_2CCl_2, $ArCHCl_2$),[62,66,69,77,78] the verdazyl alkylation products are also apparently formed initially ($ArCl_2C-Vd$, $Ph_2ClC-Vd$, $HArClC-Vd$) and readily undergo further reactions. As a result of this, the stoichiometry of these reactions and their kinetic equations depend greatly on the nature of the substrate and the experimental conditions.

The heterolysis reaction of $PhCCl_3$ is isopropyl alcohol is described by the stoichiometric equation:

$$PhCCl_3 + 6Vd^{\cdot} \xrightarrow{iso-PrOH,\ H_2O} PhCO_2Pr-iso + 3Vd^{+}Cl^{-1} + 3VdH. \quad (14)$$

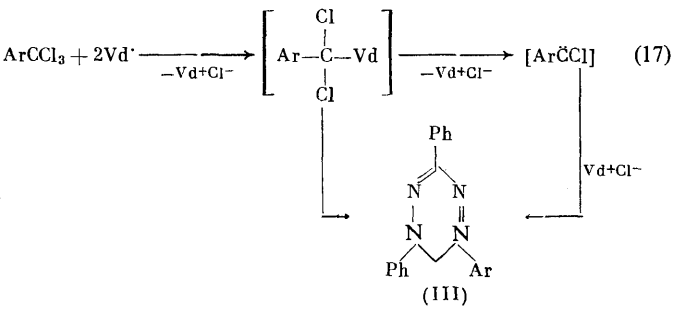
Two explanations are possible for these results. The first is that the substrate is initially solvolysed with formation of 3 moles of HCl, which then rapidly reacts with 6 moles of the indicator, while the second is that the verdazyl alkylation product formed in the first stage of the reaction is rapidly converted into $Vd^{+}Cl^{-}$ and PhCOCl and the latter is known[121] to be solvolysed ~3 orders of magnitude faster than $PhCCl_3$.[122] Regardless of the way in which this reaction takes place, it is described by the pseudo-zero-order kinetic equation

$$-d[Vd^{\cdot}]/6dt = d[Vd^{+}Cl^{-}]/3dt = k_0. \quad (15)$$

In the heterolysis of p-$MeOC_6H_4CCl_3$ in propylene carbonate, sulpholan, chloroform, and butyl acetate, the verdazyl alkylation product formed ($ArCl_2C-Vd$) is stable during the kinetic experiment and the rate of reaction in these solvents is therefore described by the pseudo-zero-order kinetic Eqn. (8).[66] In acetonitrile, γ-butyrolactone, ethyl methyl ketone, 1,1,2,2-tetrachloroethane, acetophenone, nitrobenzene, benzonitrile, and methylene chloride, the above product decomposes rapidly during the kinetic experiment with formation of $Vd^{+}Cl^{-}$. The rate of reaction in these solvents is therefore described by the pseudo-zero-order kinetic equation[62,66,76]

$$-d[Vd^{\cdot}]/2dt = d[Vd^{+}Cl^{-}]/2dt = k_0. \quad (16)$$

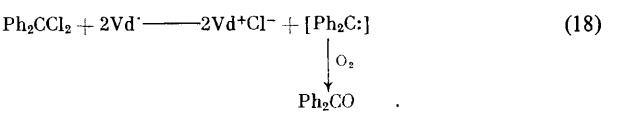
In preparative experiments carried out with $PhCCl_3$, p-$MeOC_6H_4CCl_3$, and p-$MeC_6H_4CCl_3$ in acetonitrile, the triazine (III) was isolated:[62,67,123]



(III)

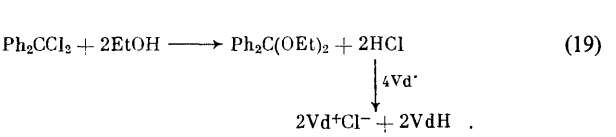
Compound (III) is apparently formed via an intermediate arylchlorocarbene or via the recyclisation of the verdazyl alkylation product.

Reaction (18) takes place[68] in the heterolysis of Ph_2CCl_2 in aprotic solvents in the presence of verdazyl and its rate is described by Eqn. (16):



The verdazyl alkylation product is apparently formed initially and then decomposes rapidly into $Vd^{+}Cl^{-}$ and diphenylcarbene. The latter is oxidised by oxygen to benzophenone.

The heterolysis of Ph_2CCl_2 takes place in ethanol in accordance with the equation:[69]



In conformity with the stoichiometry of this reaction, its rate in each individual experiment is described by a pseudo-zero-order kinetic equation:

$$-d[Vd^{\cdot}]/4dt = d[Vd^{+}Cl^{-}]/2dt = k_0. \quad (20)$$

In 85% aqueous dioxane, the verdazyl alkylation product Ph_2CCl_2 is stable during the kinetic experiment and the rate of reaction is described in this case by the kinetic equation (8).[69,77] Thus the stoichiometric ratios $[Ph_2CCl_2]:[Vd^{\cdot}]:[Ph^{+}Cl^{-}]$ depend greatly on the nature of the solvent in the heterolysis of the Ph_2CCl_2 in the presence of verdazyl. In an aprotic medium, they are 1:2:2, in ethanol they are 1:4:2, and in 85% aqueous dioxane they are 1:2:1.

A similar wide variety of stoichiometric ratios has been observed also in the heterolysis of trichloromethylbenzenes.[61,62,66,76] This is a characteristic feature of organic polychloro-compounds which afford unstable alkylation products on interaction with verdazyl.

A characteristic feature of the verdazyl method is that the indicator always reacts with the solvent-separated ion pair of the substrate. This occurs also in an aprotic medium where there is no

nucleophile other than Y—Vd· and in a protic medium where verdazyl must compete with a solvent molecule for the cationoid. For example, in 85% aqueous dioxane in the presence of 1×10^{-4} M Vd·, the heterolysis of Ph_2CCl_2 and *p*-$MeOC_6H_4CHCl_2$ takes place fully via the pathway leading the formation of verdazyl alkylation products and not hydrolysis products. This shows that the solvent-separated ion pair reacts very rapidly with verdazyl.

The verdazyl method made it possible to investigate in detail the influence of small amounts of water (0.05—0.3 M) on the rates of S_N1 and $E1$ reactions in aprotic solvents and to determine the relative yields of products formed with participation of Y—Vd· and water in S_N1 reactions.[18,21,39,41—44,46,47,49,50,52,54,59,62,69,70] Water cooperates with the heterolysis reactions in all cases by virtue of the formation of hydrogen-bonded complexes ($RX\ldots H_2O$) and increases the rate of reaction. The kinetic effect of water is determined by the parameter b in Winstein's equation (21) and greatly depends on the nature of the substrate and the solvent:

$$k_{H_2O}=k(1+b[H_2O]). \qquad (21)$$

Here k_{H_2O} and k are the rate constants for heterolysis in the presence of water and in its absence.

The kinetic effect of water yields information about possible errors in the determinatin of the rate of heterolysis due to undetermined admixtures of water in the aprotic solvent. The lowest value of b (1—3 litre mol^{-1}) were found for the heterolysis of t-butyl and adamantyl substrates. Usually b = 5—10 litre mol^{-1}, reaching 30—50 litre mol^{-1} in some cases (7α-bromocholesteryl benzoate in PhCN and $PhNO_2$).[59,70] Analysis of the data presented shows that the undetermined admixtures of water (<0.05 M) have hardly any effect on the rate of heterolysis of t-BuX and 1-AdX in aprotic solvents; for b = 10 litre mol^{-1}, the error in the determination of the rate can be 10—15%, while for b = 50 litre mol^{-1} the error is 30%. The values quoted refer to polar aprotic solvents (MeCN, propylene carbonate, $PhNO_2$, PhCN). On reducing the polarity of the solvent, the kinetic effect of water increases, but the water content then falls so much that the real effect becomes insignificant.

On heterolysis of Ph_2CHX (X = Cl, Br) in the presence of Vd· in moist acetonitrile with $[H_2O] \simeq 0.045$ M, two reaction products are formed from the substrate—the verdazyl alkaylation product and diphenylmethanol:[21,39]

$$Ph_2CHX \begin{cases} \xrightarrow{2Vd^{\cdot}} Ph_2CH{-}Vd + Vd^+X^-, \\ \xrightarrow{H_2O} Ph_2CHOH + HX \end{cases} \qquad (22)$$

$$Ph_2CHOH + HX \xrightarrow{2Vd^{\cdot}} Vd^+X^- + VdH\ .$$

Regardless of the relative yields of these products, the rate of reaction is described by the kinetic equation (8).

The method makes it possible to determine the amount of Ph_2Cd—Vd and VdH formed in the kinetic experiment. As already mentioned, an equimolecular mixture of Vd^+X^- and VdH is quantitatively converted into Vd· when acted upon by alkali. If formaldehyde is added, then the excess Vd^+X^- is also converted quantitatively into verdazyl.[124,125] In practice, this is achieved by adding a drop of an alkaline solution of formaldehyde to the reaction mixture. Since the relative yields of Ph_2Cl—Vd and VdH are determined by the competition between Vd· and H_2O for the formation of the solvent-separated ion pair $Ph_2CH^+|Solv|X^-$, then, knowing the concentrations of both nucleophiles in the solution, it is possible to calculate their relative reactivities in the reaction with the solvent-separated ion pair. In the heterolysis of Ph_2CHX (X = Cl, Br) in MeCN at 25 °C, the ratio $k_{Vd^{\cdot}}/k_{H_2O} \simeq 10^4$. Consequently Vd· is a very powerful nucleophile compared with H_2O. Indeed in the case of a strong nucleophile such as N_3^-, the ratio k_{N_3}/k_{H_2O} for Ph_2CHCl is only 170.[126]

In the heterolysis of 1-AdI in moist acetonitrile, $k_{Vd^{\cdot}}/k_{H_2O} \simeq 10^4$, while in the heterolysis of 1-AdOTs the ratio is $\sim 10^3$.[46,49]

The high reactivity of verdazyl compared with water in the reaction with the solvent-separated ion pair is apparently due to the different mechanisms of these reactions—the reaction with H_2O involves an S_N2 process during which the cationoid should be desolvated, while the reaction with Vd^+ apparently involves an outer-sphere electron transfer (an *SET*2 reaction) without the decomposition of the solvation shells of the reactants. This explains why triphenylverdazyls proved to be such effective internal indicators for unimolecular heterolysis reactions.

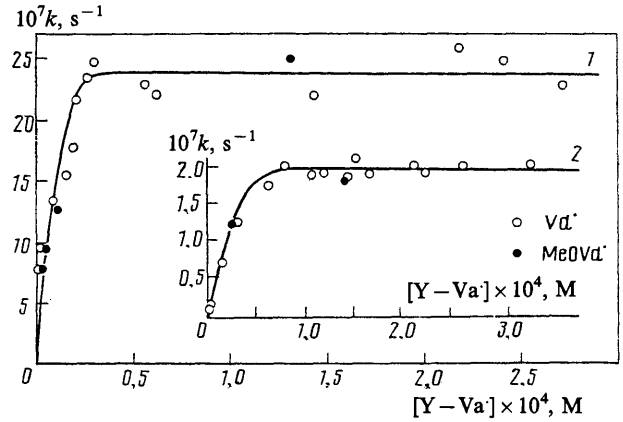


Figure 3. The influence of the concentration and nature of Y—Vd· on the rate of heterolysis of Ph_2CCl_2 in acetonitrile (line *1*) and acetone (line *2*) at 25 °C.

The data currently available for the heterolysis of organic substrates in the presence of verdazyls (Ph_2CHBr,[40—45,72] Ph_2CHCl,[21] 1-AdOTs,[46,54,56,80] 1-AdI,[47,49] 1-AdOCOCl,[27] 1-AdOPic,[52,56,80] 7α-bromocholesteryl benzoate,[59,70,75] PhCHClMe,[60,65,69] *p*-MeO.$C_6H_4CCl_3$,[62] Ph_2CCl_2,[69,77] t-BuBr,[68,73] t-BuCl,[71] *p*-$MeOC_6H_4$.$CHCl_2$,[77,78] cumenyl chloride,[79] 2-bromo-2-methyladamantane,[68] and 2-chloro-2-methyladamantane[71]) show that these radicals always react with the solvent-separated ion pairs of the substrate—both in S_N1, $E1$, and $F1$ reactions and in solvolytic reactions. This is a characteristic feature of the verdazyl method. The solvent-separated ion pair is formed after the rate-limiting stage of the heterolysis. Clearly verdazyls can be used as indicators subject only to the condition that the rate of the reaction of the solvent-separated ion pair with Y—Vd· is higher than the rate of formation of this intermediate. It is easy to assume that, on reducing the

concentration of the indicator, it is possible to achieve a situation where the reaction of Y—Vd˙ with the solvent-separated ion pair limits the overall rate of the process. This has been demonstrated in the heterolysis of Ph_2CCl_2,[69,77] p-$MeOC_6H_4CHCl_2$,[77,78] and $(p\text{-}ClC_6H_4)_2CCl_2$.[69]

The influence of the concentration and nature of the verdazyl on the rate of heterolysis Ph_2CCl_2 in acetonitrile and acetone is illustrated in Fig. 3, while Fig. 4 demonstrates their influence on the rate of solvolysis of Ph_2CCl_2 and p-$MeOC_6H_4CHCl_2$ in 85% aqueous dioxane.

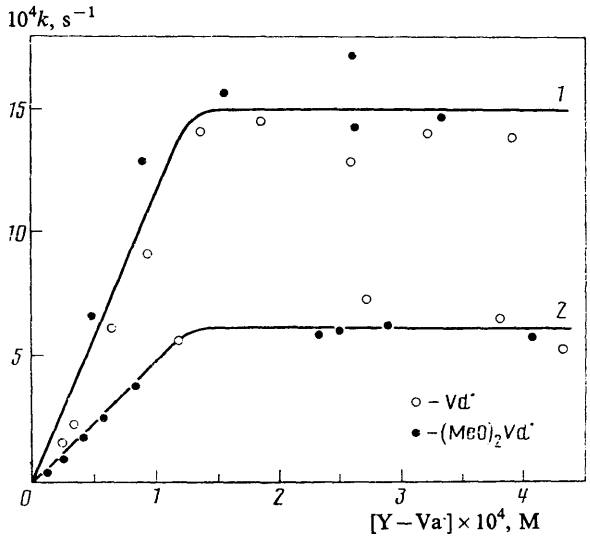


Figure 4. The influence of the Vd˙ concentration on the rate of heterolysis of p-$MeOC_6H_4CHCl_2$ (line *1*) and Ph_2CCl_2 (line *2*) in 85% aqueous dioxane.

Evidently the k—[Y—Vd˙] relation consists of two sections; at relatively high indicator concentrations, the rate of reaction is independent of the concentration of Y—Vd˙ and of the nature of its substituent, while at low indicator concentrations a direct proportionality is observed between the quantity k and the Y—Vd˙ concentration. In the former case, the rate of reaction is described by Eqn. (4), while in the latter it is described by a second-order kinetic equation:

$$v = k_2[RX][Y—Vd˙]. \quad (23)$$

Thus, on reducing the indicator concentration, the rate-limiting state of the reaction changes: at comparatively high verdazyl concentrations, the rate-limiting stage involves the formation of a cationoid intermediate (S_N1 reaction), while at a low verdazyl concentration Y—Vd˙ reacts with the solvent-separated ion pair of the substrate (*SET*2 reaction) in the rate-limiting stage.

The change in the kinetic relations and hence the change in the reaction mechanism in the heterolysis of Ph_2CCl_2 in acetonitrile, acetone (Fig. 3), ethanol (not shown in the Figure), and 85% aqueous dioxane (Fig. 4) occurs at Vd^+ concentrations of 2.0×10^{-5}, 6.2×10^{-5}, 11×10^{-5}, and 13×10^{-5} M respectively. In γ-butyrolactone and propylene carbonate, the rate of reaction is independent of the indicator concentration up to [Vd˙] ≃ 2×10^{-6} M. In the solvolysis of p-$MeOC_6H_4CHCl_2$ in 85% aqueous dioxane, the kinetic relations change at a verdazyl concentration of 11×10^{-5} M (Fig. 4). In the solvolysis of $(p\text{-}ClC_6H_4)_2CCl_2$ in alcohols, the change occurs at [Vd˙] > 1×10^{-4} M.[69] These data demonstrate that, when verdazyls are used in a proton-donating medium, the indicator concentration must be higher than 1×10^{-4} M, whereas in an aprotic medium it can be appreciably lower. In the study of the kinetics of the heterolysis of organic compounds by the verdazyl method, it is necessary to obtain proof that the rate of reaction is independent of the indicator concentration for each reaction system.

It is seen from Figs. 3 and 4 that the rates of heterolysis of Ph_2CCl_2 and p-$MeOC_6H_4CHCl_2$ are independent of the nature of the substituent in the verdazyl even when the rate of reaction depends on its concentration. This demonstrates that the reaction of Y—Vd˙ with the solvent-separated ion pair consists of many stages: in one stage, verdazyl plays the role of an electron donor (formation of a charge-transfer complex), whilst in another it behaves as an electron acceptor (decomposition of the charge-transfer complex), which leads to the compensation effect of the substituent in the indicator. Thus, by changing the concentration of the indicator, it is possible to change the rate-limiting stage of the reaction and to obtain information about the mechanism of the product-forming stage.

In the course of the development of the verdazyl method, important conclusions were reached concerning the essential features of the unimolecular heterolysis of organic compounds investigated. The application of the method demonstrated that the stage involving the external return of the ion pair ($R^+|Solv|X^- \rightarrow R^+X^- \rightarrow RX$) is not very important, although this idea is still always used in the interpretation of the reaction mechanism.[7—9,40,45,109,110] If this stage could influence appreciably the overall rate of reaction, the rate constant determined in the presence of verdazyl would have depended on the concentration and nature of Y—Vd˙ owing to the competitive decompositon of the solvent-separated ion pair in the ion pair recovery reaction and the reaction with the indicator:

$$RX \leftarrow R^+X^- \leftarrow R^+|Solv|X^- \xrightarrow{Vd˙} \text{products}.$$

Hitherto this has never been observed in the study of the kinetics of the heterolysis of all the substrates listed above in various protic and aprotic solvents.

Since the data obtained by the verdazyl method agree well with the results of other procedures, one may claim that the stage involving the external return of the ion pair is not very important both in the presence of verdazyls and without them, although the opposite view is frequently adhered to in the literature.[7,109,110,113,116,117] For example, it is believed[116,117] that the rates of solvolysis of Ph_2CCl_2 and p-$MeOC_6H_4CHCl_2$ in 85% aqueous dioxane, determined spectrophotometrically from the formation of Ph_2CO and p-$MeOC_6H_4CHO$, depend greatly on the stage involving the external return of the ion pair and it is postulated that the rate-limiting stage involves the interaction of the solvent-separated ion pair of the substrate with water. It has been demonstrated by the verdazyl method[69,77,78] that, under conditions where the rate of reaction is independent of the concentration and nature of Y—Vd˙, the results of both studies agree satisfactorily. Consequently in both cases the mechanism of the external return of

the solvent-separated ion pair is unimportant. Under the conditions of the studies of Vitullo and Vilgis,[116,117] the solvent-separated ion pair reacts with water, while under the conditions of the studies of Dvorko and co-workers[69,77,78] it reacts with Y—Vd˙. The agreement between the rate constants shows that the rate-limiting stage in these reactions is the formation of the cationoid intermediate and not the reaction of the solvent-separated ion pair with the nucleophile.

The application of the verdazyl method makes it possible to shorten greatly the time required to study the kinetics of the heterolysis reactions and to obtain reliable data in those cases where the rate of reaction depends comparatively greatly on the salt concentration. This made it possible to determine the rates of heterolysis of the majority of the substrates listed above in a large set of protic and aprotic solvents (20—40 solvents) and to carry out a quantitative analysis of the solvation effects.[11,34,48,51,53,55—57,64—66,68—70,76] It was shown that the rate of reaction is determined mainly by the polarity and electrophilicity of the solvent and that the nucleophilic cooperation of the solvent with the heterolysis does not take place. The rates of heterolysis of PhCHClMe, Ph_2CHBr, 1-AdOTs, and $PhCMe_2Cl$ are altogether independent of the nucleophilic properties of the medium, while in the heterolysis of 7α-bromocholesteryl benzoate, t-butyl halides, 1-AdI, 1-AdBr, 1-AdOPic, 2-bromo-2-methyladamantane, and p-$MeOC_6H_4CCl_3$, the negative effect of nucleophilic solvation is observed.

If the rate of heterolysis has been limited by the conversion of the contact ion pair into the solvent-separated ion pair (Scheme 3), as is generally assumed,[7,8,10] the nucleophilicity of the solvent would have promoted the reaction. In order to overcome this contradiction, a new intermediate was introduced into Winstein's scheme—a space-separated ion pair (SPSIP), formed on conversion of the contact ion pair into the solvent-separated ion pair:[49,60,62,68—70]

$$RX \rightleftharpoons R^+X^- \rightleftharpoons \underset{\text{SPSIP}}{R^+ \ldots X^-} \rightleftharpoons R^+|Solv|X^-. \qquad (24)$$

It is postulated that the rate-limiting stage of the heterolysis is the separation of ions in the contact ion pair with formation of a vacancy between them. Consequently a solvent molecule is rapidly incorporated in the interionic space within the space-separated ion pair.

On solvolysis of organic substrates via the S_N2—ion pair mechanism ($PhCH_2Cl$, PhCOCl, allyl tosylate), the rate of reaction increases with increasing nucleophilicity of the solvent.[37,61]

The application of the verdazyl method to the study of an *F*1 reaction for 1-AdOCOCl as an example yielded an unexpected resut:[27,56] the rate constants [Eqn. (4)] found in protic and aprotic solvents differed as a rule from the values obtained from the consumption of the substrate.[26,127] This is associated with the fact that the decomposiiton reaction of 1-AdOCOCl is a consecutive-parallel process and different methods for the determination of the reaction rate reflect different aspects of this process. The data obtained supplement one another. This leads to new possibilities for the study of *F*1 reactions. The use of verdazyls made it possible to demonstrate the fragmentation process proceeds via the formation of both a contact ion pair and a solvent-separated ion pair.

The rate of heterolysis of organic substrates is determined under the conditions of a stationary process where the concentration of cationoid intermediates [Int] remains constant during the kinetic experiment, i.e. for $d[Int]/dt = 0$.[128] However, time is required for the reaction system to attain a stationary state. The verdazyl method makes it possible in some cases to follow the process by determining the rate at very low conversions of the substrate ($\sim 10^{-4}$—10^{-5}%). This was observed in the heterolysis of Ph_2CCl_2 in propylene carbonate[69] and of cumenyl chloride in acetonitrile, propylene carbonate, and γ-butyrolactone.[79] In these cases, and induction period, reflecting the attainment of the stationary state by the system, appears (Fig. 5) on the kinetic curve. A delay in the attainment of a stationary state by the system may be caused by undetermined impurities in the solvent and by added salts (LiBr, $Bu_4N^+Br^-$, $Et_3PhCH_2N^+Cl^-$) or a crown-ether. These compounds apparently trap the intermediate formed before the rate-limiting stage (for example, a contact ion pair) and for a time direct the process towards the formation of an inactive complex. The addition of $LiClO_4$, which catalyses the conversion of the contact ion pair into an intermediate with a greater degree of charge separation, eliminated the induction period.

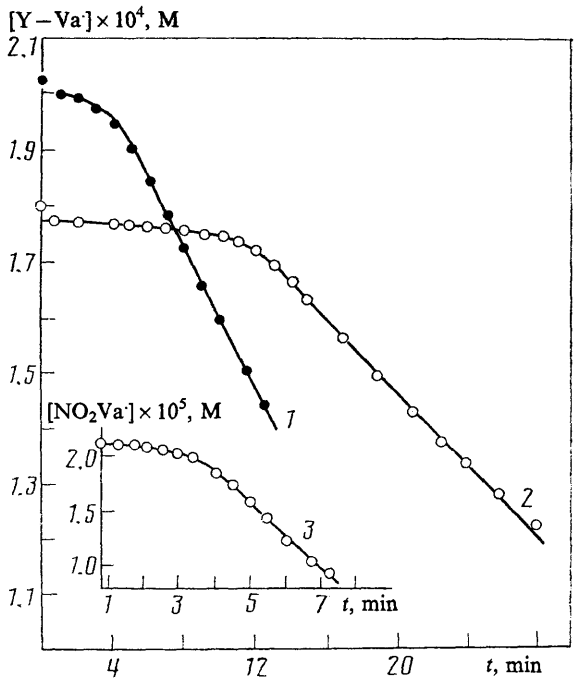


Figure 5. Kinetics of the heterolysis of $PhCMe_2Cl$ in propylene carbonate in the presence of salts at 25 °C: *1*, $[PhCMe_2Cl] = 0.00645$ M, $[Vd˙] = 2.03 \times 10^{-4}$ M, $[Bu_4N^+Br^-] = 0.1$ M, $k = 8.03 \times 10^{-6}$ s^{-1}; *2*, $[PhCMe_2Cl] = 0.00688$ M, $[(MeO)_2Vd˙] = 1.80 \times 10^{-4}$ M, $[Et_3(PhCH_2)N^+Cl^-] = 0.05$ M, $k = 4.30 \times 10^{-6}$ s^{-1}; *3*, $[PhCMe_2Cl] = 0.00636$ M, $[NO_2Vd˙] = 2.2 \times 10^{-5}$ M, [LiBr] = 0.0599 M, $k = 4.02 \times 10^{-6}$ s^{-1}.

III. Application of the verdazyl method to the study of salt effects

Salt effects constitute a fine instrument for the investigation of the details of the mechanisms of organic reactions and for the establishment of the nature of the catalytic effects.[1,7,8] This is one of

the most difficult problems in physical organic chemistry. The application of verdazyls makes it possible to study in detail the salt effects in heterolysis reactions, to elucidate their nature, and to specify in a concrete form the mechanism of the heterolysis itself. Particularly valuable data have been obtained in the study of S_N1 and $E1$ reactions in an aprotic medium.[40,43,45–47,49,50,52,54,56,61,62,65,68–73,75,76–80]

The interpretation of the unusual salt effect of perchlorate put forward by Winstein has given rise to much controversy.[1,7–9,40,45,129] It reduces to the postulate that the sharp increase in the rate of reaction in the presence of small amounts of the salt is caused by the exchange of the nucleofugal species in the solvent-separated ion pair with formation of the ion pair (IV), which is incapable of being converted into a contact ion pair:

$$\underset{}{ClO_4^-}+R^+|Solv|X^- \rightleftharpoons \underset{(IV)}{R^+|Solv|ClO_4^-}+X^- \quad . \qquad (25)$$

In other words, the presence of the unusual salt effect is explained by the suppression of the stage involving the external return of the ion pair. As already mentioned, it has been demonstrated with the aid of the verdazyl method that this stage is unimportant. Winstein's intepretation is incorrect.[40,43,45] Detailed study of the unusual salt effect by the verdazyl method led to the conclusion that the catalytic effect of perchlorate is caused by the effect of ClO_4^-,[40] Li^+,[70,75] or of the salt ion pair[68–70] on the contact ion pair of the substrate, which leads to the formation of the ion triplets (V) and (VI) or the quadrupole (VII), which are converted more readily than the contact ion pair itself into the cationoid intermediate with a greater charge separation:

$$\underset{(V)}{ClO_4^-|Solv|R^+X^-}, \quad \underset{(VI)}{R^+X^-Li^+}, \quad \underset{(VII)}{R^+X^-, M^+Y^-} \quad .$$

Comparison of data for the kinetics of the hydrolysis of Ph_2CCl_2 in acetone, obtained by the verdazyl method,[69] with the results of a study[130] where the reaction of Ph_2CCl_2 with NaI was investigated in the same solvent in the presence of $LiClO_4$ provided evidence in support of the fact that the catalytic effect of $LiClO_4$ under the conditions of the unusual salt effect is caused by the action of the salt on the contact ion pair and not on the covalent substrate. In the latter case, the catalytic effect of the salt is lower by approximately two orders of magnitude.

Analysis of data for other positive salt effects, obtained by the verdazyl method, showed that they are associated with the formation of the quadrupole (VII) and not with the increase in the ionic strength of the solution.[21,40,43,46,47,49,52,54,62,68–71] The unusual salt effect is a variety of the normal salt effect.

The concentration and nature of Y—Vd$^{\cdot}$, both in the presence of salts increasing the rate of reaction and in their absence, do not affect the rate of reaction.

The verdazyl method has also made it possible to discover a new salt effect, which was called the negative salt effect.[40,43,46,47,49,52,54,56,62,68–71,76,80] Its characteristic feature is that of the addition of a salt having an ion in common with the ion pair lowers the rate of reaction under conditions where a free carbonium ion is not formed. Such reduction in the rate of reaction is usually attributed to the salt effect caused by the Law of Mass Action, i.e. by the reaction involving reformation from the free carbonium ion:[1–3,7–9,129]

$$R^+ + X^- \rightarrow R^+|Solv|X^- \rightarrow R^+X^- \rightarrow RX.$$

However, the negative salt effect is usually manifested in an aprotic medium where heterolysis does not go so far as the formation of a free carbonium ion.

This salt effect is associated with the reaction involving the external return of the ion pair: the salt or its anion form with the solvent-separated ion pair or the space-separated ion pair a quadrupole or an anionic triplet, which are more readily converted into the contact ion pair and subsequently into the covalent substrate than the solvent-separated and space-separated ion pairs themselves:

$$RX \rightleftharpoons R^+X^- \overset{X^-}{\rightleftharpoons} R^+ \ldots X^- \rightleftharpoons R^+|Solv|X^- \xrightarrow{Y-Vd^{\cdot}} \text{products}. \qquad (26)$$

The decrease in the rate of reaction in the presence of a salt with a common ion is caused by the catalysis of the reaction involving the external return of the ion pair.

For low degrees of conversion of the substrate, where the nucleofugal species exchange reaction is unimportant, a negative salt effect of a similar kind is manifested also in the presence of a salt with a non-common ion. In all cases its nature is the same: a decrease in the concentration of the product-forming intermediate (a solvent-separated ion pair).

It is seen from Scheme (26) that the verdazyl always acts on the solvent-separated ion pair, while the salt can act both on the solvent-separated ion pair and on the space-separated ion pair. In the former case, there is competition between the salt and the verdazyl for the cationoid and the rate of reaction should depend on the nature and concentration of Y—Vd$^{\cdot}$. In the latter case, this should not be observed.

Detailed study of the influence of the concentration of the verdazyl and of the nature of the substituent in it on the rate of reaction in the presence of salts reducing the rate of reaction demonstrated that the nature of the negative salt effect depends greatly on the structure of the substrate and on the nature of the salt and the solvent. Thus the decrease in the rate of heterolysis of *p*-$MeOC_6H_4CCl_3$ in acetonitrile in the presence of LiCl is caused by the interaction of the salt with the space-separated ion pair.[62] A similar picture is observed in the heterolysis of 1-AdI in propylene carbonate in the presence of $Et_4N^+OPiC^-$.[49] In the heterolysis of Ph_2CCl_2 in acetonitrile, γ-butyrolactone, and propylene carbonate, the negative salt effect of chlorides and bromides is associated with their interaction with the solvent-separated ion pair,[69] whereas in the heterolysis of 7α-bromocholesteryl benzoate in γ-butyrolactone, the negative salt effect of the chloride is caused by the reaction of the salt with the space-separated ion pair while in nitrobenzene and *o*-xylene it is due to interaction with the solvent-separated ion pair.[70] The negative salt effect of $Et_3(PhCH_2)N^+Cl^-$ in the heterolysis of cumenyl chloride in acetonitrile and γ-butyrolacetone is also associated with the effect of the salt on the solvent-separated ion pair, while propylene carbonate it is due to its effect on the space-separated ion pair, while in propylene carbonate it is due to its effect on the space-separated ion pair.[79] In the heterolysis of t-BuBr, t-BuCl, 2-bromo-2-methyladamantane, and 2-chloro-2-methyladamantane, and 2-chloro-methyladamantane in γ-butyrolactone, the negative salt effect of the chloride and thiocyanate is associated with their interaction with the solvent-separated ion pair.[68,73] On the other hand, in the heterolysis of Ph_2CHBr in acetonitrile the salts $Et_4N^+I^-$ and $Et_4N^+Br^-$ act on the space-separated ion pair, while

$Et_4N^+Cl^-$ and $Et_3(PhCH_2)N^+Cl^-$ act on the solvent-separated ion pair.[40,72]

When the rate of heterolysis in the presence of a salt reducing the rate of reaction depends on the Y—Vd˙ concentration, then it usually depends also on the nature of the substituent in the indicator, the rate increasing with enhancement of the electron-donating properties of the radical. This is associated with the idea that the reaction of the solvent-separated ion pair with Y—Vd˙ proceeds via electron transfer from the radical to the cationoid.[91—96] In the heterolysis of Ph_2CCl_2 in acetonitrile in the presence of chlorides, the rate of reaction increases with increasing Y—Vd˙ concentration but is independent of the nature of the substituent in the radical,[69] while in the heterolysis of Ph_2CHBr in acetonitrile in the presence of $Et_3(PhCH_2)N^+Cl^-$ the rate of reaction falls on enhancement of electron-donating properties of Y—Vd˙.[72] These data confirm the conclusion that the reaction between the solvent-separated ion pair and Y—Vd˙ proceeds in several stages.

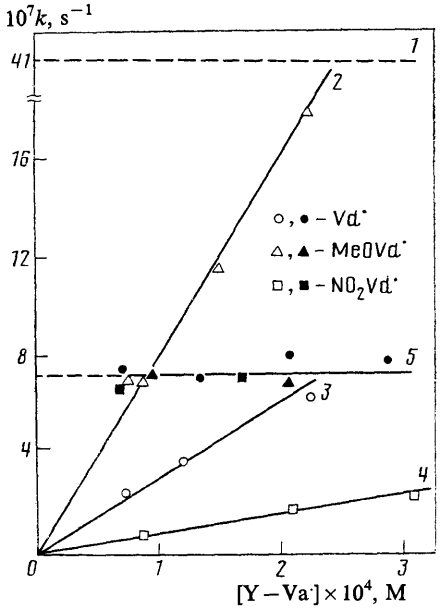


Figure 6. The influence of the concentration and nature of Y—Vd˙ on the rate of heterolysis of 1=AdOTs in γ-butyrolactone in the presence of 0.03 M $Et_4N^+Cl^-$ (lines *2—4*) and 0.03 M $Et_4N^+Br^-$ (line *5*) at 35 °C and in the absence of salts (line *1*).

The study of the k—[Y—Vd˙] relations in the presence of salts reducing the rate of reaction makes it possible to observe also fine differences between salt and solvation effects. Thus the rate of heterolysis of 1-AdOTs and 1-AdOPic in acetonitrile, γ-butyrolactone, and propylene carbonate in the presence of $Et_3(PhCH_2)N^+Cl^-$ or $Et_4N^+Cl^-$ increases with increase in the concentration of Y—Vd˙ and with increase in its electron-donating properties[52,54,56] (Figs. 6—9). Consequently the negative salt effect of the chloride is caused by the reaction of the salt with the solvent-separated ion pair. The addition of $Et_3N^+Br^-$ in the heterolysis of the substrates indicated in γ-butyrolactone and propylene carbonate also reduces the rate of reaction but only in the case of 1-AdOPic in γ-butyrolactone (Fig. 7) does the rate of reaction in the presence of this salt depend on the concentration and nature of Y—Vd˙. Consequently the verdazyl and the chloride act in all these cases on the solvent-separated ion pair, whereas the bromide ion acts on the solvent-separated ion pair in some instances and on the space-separated ion pair in others. On the other hand, in acetonitrile, where the positive salt effect o $Et_4N^+Br^-$ is manifested, the latter salt acts on the contact ion pair.

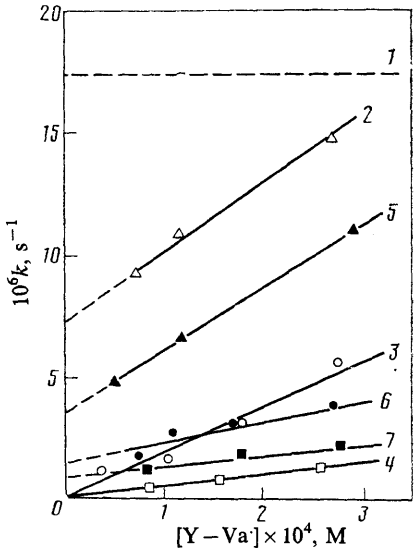


Figure 7. The influence of the concentration and nature of Y—Vd˙ on the rate of heterolysis of 1-AdOPic in γ-butyrolactone in the presence of 0.03 M $Et_3(PhCH_2)N^+Cl^-$ (lines *2—4*) and 0.03 M $Et_4N^+Br^-$ (lines *5—7*) at 25 °C [*1*, the heterolysis rate constant in the absence of salts]; verdazyl: *2* and *5*, $(MeO)_2$Vd˙; *3* and *6*, Vd˙; *4* and *7*, NO_2Vd˙.

Analysis of the nature of the salt effects in an aprotic medium[80] has shown that ClO_4^- acts on the contact ion pair, Br^- acts as a rule on the space-separated ion pair, while Cl^- acts on the solvent-separated ion pair, i.e. with increase in the hardness of the anion there is an increase in the tendency of the salt to react with the later intermediate—with the cationoid having a greater charge separation. Consequently the site where the salt acts during the ionisation of the covalent bond is determined by the principle of hard and soft acids and bases (HSAB), because an increase in the hardness of the carbonium ion is to be expected in the CIP—SPSIP—SSIP series.

The differences between the space-separated and solvent-separated ion pairs are apparently small and their negative activity in the reaction with the salt therefore depends greatly both on the structure of the substrate and on the nature of the solvent.[52,56,70—72,77—79] In the solvolysis of *p*-$MeOC_6H_4CHCl_2$ in aqueous dioxane, Cl^- acts on the space-separated ion pair, while Br^- acts on the solvent-separated ion pair,[78] which is caused by the inversion of the

nucleophilicity of the halide anion in water compared with the aprotic medium.

The application of the HSAB principle to the interpretation of the salt effects in unimolecular heterolysis reactions and other carbonium ion processes[131,132] makes it possible to explain why the catalytic effect in the carbonium generation process is manifested by the weakest nucleophile. This is associated with the fact that it begins to act in the earliest stages.

The application of the verdazyl method showed that, in the heterolysis of organic substrates, a superposition of the positive and negative salt effects is frequently observed.[52,54,56,65,68–71,73]

Figs. 8 and 9, where the $k-[Y-Vd^{\cdot}]$ relations are presented for the heterolysis of adamantyl substrates in acetonitrile in the presence of chlorides, show that the form of the $k-[Y-Vd^{\cdot}]$ curves for 1-AdOTs differs significantly from that for 1-AdOPic. In the case of 1-AdOTs (Fig. 8), an increase in the $Y-Vd^{\cdot}$ concentration results in the attainment of by k of the value of the rate constant for heterolysis in the absence of salts (indicated by a dashed line), after which k no longer changes on increase in the indicator concentration. In the heterolysis of 1-AdOPic, the value of the rate constant for heterolysis in the absence of salts is also rapidly attained as the indicator concentration rises, but in this case k continues to increase on further increase in the indicator concentration. This shows that in the latter case the negative salt effect is accompanied also by a positive salt effect, which is due to the action of the salt on the contact ion pair.

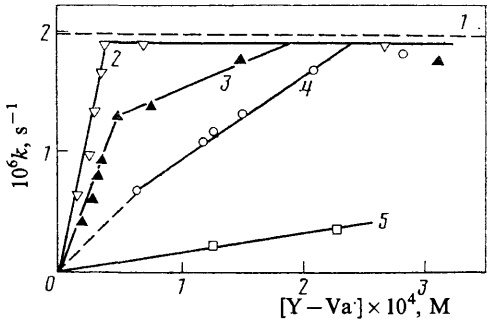


Figure 8. The influence of the concentration and nature of $Y-Vd^{\cdot}$ on the rate of heterolysis of 1-AdOTs in acetonitrile in the presence of 0.03 M $Et_4N^+Cl^-$ at 25 °C [*1*, the heterolysis rate constant in the absence of salts]; verdazyl: *2*, $(MeO)_2Vd^{\cdot}$; *3*, $MeOVd^{\cdot}$; *4*, $Vd^{\cdot}$; *5*, $NO_2Vd^{\cdot}$.

The superposition of the salt effects is manifested particularly well when one follows the influence of the salt concentration on the rate of reaction in the presence of the same concentration of verdazyls. Fig. 10 shows how markedly the manifestation of the salt effect changes as a function of the nature of the indicator in the heterolysis of t-BuBr in γ-butyrolactone in the presence of $Et_3(PhCH_2)N^+Cl^-$:[68,73] in the presence of $MeOVd^{\cdot}$, the salt hardly affects the rate of reaction, in the presence of $Vd^{\cdot}$ and $NO_2Vd^{\cdot}$ the rate of reaction falls with increase in the salt concentration, while in the presence of $(MeO)_2Vd^{\cdot}$ it increases. These relations can be explained by the superposition of the negative and positive effects of $Et_3(PhCH_2)N^+Cl^-$, the negative salt effect being due to the reaction in the salt (as well as the verdazyl) with the solvent-separated ion pair, while the positive effect is due to the reaction with the contact ion pair. In the presence of $MeOVd^{\cdot}$, both effects are approximately the same, in the presence of $Vd^{\cdot}$ and especially $NO_2Vd^{\cdot}$ the negative salt effect predominates, while in the presence of $(MeO)_2Vd^{\cdot}$, which traps the solvent-separated ion pair almost completely and hence suppresses the negative salt effect, the positive salt effect predominates.

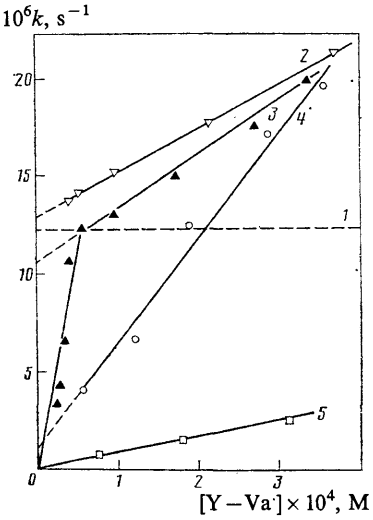


Figure 9. The influence of the concentration and nature of $Y-Vd^{\cdot}$ on the rate of heterolysis of 1-AdOTPic in acetonitrile in the presence of 0.03 M $Et_3(PhCH_2)N^+Cl^-$ at 25 °C [*1*, the heterolysis rate constant in the absence of salts]; verdazyl: *2*, $(MeO)_2Vd^{\cdot}$; *3*, $MeOVd^{\cdot}$; *4*, $Vd^{\cdot}$; *5*, $NO_2Vd^{\cdot}$.

It is seen from Figs. 8–10 that at certain $Y-Vd^{\cdot}$ concentrations the negative salt effect is completely eliminated. The relative reactivities of the verdazyl and the salt in the reaction with the solvent-separated ion pair were calculated from these data.[52,54,56,69,70–79] In the heterolysis of 1-AdOTs, 1-AdOPic, $PhCMe_2Cl$, and t-BuBr, the solvent-separated ion pair reacts ~2 orders of magnitude faster with the verdazyl than with the salt. This agrees with the hypothesis that $Y-Vd^{\cdot}$ reacts with the solvent-separated ion pair and not with the free carbonium ion. In the heterolysis of Ph_2CCl_2, the verdazyl and the chloride react with the sovent-separated ion pair at approximately the same rates.[69]

The decrease in the rate of heterolysis in the presence of a salt having a common ion is almost always explained by the salt effect caused by the Law of Mass Action, i.e. by the formation of a free carbonium ion [see Scheme (3)].[1,3,8,129] It was demonstrated above that such a decrease in the rate can be associated with the action of the salt on the solvent-separated or space-separated ion pair. The verdazyl method makes it possible to specify in a more concrete form the cause of the decrease in the rate of reaction in the presence of a salt having a common ion.

As an example, we shall consider the heterolysis of p-$MeOC_6H_4CHCl_2$. The rate of solvolysis of this substrate has been determined[117] in 75% aqueous dioxane from the formation of p-$MeOC_6H_4CHO$. It was shown that the addition of chlorides (LiCl, $Bu_4N^+Cl^-$) diminishes the rate of reaction; it was concluded that the reaction proceeds via the formation of a fre carbonium ion. The study of the kinetics of the solvolysis of p-$MeOC_6H_4CHCl_2$ by the verdazyl method under similar conditions showed that Cl^- and the verdazyl act on different intermediates.[78] If it is supposed that Vd$^\cdot$ reacts with the free carbonium ion, then Cl^- should react with the solvent-separated ion pair. On the other hand if Vd$^\cdot$ reacts with the solvent-separated ion pair, then Cl^- should react with the space-separated ion pair. Consequently, in the heterolysis of p-$MeOC_6H_4CHCl_2$ in 75% aqueous dioxane, Cl^- never reacts with the free carbonium ions; the observed decrease in the rate of reaction is caused by the negative salt effect associated with the reaction of the salt with the substrate ion pair. In the solvolysis of p-$MeOC_6H_4CHCl_2$, a free carbonium ion is not formed.[78]

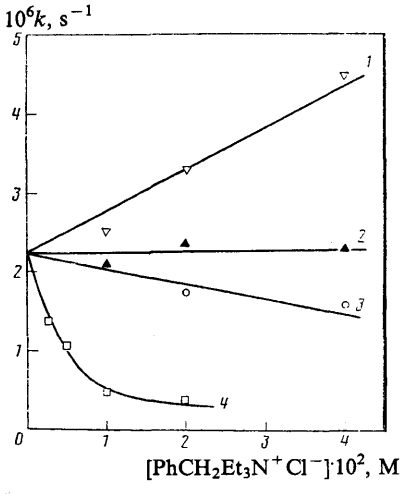


Figure 10. The influence of the concentration of $Et_3(PhCH_2)N^+Cl^-$ and of the nature of Y—Vd$^\cdot$ (3.2×10^{-4} M) on the rate of heterolysis of t-BuBr in γ-butyrolactone at 25 °C; verdazyl: *1*, $(MeO)_2Vd^\cdot$; *2*, $MeOVd^\cdot$; *3*, $Vd^\cdot$; *4*, $NO_2Vd^\cdot$.

The study by the verdazyl method of the salt effects in unimolecular heterolysis reactions confirmed the reaction mechanism represented by Scheme (24).

IV. Conclusion

The application of the verdazyl method to the study of the kinetics and mechanisms of S_N1, $E1$, and $N1$, and solvolysis reactions made it possible to reduce greatly the duration of the experiment and to obtain an extensive set of kinetic data which in many cases are inaccessible by other methods. These data have been used for the quantitative analysis of the solvation effects over a wide range of substrates. The application of the method to the study of S_N1 reactions has been shown to be especially effective. Other available methods for the study of the kinetics of these reactions generally yielded invalid results owing to the impossibility of taking into account the salt effects.

The application of the verdazyl method made it possible to investigate in detail the salt effects, to elucidate their nature, and to specify in detail the mechanism of the heterolysis of the covalent bond. For example, it has been shown that the conclusion that a free carbonium ion is formed, reached on the basis of the decrease in the rate of reaction in the presence of a salt with a common ion, is unjustified. In the study of $F1$ reactions, the verdazyl method proved to be an important complement to other procedures.

The verdazyl method has been widely tested.[18,21,22,27,29–80] The kinetics and mechanisms of the heterolysis of 21 substrates have been investigated with its aid. The results obtained for the solvation and salt effects have led to a new mechanism of the heterolysis of the covalent bond [see Scheme (24)] which includes the formation of a space-separated ion pair. It has been shown that the nature of the cationoid, which is subjected to nucleophilic attach by the salt anion, is determined by the principle of hard and soft acids and bases.

The verdazyl method is being vigorously developed at the present time. Further expansion and deepening of its possiblities should lead to significant mechanistic results.

The verdazyl method makes it possible to study the kinetics of the solvolysis of substrates, for example PhCOCl, which react via an S_N2 mechanism.[61] Verdazyls can also be used to study the kinetics of the photolysis of chlorohydrocarbons,[133,134] and for the selection of stabilisers for the latter.[135]

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Translated from *Uspekhi Khimii* **60** 2113–2142 (1991) U.D.C. 541.138.3–183; 543.253; 541.128; 547.484.34

The electroreduction of organic compounds in the presence of catalysts causing catalytic evolution of hydrogen and the electrosynthesis of chiral compounds

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ABSTRACT. **A critical examination has been made of the mechanism of catalysts (particularly alkaloids) of the electrochemical catalytic evolution of hydrogen in their effect on the electroreduction of various organic compounds and on the induction of optical activity when prochiral compounds participate. Particular attention has been paid to processes occurring at electrodes modified by chiral compounds and to the preparation of optically active products in media containing asymmetric cosolvents.**

The bibliography contains 98 references.

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I. Introduction

At the end of the sixties it was established by three groups of investigators, independently of one another in different countries, that catalysts causing the appearance on polarograms of currents of the catalytic evolution of hydrogen may also facilitate the electroreduction of certain classes of organic compounds. In addition, if the catalyst is optically active then when prochiral compounds participate in the electrode reaction the formation of enantiomers is possible, i.e. it is possible to effect asymmetric electrosynthesis during electroreduction or electrooxidation in the presence of such catalysts.

In spite of the significant number of studies devoted to such electrode processes their mechanism is still unclear. An attempt is made in the present review to bring together the results of the many investigations in this area and to discuss critically, in chronological order if possible, the development of the ideas of the various schools of investigators on the effect of catalysts on the catalytic evolution of hydrogen when facilitating the electroreduction of several classes of organic compounds and, in the case of prochiral substrates and optically active catalysts, on the mechanism of formation of enantiomeric products.

II. The nature of the electrochemical catalytic evolution of hydrogen

The phenomenon of the catalytic evolution of hydrogen in the polarograph was first revealed in the thirties by the well-known Czechoslovakian scientist Brdicka (for the history and nature of the phenomenon see the review[1]).

Brdicka discovered that the onset of cathodic polarographic waves in solutions of certain compounds is explained not by the reduction of these compounds but by the electrochemical evolution of hydrogen, which is facilitated (catalysed) in their presence. Such substances are organic bases (B), containing heteroatoms with an unshared pair of electrons (nitrogen, phosphorus, oxygen, sulphur, arsenic, etc.) which may add a hydrogen ion (from any proton donor DH^+) and form onium cations.

$$B+DH^+ \rightleftarrows D+BH^+ . \quad (I)$$

The onion cations BH^+ may decompose on the electrode (transfer of the electron usually occurs reversibly) with the formation of particles having the character of free radicals.

$$BH^+ + e^- \rightleftarrows BH^\cdot . \quad (II)$$

The bimolecular reaction of these radicals[1] leads to the formation of a hydrogen molecule and regeneration of the catalyst in the base form.

$$2BH^\cdot \rightarrow 2B+H_2 . \quad (III)$$

Base B is once again protonated and the whole cycle is repeated so that the result of the process is discharge of the proton donor by the catalyst with the formation of hydrogen. Cations such as H_3O^+, NH_4^+, uncharged molecules such as H_2O, CH_3COOH, etc. and anions able to give up a proton, such as $H_2PO_3^-$, may act as donors.[1]

III. First observations of the phenomenon

As already mentioned, the catalysts indicated also facilitate the electroreduction of certain classes of organic compounds. Grimshaw and collaborators[2] showed that the waves of the electroreduction of coumarin and 4-methylcoumarin in citrate buffer solution in the presence of alkaloids (narcotine, nicotine, codeine, brucine, sparteine

and yohimbine) became less negative, while under preparative electrolysis conditions the yield of the dimeric pinacol falls in the majority of cases but the yield of the secondary alcohol, dihydrocoumarin, is increased compared with experiments in the absence of alkaloid.[2] On the basis of the scheme outlined above for the catalytic evolution of hydrogen it was proposed[2] that the radical BH· formed by reaction (II) transfers a hydrogen atom to the intermediate reduction product of the ketone, a free radical, which enables the yield of secondary alcohol to be increased as a result of the fall in yield of pinacol. It was shown in the same study[2] that in several cases the alcohol obtained was optically active. The difference in the action of the alkaloids studied was explained by their different adsorbability to the electrode surface.

It was shown by us[3] that the products of electroreduction of aromatic nitroalcohols, viz. the corresponding hydroxylamines and amines, accelerate the electroreduction of the starting material so that the process is autocatalytic. The acceleration of the electroreduction of nitroalcohols by certain amines (pyridine, 2-picoline, 2,6-lutidine), amino acids (cysteine) and alkaloids (ephedrine, quinine) is explained[3] by the fact that the protonated form of the amine facilitates protonation of the depolariser. It was shown[3] in separate experiments by adding tetraalkylammonium salts that the shift in the reduction wave of nitro compounds, observed in the presence of amines, in the direction of less negative potentials in this case, was not linked with a change in the structure of the electric double layer on the electrode surface.

In subsequent work it was shown[4] that pyridine and diethylaniline accelerate the electroreduction of nitroethanol and also increase the first kinetic wave of the reduction of acetophenone which is observed on polarograms in a medium with a sufficiently high proton-donating activity, such as in acetate buffer solutions of pH greater than 5.0.[5] These phenomena were explained[4] by acceleration of the protonation reaction during electroreduction of the compounds indicated by catalysts causing the catalytic evolution of hydrogen. It was established in separate experiments[4] that these catalysts may facilitate the electroreduction of organic compounds by accelerating the protonation reaction occurring both on the electrode surface and in the bulk of the reaction layer.

Horner and collaborators showed[6] that in the electroreduction of acetophenone in methanol solution containing optically active ephedrine hydrochloride (at a concentration of 0.5 M) as electrolyte the corresponding alcohol was obtained with an optical activity of 5%. The pinacol formed (yield 40%) possessed no optical activity.[6] It was proposed that ephedrine adsorbed on the electrode influenced the reduction. On reducing the ephedrine concentration to 0.3 M the optical activity of the alcohol was reduced to 3.1%, but was unchanged on increasing it to 1 M. The effect of changing the temperature from −20 °C to boiling the solution on the optical purity of the resulting alcohol was also studied.[6] This effect proved to be maximal at 25−35 °C.

IV. Effect of various factors on the facilitation of electroreduction and the induction of chirality

After the short communications,[2,6] more detailed papers followed from the same authors[7–9] in which details of the investigations carried out were given, and some new data were presented. In one study[7] the electroreduction of 5-methoxy-4-methylcoumarin in the presence of the same set of alkaloids was also reported.

The reduction of acetophenone N-benzylimine in the presence of tetrasubstituted chiral ammonium salts, of the type of trimethylbenzylammonium iodide or dimethylated (at nitrogen) ephedrine, leads to the amine or to the dihydro dimer depending on the conditions.[8] Amines with an optical purity of 5−7% were obtained on electrolysis. Most investigations have been conducted with aliphatic-aromatic ketones, and the effect of the alkyl chain length of the alkyl aryl ketone on the ratio of the resulting pinacol and alcohol has been studied.[9] In methanol solutions containing tetramethylammonium salt as base electrolyte, the yield of alcohol grew with an increase in alkyl chain length at the expense of a reduction in the yield of pinacol.

The effect has also been studied of the length of the alkyl chain of the alkylammonium salt on the yield of hydrodimer in the electroreduction of cinnamic acid ester.[10] The results of these studies are summarised in a review.[11]

Subsequently Horner and collaborators showed[12] that inversion of the absolute configuration of the catalyst−inducer led to inversion of the configuration of the alcohol obtained. The optical purity and configuration of the alcohol may change depending on the extent of methylation of the ephedrine nitrogen atom (a maximum optical activity of 13.9% was achieved with completely methylated ephedrine). On replacing the hydroxyl group of ephedrine by hydrogen the optical purity of the resulting alcohol was reduced but the configuration was retained. These data are correlated in a review,[13] but a detailed description of these and other experiments is contained in the thorough paper of Horner and Degner.[14] In particular it was recorded that methylation of the ephedrine nitrogen atom permits not only an increase in optical purity but also inversion of the configuration of the resulting carbinol. It is interesting that introduction of a hydroxyl group into the position β to the quaternary nitrogen atom of desoxyephedrine leads to a change in the configuration of the alcohol obtained.[14] It was also shown that the pinacol formed on reduction of acetophenone in the presence of chiral inducers did not possess optical activity. In the presence of tetrasubstituted ammonium salts and ephedrine the *meso*-form of the pinacol is mainly formed while in the presence of ephedrine hydrochloride the DL-form results almost exclusively. The absence of optical activity for the pinacol prompted the authors to consider that the chirality is induced at the transfer of the second electron (and proton) to the ketone molecule.[14]

These studies served as a stimulus for similar investigations in several other laboratories. Particularly major contributions in this direction have been made by the French scientists Jubault, Raoult, Hazard and Tallec and also by Kariv, Miller and Gileadi (Israel) and recently by Wendt (FRG) and Nonaka (Japan).

In the preparative electroreduction of acetophenone in acetate buffer in methanol as base electrolyte in the presence of alkaloids, the yield of alcohol was increased with a concomitant reduction in the yield of pinacol, which may be explained by the inhibition of radical dimerisation by the adsorbed alkaloid.[15] The phenylethyl alcohol formed in the presence of alkaloids possessed optical activity, the maximum optical yield (14.9%) being achieved in the presence of quinine. Comparison of the optical yields achieved in the presence of quinine and quinidine on the one hand and cinchonine and cinchonidine (this pair differs from the first by the absence of a methoxyl group in the quinoline ring) on the other, showed that in the presence of alkaloids having no methoxyl group the yield was significantly less. This was linked[15] with the weaker adsorbability of the latter (although the adsorbability of the alkaloids was not assessed in this study). It was considered[15] that a specific interaction

took place between the adsorbed alkaloid and the reactant on the electrode which caused the appearance of optical activity in the product. The fact that in the presence of alkaloids of the opposite configuration, as in the pairs indicated above, the sign of the rotation of the products is reversed was considered as confirmation of this conclusion. Under the conditions of the experiments,[15] electro-reduction occurred up to potentials of the onset of catalytic evolution of hydrogen consequently the authors[15] doubted the hypothesis of Grimshaw and collaborators[2,7] on the transfer of hydrogen from the catalyst to the free radical of the ketone.

Subsequently the same authors[16] studied the electroreduction of acetophenone in the presence of several alkaloids and particularly in the presence of quinidine in aqueous methanolic acetate buffer solutions (pH 4.8). In these experiments quinidine was first reduced electrochemically to a mixture of products of hydrogenation of the nitrogen-containing quinoline ring, the methoxyl group remaining unaffected. In the presence of hydrogenated cinchonine the polarographic wave of acetophenone was shifted somewhat towards negative potentials while the catalytic wave of hydrogen in the presence of acetophenone became less negative. While criticising the mechanism of action proposed by Grimshaw and collaborators for the catalyst it was indicated[16] that the catalytic evolution of hydrogen sets in at more negative potentials than the electro-reduction of acetophenone itself. However, it follows from Fig. 1[16] that even in the absence of acetophenone at a potential of −1.8 V (at which the greatest optical yield of alcohol is observed) the catalytic current for hydrogen is about 10% of the limiting current of the acetophenone wave, and as already mentioned acetophenone markedly facilitates the catalytic evolution of hydrogen. It was shown[16] that methylation of the quinidine nitrogen atom sharply reduces the optical yield and changes the sign of the rotation of the resulting alcohol. Retention of the inducing ability of methylated quinidine is also considered as an argument against the criticised scheme for the process proposed by Grimshaw and collaborators.[2,7] However it is known[17,18] that on discharge of tetraalkylammonium cations containing different substituents on the nitrogen atom, one of the substituents is removed from the free radical (or is transferred to the substrate) and in this way a trisubstituted amine is formed, which is capable of being protonated and catalysing hydrogen evolution. In our opinion the change in sign of the rotation of the product is probably explained by the formation of such an amine, which may differ in conformation from the initial alkaloid, or by the alkylation of the substrate. In addition the free radical formed on discharge of tetrasubstituted ammonium may serve as the transferer of the electron.[18,19]

The fission of alkyl on discharge of a completely alkylated amine apparently does not always occur. As long as fission of alkyl and protonation of the dealkylated catalyst does not occur then the action shown by the completely alkylated catalyst is caused by the creation of an asymmetric field near the substrate on formation of a hydrophobic adduct between them. The significantly lower optical yield observed in this situation is seemingly achieved on transfer of a hydrogen atom from the discharged protonated amine, within the restrictions of its adduct with the substrate.[16] The completely alkylated inducer may serve only as the transferer of an electron from the electrode to the substrate. The change in sign of the rotation of the product, on reduction of the substrate in the presence of completely alkylated amine,[16] may be explained by the fact that protonation of the substrate anion-radical in its adduct only occurs at the expense of proton donors of the solution, which evidently approach the substrate from the side opposite the inducer. The strength of the asymmetric field generated by the alkylated alkaloid on that part of the adduct opposite to it where proton is being added from the solution is markedly less than when proton is added from the alkaloid itself. Consequently the optical yield on induction by an alkylated alkaloid is significantly less than in the case of a protonated alkaloid.

The absence of a correlation between the ability of various alkaloids to catalyse the evolution of hydrogen and the size of the optical yield was also considered[16] to be an argument against the mechanism proposed.[2,7] However it is relevant to emphasise that only in the case of simple catalysts causing volume catalytic waves of hydrogen was a link successfully established between the structure of the catalyst (more precisely its pK_a) and its ability to catalyse the evolution of hydrogen (see Ref. 1, p. 244). In the case of catalysts of complex structure, such as alkaloids, that link has not yet been successfully established.

The effect of the potential of the mercury cathode during electrolysis on the optical yield of alcohol and the alcohol : pinacol ratio has been studied.[16] The maximum optical yield (up to ~17%) was observed at −1.8 V (relative to a mercury sulphate reference electrode). Maximum adsorption of the acetophenone–catalyst complex was achieved at these same potentials,[16] while maximum yield of alcohol was obtained at the very negative potential of −2.10 V. The optical yield was increased on reducing the temperature which is linked with the increase in adsorbability of the complex indicated.

Study of the electroreduction of acetophenone in the presence of ephedrine showed that in strongly acidic and strongly basic media the optical yield falls and an inversion of its configuration occurs compared with the product obtained at medium pH values. This is explained by the fact that at extreme pH values protonation occurs at the expense of proton donors in solution and in the region of medium pH at the expense of protons from ephedrine (in strongly acidic medium acetophenone itself is protonated and in alkaline ephedrine is in the base form). Other conditions being equal, an increase in optical yield of the carbinol occurs on reducing the dielectric constant of the medium (water–methanol, methanol, methanol–isopropanol), which is linked with the increase in stability of the ephedrine–acetophenone complex in which proton transfer occurs. It was noted that replacement of the mercury cathode by lead did not change the optical yield of alcohol.

Phenylglyoxylic acid was used as a subject for reduction for the first time by Jubault, Raoult and Peltier to study the influence of alkaloids on the induction of optical activity.[21] Unlike acetophenone this acid is reduced over a wide pH range directly to phenylglyoxylic alcohol (with $n = 2$) and the process takes place at less negative potentials. This circumstance and also the absence of dimer significantly facilitate the study of the mechanism of the process. The effect of the nature of the alkaloid (15 different inducers were taken) on the optical yield of the product has been studied in detail.[22] In general the greater the adsorbability of the alkaloid-inducer the greater was the optical yield, other conditions being equal. However a specific effect of the alkaloid also became apparent. Thus the strongly adsorbed narcotine induced practically no optical activity but strychnine acts almost twice as strongly as brucine while showing approximately the same ability to be adsorbed.[22] A detailed study of the effect of various factors on the optical yield led the authors to the conclusion[22] that the process of inducing optical activity occurs with the participation of the inducer adsorbed on the electrode and all the factors aiding its adsorption lead to an increase in the optical yield of product. For example,

with an increase in the temperature of the experiment and on adding an organic solvent to the solution (both reduce adsorption of the alkaloid) the optical yield was reduced. The addition of quinine, which is strongly adsorbed under these conditions but is not an inducer, to the inducer (strychnine) also reduces the optical yield by displacing strychnine from the electrode surface. The dependence of the optical yield of product on the alkaloid concentration is close in shape to the adsorption isotherm of the alkaloid. This also confirms the important role of catalyst adsorption in the induction of optical activity. As already mentioned[22] it is apparently true[15] that the induction of optical activity occurs on forming a complex between the inducer and the substrate itself or an intermediate in its reduction, such as the anion-radical or free radical. The preparation of an optically active product, L-menthyl (*S*)-mandelate, on electroreduction of phenylglyoxylic acid ester with L-menthol in the absence of other inducers points in favour of that hypothesis.[21] In the latter case the induction of optical activity is provided by the asymmetric field of L-menthol.

It must however be noted that the maximum optical yield when reducing phenylglyoxylic acid in the presence of strychnine is observed at a strychnine concentration of 10^{-3} M, at higher concentrations the optical yield falls.[12] A similar phenomenon has been explained[15] by 'association of the alkaloid'. Seemingly this effect is caused either by inhibition of the process due to the formation of a dense film of alkaloid adsorbed on the electrode,[23] or by double-layer adsorption of the alkaloid,[24] which hinders the formation of a complex between the substrate and the alkaloid.

The optical yield depends markedly on the pH of the medium.[22] When reducing phenylglyoxylic acid in the presence of strychnine it is maximal in pH 4.8 acetate buffer solution and gradually falls to zero in strongly acidic and strongly alkaline media. It is claimed that this is linked with hindrance of the formation of a complex between the inducer and one of the forms of the substrate in these media. It must be noted that in the case of the reduction of acetophenone in the presence of ephedrine, passing from a strongly acidic to a strongly alkaline medium leads only to a change in the sign of rotation of the product.[20]

Several valuable recommendations have been made[22] for preparative asymmetric reduction. The benefit of agitating the surface of the mercury cathode (i.e. cleaning it) and of introducing the substrate into the electrolyser in appreciable portions was particularly noted.

Jubault and collaborators[25] have analysed the effect of various alkaloids on the shape of the reduction curve of phenylglyoxylic acid and showed that strongly adsorbed alkaloids such as strychnine at small concentrations (2×10^{-5} M) in weakly acidic media shift the reduction wave to a lower cathode potential, i.e. the electrode process is accelerated, while at large concentrations it is inhibited. On 'instant current–time' curves, taken during the life of the mercury drop, in the presence of low strychnine concentrations the current reaches a maximum value (corresponding seemingly to the achievement of adsorption equilibrium with the inducer), then is reduced somewhat and once again increases but more slowly (evidently due to the increase in the surface of the dropping electrode). The current is markedly greater in the presence of strychnine than in its absence. The authors explain this by the development of the ψ_1 effect, i.e. by a reduction in the potential fall beyond the Helmholtz plane and by the consequent increase in the actual potential difference between the electrode and reacting particles (see for example[26]), as a consequence of the adsorption of protonated forms of strychnine on the electrode. However, as follows from Fig. 1, the rise of the reduction wave current for phenylglyoxylic acid is observed at a potential of −0.63 V relative to a saturated calomel electrode (vs. SCE). On introducing 1.81×10^{-5} M strychnine into the solution the lower part of the wave is shifted to a less negative potential by approximately 30 mV. This wave is located close to the point of zero charge and all the values of the ψ_1 potential are in this case about 20 mV[26] (allowing for the fact that the potentials were given[26] relative to the normal calomel electrode). Seemingly the effects of the double layer, if they develop, play a secondary role in this case. In our opinion the reduction is facilitated by the interaction of the intermediate product with the protonated inducer or even with its uncharged form which transfer a hydrogen atom to the particle being reduced. In the first case the shift of the wave to a lower cathode potential is explained (see Ref. 1, p. 198 or Ref. 27) by linking the reduced form with a reversible redox system (in this case phenylglyoxylic acid, which is reduced reversibly judging by the shape of the polarogram in Fig. 1). An even more weighty argument in favour of the effects of the double layer not playing a decisive role in the acceleration of the electrode process in the present case are the data[25] that the $i-t$ curves of the reduction of phenylglyoxylic acid methyl ester in acetate buffer are increased sharply in the presence of strychnine at a potential even more positive than the point of zero charge, when the ψ_1 potential, although small, is positive. In addition, it is known (for example, Chapter VII, Ref. 28) that transfer of the first electron to the carbonyl-containing compound is reversible in many cases and the structure of the double layer does not affect reversible electrode processes. As already mentioned above, the shape of the reduction wave of phenylglyoxylic acid (Fig. 1) corresponds to a reversible transfer of an electron in the potential-determining step of the process.

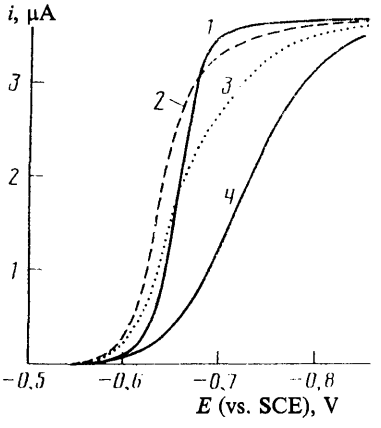


Figure 1. Polarogram of the reduction of phenylglyoxylic acid (5×10^{-4} M) in 0.5 M acetate buffer (pH 4.8) in the presence of strychnine at concentrations (10^{-5} M): *1*, 0; *2*, 1.81; *3*, 2.94; *4*, 16.7.[25]

It is interesting that the addition of alkaloids proved to have no marked effect on the reduction of *p*-nitrobenzoic and picric acids which seemingly indicates some specificity in the reaction of

substrate and inducer. On the other hand strychnine accelerates the reduction of pyruvic acid.[25]

Proceeding from the hypothesis that the formation of an adduct between the substrate and an asymmetric inducer is necessary for the induction of optical activity in an electroreduction product, Jubault and collaborators[29] selected as a model for thorough investigation the phenylglyoxylic acid ester of (−)-menthol in which the asymmetric inducer is one part of the molecule and the prochiral substrate being reduced is the other. In the majority of cases the (*R*)-conformer of mandelic acid menthyl ester predominates in the products of electroreduction of this ester. Its optical yield depends markedly on the pH of the medium,[29] it is maximal (20.6%) in 1 N H_2SO_4 and falls with increasing pH, it passes through a minimum at pH 3−4 and increases once again in neutral and alkaline solution. It is important to note that addition of di-n-butylamine in ammonia buffer solution increases the optical yield from 19.8 to 30%, while a tetrasubstituted ammonium salt reduces the yield under these conditions to 5%. The effect of pH is explained by competition between the reactions of protonation of the intermediate anion-radical and its transformation with inversion of configuration. Naturally the rate of protonation is highest in acid solutions. Protonation also explains the effect of dibutylamine added to the alkaline solution which forms an adduct with the anion-radical in which proton transfer is effected. A similar mechanism, in the opinion of the authors,[29] also takes place in electroreduction in the presence of inducer-alkaloids. The inhibitory action of tetra-alkylammonium cations is explained[29] by displacement of the particle being protonated from the electrode surface. It was established[29] that the maximum optical yield is observed on electrolysis in the vicinity of the zero charge potential. At higher negative potentials the optical yield is reduced which is explained by acceleration of the (*R*)→(*S*) transformation of the anion-radical by the electrode field.[29] The increase in optical yield in acidic medium on increasing the intensity of stirring the solution in the electrolyser is linked with the additional supply of proton donors to the electrode surface where their concentration is reduced as a result of their reaction with the substrate.[29]

Most interesting results were obtained subsequently by Raoult, Jubault and Peltier[30] in a detailed study of the effect of strychnine and *N*-methylstrychnine (which is devoid of proton-donating ability) in the electroreduction of phenylglyoxylic acid, its methyl ester, the two oximes of the acid (*anti* and *syn*), the two isomeric oximes of the methyl ester and the phenylhydrazone of the acid. The introduction of alkaloid into the polarograph solution of the compounds indicated changes the shape of the polarograms, which is a reflection of the change of the kinetics of the individual stages of the process. Reduction of the keto group requires altogether the participation of two electrons and two protons and is accompanied by the formation of a secondary alcohol. The oximes are reduced with the participation of four electrons and protons to primary amines. The preferred configuration of the product, in the authors' opinion,[30] is determined either by stereoselective protonation of the intermediate reduction product, the anion-radical, with an optically active proton donor, the inducer (as also proposed[5,31]), or by the substrate-inducer interaction[14,22,25,29] which, in the authors' opinion,[30] is preserved during many stages of the process. The formation of an adduct with the optically active inducer determines the preferred configuration of the product and the nature of the proton donor plays no role in this case.

In acidic medium (1 N H_2SO_4) addition of increasing quantities of both strychnine and methylstrychnine to the solution leads to a shift of the $E_{1/2}$ of waves of all the compounds studied to a more negative potential. The greatest shift is observed at small concentrations of additive but with its growth the size of $E_{1/2}$ tends to a limit. The displacement of the $E_{1/2}$ of waves for the reduction of the keto group is far greater than for the oxime. It is evident that under these conditions (i.e. at an excess of a strong proton donor) both additives inhibit the electrode process by blocking the electrode surface on which their adsorption depends.

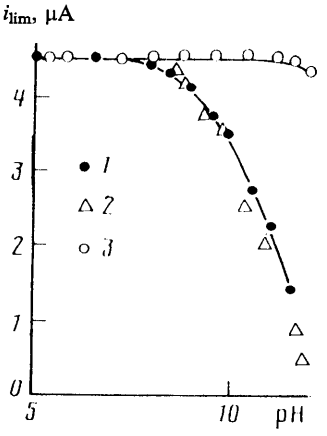


Figure 2. Effect of pH on wave height in the reduction of the oxime of phenylglyoxylic acid ester (5×10^{-4} M) in Britton-Robinson buffer solutions (with 10% ethanol). *1*, Without additions; *2*, in the presence of 9×10^{-5} M methylstrychnine; *3*, in the presence of 9×10^{-5} M strychnine.[30]

In the case of the oxime of phenylglyoxylic acid ester at a solution pH above 7, strychnine and also ammonium ions facilitate reduction while methylstrychnine has almost no effect on the polarograms. It is important to note that in the absence of additives at pH values above 7, a reduction is observed in the wave height for this oxime and it acquires a kinetic character. Methylstrychnine has no effect on the height of the kinetic wave while strychnine increases it to the level of the diffusion current (Fig. 2). The latter effect is caused by the proton-donating properties of protonated strychnine, the strychninium ion. The same properties explain the appreciable displacement of $E_{1/2}$ of the reduction wave of the oxime ester to a lower cathode potential in neutral media on introducing strychnine into the solution. At pH > 10 the $E_{1/2}$ of this wave in the presence of strychnine was almost the same as in the absence of additives or in the presence of methylstrychnine.[30] In weakly acidic medium both strychnine and methylstrychnine inhibit the process, the action of the latter being much stronger. It is interesting that the pK_a of the strychnine cation is 7.4 since with an increase in pH above 7.4 the displacement of $E_{1/2}$ by strychnine is reduced.

In the reduction of the *anti*-oxime of phenylglyoxylic acid in pH 5.4 acetate buffer solution, the addition of strychnine (see Fig. 3) leads to a shift in the lower part of the wave in the direction of greater cathode potentials and simultaneously to the appearance of a more negative wave, which becomes less negative on increasing the

strychnine concentration and blends in with the main reduction wave. The unique wave emerging in the presence of strychnine proved to be far steeper and almost 1.5 times greater than in its absence (see Fig. 3). The authors[30] explain this phenomenon by the suppression of the surface protonation of the oxime on adsorption of strychnine and by the increase of the wave by limited volume overprotonation of the oxime. In our opinion a change occurs in the mechanism of the process in this case. The strychninium cation is discharged and the radical formed transfers its hydrogen atom to the substrate,[2,4] reducing it. The change in the shape of the wave occurring in this way reflects the transition from an irreversible reduction of the oxime to a reversible discharge of the strychninium ion[1] (in this case $E_{1/2}$ of the catalytic hydrogen wave is about −1.1 V). The discharge of the strychninium ion is therefore the rate-determining step of the whole process.

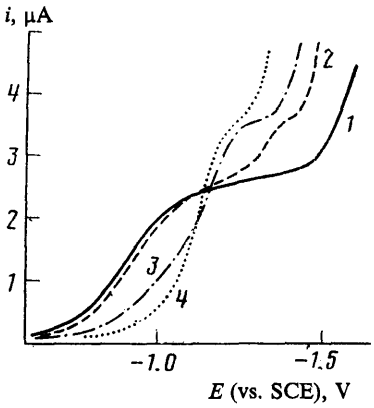


Figure 3. Polarograms of the reduction of the oxime of phenylglyoxylic acid in acetate buffer solution (without ethanol) at pH 5.4. *1*, Without additives; *2*–*4*, in the presence of strychnine (10^{-5} M); *2*, 1.5; *3*, 4.5; *4*, 10.[30]

In several cases facilitation of electroreduction was observed[30] on introducing methylstrychnine into a solution of certain compounds in pH 9.8 buffer containing Li cation (i.e. under conditions when there is no prior protonation) (Fig. 4). This was explained[30] by the formation of hydrophobic ('physical') positively charged complexes (more precisely adducts) between tetrasubstituted ammonium cation and the organic molecule,[32] which increases the substrate concentration close to the electrode.[33] It is however impossible to exclude the possibility that the observed shift is also linked with effects of the double layer since they are displayed in the case of the more cathodic waves on polarograms which may correspond to the reduction of both negatively charged ions, formed on dissociation of the substrate, and of the intermediate anion-radicals. For example, it follows from Fig. 4 that addition of methylstrychnine to a solution of the *anti*-oxime of phenylglyoxylic acid ester in Britton-Robinson buffer (pH 9.8) has practically no effect on the first wave but displaces the second wave appreciably, by almost 200 mV, to a less negative potential and simultaneously removes the fall in current after the first wave (evidently caused by the depolariser). Removal of the fall may be linked with an increase in adsorption of depolariser as a result of the formation by it of an adduct with methylstrychnine and the significant shift of $E_{1/2}$ of the second wave may be linked with the additional effect of a reduction in ψ_1-potential as a result of the adsorption of methylstrychnine cation.

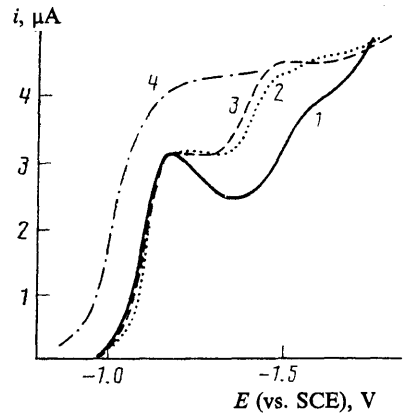


Figure 4. Polarograms of the reduction of the oxime of phenylglyoxylic acid methyl ester (5×10^{-4} M) in pH 9.8 Britton-Robinson buffer solution (with 10% ethanol and 0.01 M Li^+) of pH 9.8. *1*, in the absence and *2*, *3*, in the presence of methylstrychnine (10^{-5} M); *2*, 4.5; *3*, 5.0. *4*, Polarogram of phenylglyoxylic acid ester in 0.5 M ammonia buffer pH 9.8 with 10% ethanol.[30]

In our opinion, the increase in the region of the adsorption potentials of *p*-bromoacetophenone and tetraethylammonium salts when both are present in aqueous medium, described by van Tilborg and collaborators,[34] also indicates the formation of a strongly adsorbing adduct between them, although the authors considered[34] that adducts are not formed and the role of the R_4N^+ cation in facilitating reduction of the ketone is 'polarisation of the C=O bond on collision of R_4N^+ with the carbonyl group'. At very high concentrations of the tetraethylammonium salt, its cations, in the opinion of the authors,[34] displace the ketone from the electrode surface so that the ketone is situated on a layer of ammonium cations adsorbed on the electrode. This also shows the salts own action on the induction of asymmetric reduction on desorption of chiral cations on the electrode.

Subsequently van Tilborg and collaborators[35] studied the effect of tetraalkylammonium salts on the reduction of acetophenone in dry acetonitrile. A very interesting phenomenon was discovered. With LiF as base electrolyte acetophenone was not reduced down to a potential of −3.0 V. On adding a tetraalkylammonium salt to the solution a two-step reduction wave was observed. At a low concentration of R_4NClO_4 the height of the first wave of acetophenone changed with the growth in its concentration according to a curve reminiscent of the shape of the Langmuir isotherm. In the opinion of the authors[35] it therefore follows that reduction occurs only of adsorbed acetophenone. The dependence of the limiting current on the square root of the height of the mercury column implies kinetic limitation of the current. On increasing the

tetraalkylammonium salt concentration the limiting current becomes diffusion in character and changes in proportion to the acetophenone concentration. Judging by one study[35] the dependence of i_{lim} of the acetophenone wave on its concentration becomes nonlinear at values comparable with the concentration of tetraalkylammonium ions. In our opinion only the adduct of acetophenone with the R_4N^+ cation is reduced on the electrode under these conditions.[35] The kinetic character of the current at an excess of acetophenone is caused by R_4N^+ cations on the electrode surface, freed after reduction of acetophenone, combining with other acetophenone molecules diffusing from the solution. The comparatively low rate of formation of such adducts is evidently the reason for the kinetic limitation of the current.

It is also necessary to note the extremely interesting shape of the current intensity–time curves observed in several cases in the process of growth of the mercury drop.[30] When strychnine or methylstrychnine are present in the solution the reduction current of the oxime of phenylglyoxylic acid ester grows from the moment of formation of the mercury drop, reaches a certain limit, falls and then begins to grow once again (Fig. 5). The presence of the first maximum is evidently caused by the inhibition of the electrode process at complete coverage of the surface of the dropping electrode by the adsorbed additive. The subsequent rise in current when methylstrychnine is present is seemingly linked with the formation of hydrophobic adducts and their adsorption on the electrode which may compete successfully with the adsorption of the additive itself. When strychnine has been added to the solution, this rise in current may be explained by the development of a catalytic effect. Numerous examples of such a current increase are given in the studies considered above.

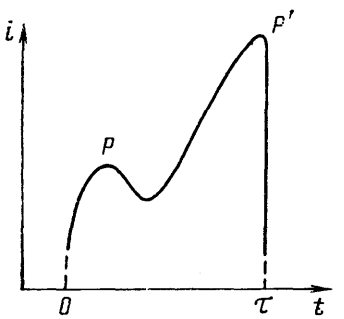


Figure 5. Diagram outlining the shape of $i-t$ curves at the time of the growth of the mercury drop in buffered solutions of phenylglyoxylic acid (and its esters and oximes) in the presence of strychnine and methylstrychnine.[30]

As already mentioned, the optical yield of product on reduction of phenylglyoxylic acid and its oximes in the presence of strychnine depends on the pH of the medium and on the electrode potential.[22,36] For example, on reducing both the *syn* and *anti* isomers of the oxime of phenylglyoxylic acid in acetate buffer in the presence of strychnine at a mercury cathode in the potentiometric mode at a cathode potential of −0.95 V (vs. SCE), the (*R*)-enantiomer of phenylglycine is formed in 17.1% optical yield.[36] On increasing the cathode potential the optical yield of (*R*)-enantiomer falls, reaching zero at −1.14 V, and on increasing the cathode potential further the (*S*)-enantiomer is formed predominantly. The optical yield of the (*S*)-enantiomer increases with the potential and reaches 11.1% at a potential of −1.35 V.[36] As had been shown by Jubault,[37] the optical yield also depends strongly on the strychnine concentration (c_{str}). Using the example of the electroreduction at the mercury cathode of phenylglyoxylic acid and its *anti*-oxime in pH 4.7 acetate buffer solution, it was shown that the optical yield initially rose rapidly with an increase in c_{str} reaching a maximum at $c_{str} = 1 \times 10^{-4}$ M, and then fell slowly, moving towards a fairly constant value. It is interesting that the optical yield reaches its greatest values at an electrode potential of −0.85 V (vs. SCE) for the acid and −0.95 V for the oxime and was reduced to zero on further increasing the cathode potential. Under conditions of high strychnine concentrations ($c_{str} > 2 \times 10^{-3}$ M for the acid and $c_{str} > 2 \times 10^{-4}$ M for the oxime) even the sign of rotation of the resulting mixture of enantiomeric products was changed. At low c_{str} and low cathode potentials (*R*)-(−)-mandelic acid and (*R*)-(−)-phenylglycine respectively predominated and at larger cathode potentials and high c_{str} mainly the (*S*)-(+) enantiomers predominated (Fig. 6). This phenomenon is as yet unexplained. In our opinion, at high concentrations strychnine not only completely covers the electrode surface with a monolayer but is also adsorbed in a second layer, like quinine.[24] The complex of strychnine ion and substrate adsorbed on the electrode surface gives the (*R*)-(−)-enantiomer on reduction but in the second layer a different orientation of strychnine, in comparison with that on the electrode surface, is possible and it may interact differently with the substrate leading to an effect opposite to that on the electrode surface, i.e. to the formation of the (*S*)-(+)-enantiomer. As c_{str} is increased the quantity of strychnine in the second layer grows and its quantity in the first layer (directly on the electrode surface) remains unchanged. Consequently the quantity of (*R*)-form resulting remains unchanged and the proportion of (*S*)-form increases with the growth in c_{str}. This is reflected in the curves given by Jubault.[37] The optical yield approaches zero at not very negative potentials as c_{str} increases.[37] It may be proposed that in this case the formation of (*R*)-form in the first layer is compensated by the formation of approximately the same quantity of (*S*)-form in the second layer. As the cathode potential is increased at high c_{str}, polylayer adsorption occurs due to the electrostatic attraction for strychnine cations and the positively charged adducts of these cations with substrate molecules. This results in the quantity of adducts in the second and subsequent layers becoming greater than in the first layer and the proportion of (*S*)-enantiomer formed exceeds the proportion of (*R*)-form. A change of electrode potential when complex organic molecules, which are inducers, are adsorbed on it frequently causes reorientation of the adsorbed molecules, which may be displayed in the direction of the rotation of the plane of polarisation of the product formed on reduction. This may be an explanation of the extremely interesting observations described.[36,37]

Halogen atoms in organic molecules are apparently particularly prone to interact with tetrasubstituted ammonium cations with the formation of hydrophobic adducts.[38] Consequently on adding 1,1-dibromo-2,2-diphenylcyclopropane to an acid polarograph solution of the alkaloids strychnine, emetine, yohimbine and also methylstrychnine salts an appreciable shift is observed in the reduction wave of this compound to a lower cathode potential.[39] The electroreduction of the compound indicated occurs with the

overall consumption of $2e^-$, by the fission of bromine ion and by protonation of the intermediate anion. The $E_{1/2}$ potential of the reduction wave did not depend on pH and was −1.46 V (vs. SCE), however in the presence of alkaloids it became more positive when reducing the pH. On changing pH from 10 to 4 in the presence of strychnine, $E_{1/2}$ was displaced from −1.45 V (vs. SCE) to −1.25 V. An even larger shift was observed in the presence of emetine, viz. from −1.41 to −1.05 V, for the same change of pH. Methylstrychnine also facilitates the reduction, in its presence $E_{1/2}$ = −1.27 V and did not depend on pH. These phenomena were explained[39] by the interaction of the cationic form of the alkaloid with the depolariser. The fact that strychnine facilitates the reduction to a markedly greater extent than methylstrychninium and in its presence $E_{1/2}$ depends on pH, indicates an effect on the size of $E_{1/2}$ and on the kinetics of protonation of the intermediate. The formation of optically active electroreduction products indicates the important role of protonation when carrying out electrode processes. The (*R*)-enantiomer was formed in the presence of strychnine and emetine and the (*S*)-form in the presence of yohimbine. The optical yield was zero on introducing into the solution methylstrychnine, having no labile hydrogen.[39] In the presence of alkaloid the reduction of dibromide was facilitated both by the electrocatalytic action of the adducts formed with the participation of the alkaloid cation (by transfer of a proton of the inducer or a hydrogen atom from the uncharged alkaloid) and by the change in structure of the double layer, i.e. by a reduction in the absolute value of the ψ_1 potential in the presence of the strongly adsorbed cations (protonated alkaloids or methylstrychninium) which facilitate the irreversible electrochemical fission of the C−Br bond.

Kopilov and co-workers[31,40,41] have studied the electroreduction of the three acetylpyridines in aqueous alcoholic acetate buffer solutions in the presence of alkaloids. Both secondary alcohols and pinacols are formed when reducing acetylpyridines. In the presence of strychnine and brucine, 2- and 4-acetylpyridine give an optically active alcohol.[41] Only the racemate is formed from the 3 isomer. In all cases the pinacols were optically inactive. When reducing 2-acetylpyridine the maximum optical yield (31.2%) was achieved in the presence of brucine. In the presence of quinidine none of the acetylpyridines gave an optically active reduction product. It is interesting that addition of alkaloid to the 2 and 4 isomer markedly increased the yield of alcohol by reducing the quantity of pinacol formed,[31,41] while the yield of alcohol from 3-acetylpyridine was reduced in the presence of alkaloid. In the opinion of the authors[41] the stage determining the optical yield is the protonation of the intermediate by the chiral alkaloid present on the electrode surface in the cationic protonated state. In contrast to the 2 and 4 isomers the 3 isomer gives a stable zwitterion, the intermediate product of which is protonated not by the alkaloid but by the acid of the buffer solution.[41] The increase in the yield of alcohol from the 2 and 4 isomers in the presence of alkaloid also indicates the important role of protonation of the alkaloid in this process. In the case of the 3 isomer, when the alkaloid does not participate in the protonation, the yield of alcohol is markedly reduced in its presence.[41]

The effect of eleven different alkaloids on the electroreduction of the isomeric acetylpyridines has been studied.[31] The highest optical yield of alcohol was achieved in the presence of strychnine, viz. 47.5% for the 2 isomer and 41% for the 4 isomer. In all cases when asymmetric reduction occurred the (+)-enantiomer was formed. Only in the presence of yohimbine was the (−)-isomer obtained with yields for the 2 and 4 isomers for 5 and 4% respectively. The reduction products of the acetyl pyridines possessed no optical activity in the presence of quinine, quinidine, reserpine, eserine and ephedrine,[31] although, as already mentioned, some of these alkaloids are inducers of asymmetry when reducing other compounds. In our opinion, an important factor assisting asymmetric induction is the possibility of forming an associate between the substrate and the inducer which is evidently determined by the specificity of the interaction between them. This specificity is displayed in the varying shift of the $E_{1/2}$ potential of the polarographic wave of the reduction of alkyl bromides in the presence of tetrasubstituted ammonium salts, depending on the nature of the alkyl group.[42] It was also noted[31] that in those cases when asymmetric induction was observed, a marked increase occurs in the yield of alcohol at the expense of a reduction in the yield of pinacol, i.e. the formation of an adduct aids protonation of the intermediate reduction product by hydrogen from the inducer and also facilitates transfer of a second electron.

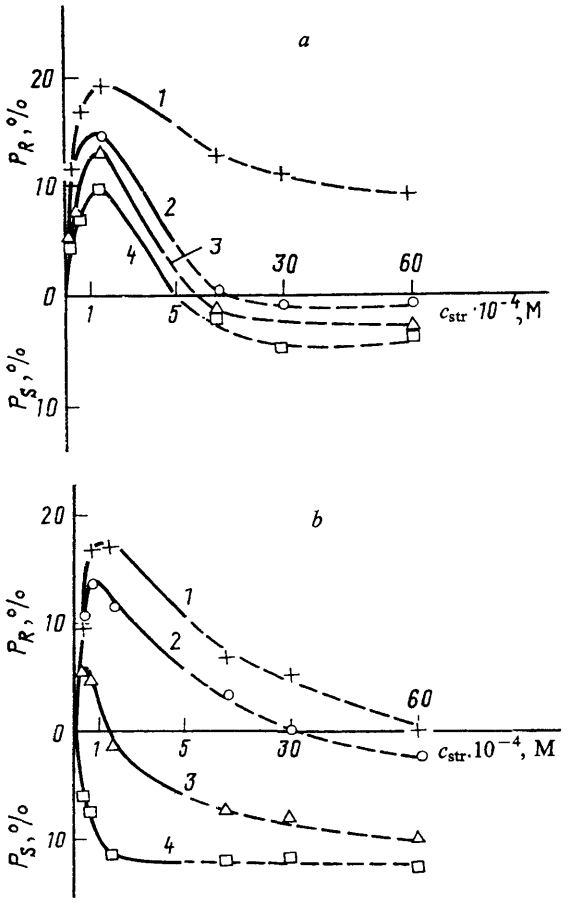


Figure 6. Dependence of enantiomer composition [%(*R*) and (*S*) forms] of the reduction products of (*a*) phenylglyoxylic acid and (*b*) its oxime in pH 4.7 acetate buffer solution on the concentration of strychnine (above c_{str} 0.5 mM the concentration scale is reduced 5-fold) at electrolysis potentials (vs. SCE, V) in (*a*) of *1*, −0.85, *2*, −1.10, *3*, −1.20, *4*, −1.30 and in (*b*) of *1*, −0.958, *2*, −1.05, *3*, −1.15, *4*, −1.30.[37]

A similar phenomenon was repeatedly observed in the reduction of acetophenone in the presence of ephedrine derivatives.[43,44]

A fairly detailed study of the effect of various factors on the optical yield and pinacol: secondary alcohol ratio in the electroreduction of acetophenone, particularly in the presence of methylephedrine[44] showed that the maximum optical yield of alcohol (18%), when carrying out electrolysis under previously selected standard conditions,[43] was achieved at a cathode potential of –1.37 V and falls to 12–13% on increasing the potential to –1.80 V, while the yield of product (alcohol) was increased by this from 14 to 70%. The reduction in optical yield with the growth in cathode potential is explained by the increase in the rate of direct transfer of the second electron to the radical and not to its adduct with the inducer. As proposed previously[14] optical activity is induced on transfer of the second electron. Maximum optical yield is achieved at solution pH 3.0.[44] The nature of the solvent also affects the optical yield of alcohol, the maximum value is observed on carrying out the electrolysis in ethanol. Addition of water to the alcohol or dioxan leads to a reduction in optical yield, the minimum yield occurring in pure aqueous solution. On reducing the temperature the optical yield grew again, the maximum (20%) was reached at –10 to –30 °C, but then was reduced once more.[44]

If the proton-donating ability of the inducer is eliminated, such as by complete methylation of ephedrine, and the electroreduction of acetophenone is carried out in anhydrous acetonitrile in the presence of this inducer, then the pinacol becomes practically the sole reduction product with an enantiomeric excess of 26.3%.[45] This, by the way, is the first case of the asymmetric synthesis of a pinacol. It is curious that in the presence of proton donors, i.e. under conditions when two radicals and not two anion-radicals react, the optical yield of pinacol is reduced to zero.[45] Asymmetric induction arises only on dimerisation of anion-radicals when at least one of them forms a tight ion pair with the inducer cation.[45]

As on reduction of phenylglyoxylic acid and its derivatives,[22,36] the maximum optical yield of pyridylethanol is observed at an electrode potential of –0.7 to –0.8 V and it is reduced at more negative potentials.[31] The optical yield of carbinol when reducing acetophenone in the presence of an inducer, such as substituted ephedrine, reaches a maximum (18%) at a potential of –1.37 V and is reduced somewhat with an increase in the cathode potential, although the overall yield of carbinol grows at the expense of a reduction in yield of the corresponding pinacol.[44] The optical yield also varies with the inducer concentration. In the case of strychnine it reaches a maximum value at $c_{str} = 5 \times 10^{-4}$ M. A reduction in temperature causes an increase in the optical yield,[31] which is seemingly explained both by an increase in adsorption of the components and by facilitation of the formation of an adduct between the intermediate reduction product and strychnine. A change in the alcohol content and replacement of ethanol by methanol and isopropanol in the mixture with aqueous acetate buffer has little effect on the optical yield of pyridylethanol, but addition of acetone sharply reduces the optical yield of the 4 isomer.[31] The relationships of the yield of both the 2 and 4 isomers of pyridylethanol to the solution pH pass through a maximum at pH 4.5, falling in more acidic and more alkaline solutions.[31] On gradually adding quinidine with strychnine to the solution the optical yield of alcohol was reduced continuously.[31] Quinidine itself is not an inducer of optical activity but its strong adsorption on the electrode aids displacment of strychnine and its adducts with the intermediates of acetylpyridine reduction. It was considered[31] that the alcohol becomes optically active at the stage of protonation of the product of the $2e^-$ reduction of the carbonyl group, viz. the enol (if the compound is protonated at the nitrogen atom) or the anion. Protonation proceeds through a hydrogen ion belonging to the strychnine cation which is on the electrode in the adsorbed state. Consequently strychnine methylated at nitrogen does not induce optical activity.[31]

It is important to note that the surface character of the chemical stage of the electrode process responsible for the induction of the optical activity requires specially pure reagents and mercury for the electrode.[40] Careful purification of all the components of the solution and the mercury, reducing the current density by increasing the surface of the mercury cathode, gradual dropwise addition to the electrolyser of the initial acetylpyridine solution[16] and reduction of the duration of electrolysis, i.e. use of all the factors reducing the effect of contaminants adsorbed on the electrode, led to an increase to 50% in the optical yields on electroreduction of 2- and 4-acetylpyridines in the presence of strychnine and to 80% in the total yield of alcohols.[40]

When studying the reduction of acetylpyridines in the presence of alkaloids, Wendt and collaborators[46] found that the reduction wave of 2-acetylpyridine in pH 4.5 acetate buffer solution after addition of 5×10^{-4} M strychnine became appreciably more positive and significantly more steep (Fig. 7). As correctly recorded,[46] this is linked with the proton-donating properties of the strychnine ion, which is adsorbed on the electrode and reacts with the intermediate product, the free radical.

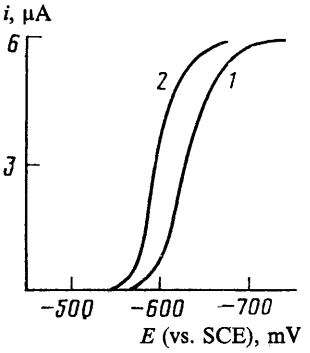


Figure 7. Polarogram of *1*, 2-acetylpyridine (1 mM) in pH 4.5 aqueous acetate buffer solution and *2*, the same in the presence of 0.5 mM strychnine.[46]

In our opinion it is not excluded that, simultaneously with the transfer of an electron (and possibly a proton as well) to acetylpyridine, discharge of the strychninium ion also occurs thereby increasing the steepness of the overall wave due to the reversible discharge of the strychninium ion[47] (see following Chapter).

V. The reversible character of the discharge of the catalyst and the features of the adsorption of organic compounds on the electrode surface

First some additional information is given on the mechanism of the catalytic evolution of hydrogen by organic catalysts and on the rules for the adsorption of organic compounds on electrodes.

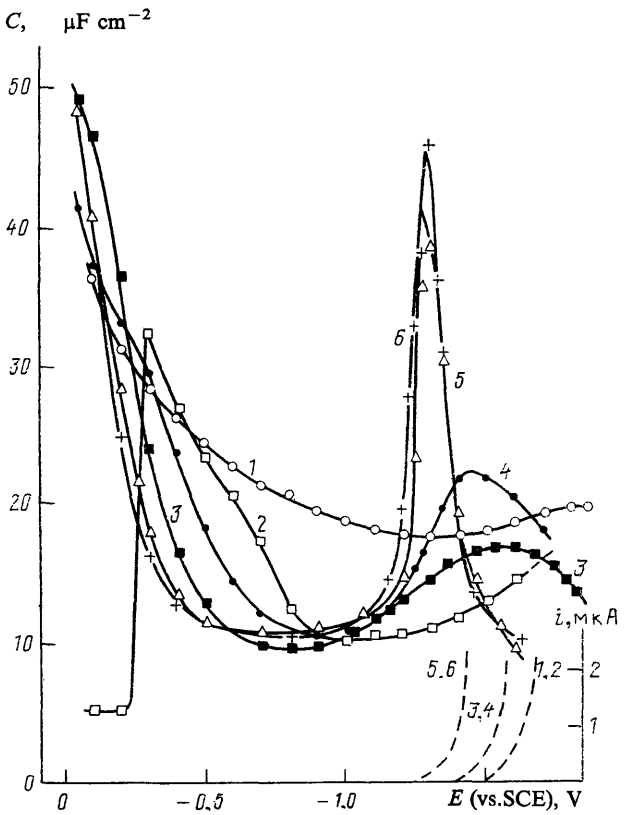


Figure 8. Differential capacity (C) curves (frequency of alternating current 179 Hz) for 0.1 mM alkaloid solutions in 0.5 M acetate buffer: *1*, buffer solution; *2*, *N*-methylstrychnine iodide; *3*, emetine; *4*, codeine; *5*, brucine; *6*, strychnine. Below are the initial portions of classical curves of the catalytic waves of hydrogen and buffer.[47]

As already mentioned at the beginning of this review, the transfer of an electron to the catalyst in the protonated form [i.e. reaction (II)] usually proceeds reversibly. The reversible character of the discharge process for pyridinium ions has been demonstrated.[48] The reversibility of electron transfer to a protonated molecule of the alkaloid pachycarpine on catalytic evolution of hydrogen into its solutions in buffer has also been proved.[49] The reversibility of the electron transfer step on catalytic evolution of hydrogen from buffer solutions of strychnine and brucine is indicated by the pseudocapacity peaks on the differential capacity curves (Fig. 8), which are caused by the discharge–ionisation process of the protonated form of the catalyst when applying an alternating current to the electrode. That the peaks mentioned are peaks of reaction pseudocapacity and not of adsorption–desorption is indicated by the correspondence of their potentials with the potentials at which the rise in current occurs in the catalytic hydrogen waves on classical polarograms obtained in solutions of these catalysts (curves in the lower portion of Fig. 8) and also by the drop in capacity after these peaks.

It is noteworthy that the catalytic hydrogen waves in buffer solutions of strychnine undergo a significant shift, with growth of the catalyst concentration, towards less negative potentials, of approximately 140 mV over a ten-fold increase in strychnine concentration (Fig. 9). There are several reasons for this. An increase in depolariser concentration always causes an earlier discharge of it, i.e. discharge at less negative potentials in the present case. In addition the subsequent bimolecular reaction in the catalytic cycle [reaction (III)] is sharply accelerated on increasing the catalyst concentration, which in its turn also leads to an appreciable shift of the reversible wave in the direction of less negative potentials.[50]

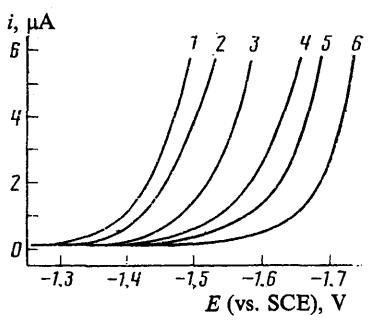


Figure 9. Classical polarographic curves for the catalytic evolution of hydrogen from buffer solutions with different strychnine concentrations (10^{-5} M): *1*, 50; *2*, 14.3; *3*, 6.52; *4*, 4.55; *5*, 2.38; *6*, 0.[47]

According to the theory of A N Frumkin[51] the adsorption of organic molecules on the electrode is maximal at the so-called potential of maximum adsorption (E_M) which is close to the zero charge potential of the electrode or the maximum of the electrocapillary curve. On moving the potential of the electrode both to the positive and to the negative side the adsorbability of compounds β falls according to the equation

$$\beta=\beta_0 \exp(-a\varphi^2), \quad (1)$$

where β_0 is the maximum adsorbability at potential E_M, φ is the potential measured from E_M, i.e. $\varphi = E-E_M$, a is a constant characteristic of each substance. The significant decrease in adsorbability of the catalyst, which depends on the extent of the difference between the electrode potential and E_M, is the reason for the characteristic hump-like shape of the surface catalytic hydrogen waves (see Chapter VI, Ref. 1 and Ref. 52).

The catalytic hydrogen waves become less negative at increased concentrations of strychnine. Under these conditions the adsorbability of strychnine is increased significantly which once again leads to an increase in the catalytic current and a shift in the wave to a less negative potential. The three factors indicated also

determine, in our opinion, the sudden shift mentioned above in the catalytic hydrogen wave in a buffer solution of strychnine on increasing the concentration of the latter, as follows from Fig. 9.

The gradual reduction in the quantity of catalyst adsorbed, which is observed on increasing the cathode potential, is the reason (see chapter VI, Ref. 1) for the fact that the slope of the semilogarithmic plots of the catalytic hydrogen waves is far greater than in the case of the usual reversible waves. The catalytic waves in buffer solutions of strychnine (Fig. 9) are an example. However under conditions of complete occupation of the electrode surface by the adsorbed catalyst, when there is no appreciable desorption, the slope of the semilogarithmic plot (in the absence of subsequent bimolecular reaction as takes place in the case of the catalytic hydrogen waves caused by pachycarpine) is 59 mV at 25 °C,[49] i.e. it corresponds to the value predicted theoretically.

VI. The mechanism of action of asymmetric inducers

Returning to the data on the effect of strychnine on the steepness of the reduction wave of acetylpyridine (Fig. 7) it is noted that discharge of the strychnine ion occurs at appreciably more negative potentials than acetylpyridine reduction. If the product of the reversible discharge of strychnine adsorbed on the electrode reacts rapidly with the product of electron transfer to acetylpyridine (i.e. with its anion–radical or, on protonation, with the radical)

$$StrH^+ + e^- \rightleftharpoons StrH^{\cdot}, \qquad (IV)$$

$$StrH^{\cdot} + AcPy^{-} \ (\text{or } AcHPy^{\cdot}) \rightarrow Str + AcHPy^{-} \ (\text{or } AcH_2Py)_2 \qquad (V)$$

then these interactions shift the discharge of strychnine to a lower cathode potential. Finally, the electroreduction of strychninium ions may also be facilitated by the formation by them of adducts with acetylpyridine. This was shown in the example of the catalytic hydrogen wave caused by cinchonine which becomes less negative in the presence of acetophenone.[16]

All the above-cited on the possibility of the start of discharge of protonated catalyst ions in the presence of substrate at far less negative potentials than in the case of the catalytic hydrogen wave in a pure catalyst solution, also explains the observation described above (Kariv and collaborators[15]) according to which the effect of the alkaloid on the reduction of the substrate is displayed up to the potential corresponding to the appearance of catalytic hydrogen wave.

It is necessary to note that the corresponding alcohol is formed in 47.5% optical yield in the preparative electrolysis of acetylpyridine in the presence of strychnine at the mercury cathode.[46] On a lead cathode, which is close in properties to mercury, a high optical yield is also achieved, while on a cadmium electrode, to which strychnine is almost not adsorbed, only racemic products were formed.[46] The factors aiding displacement from the electrode of starting materials and intermediates adsorbed onto it, such as the addition of a strongly adsorbing alkaloid or tetrabutylammonium salt, clearly reduce the yield of dimeric pinacol and as a result increase the yield of alcohol.[46] It is possible however to add that the electrolytes introduced into the solution not only displace starting materials and intermediates of their reduction from the electrode surface but often increase their solubility due to the so-called 'salting in' effect (see for example review[53]). The problem of the effect of the adsorption of organic substances on the kinetics and selectivity of their conversions both on a platinum anode and on a mercury cathode was considered even earlier.[54] The action of the inducer clearly grows due to a significant growth in its concentration in the reaction zone as a result of adsorption. The extremely thorough investigation of Koster, Wendt and Lebouc[55] is devoted to the role of the adsorption of components of the chemical reaction of protonation on the electrode in the kinetics of the electroreduction of prochiral compounds in the presence of inducers. The mechanism and kinetics of the electro-reduction of the three isomeric acetylpyridines on electrodes of various metals were studied. The reduction of the acetylpyridines on the dropping mercury electrode and, preparatively, on a large mercury cathode in the presence and absence of strychnine, tetrabutylammonium salts and camphoric acid were examined particularly carefully. The adsorbability of the acetylpyridines, of their reduction products and of strychnine on solid electrodes of various metals was also studied. At pH $\leqslant$ 10 the strychnine cation, which is as well adsorbed on a lead electrode as on mercury (or amalgamated copper), causes an intense catalytic evolution of hydrogen. Strychninium is adsorbed far more strongly than the acetylpyridines and their reduction products. A somewhat weaker adsorption of strychnine and a weaker action on the catalytic evolution of hydrogen was displayed when using bismuth and antimony cathodes. No adsorption of strychnine or catalytic hydrogen evolution was observed on cadmium and zinc electrodes.[55]

The effect of the nature of the cathode metal on optical yield when reducing in the presence of ephedrine methochloride was also studied by Horner and Schneider.[43] The optical yield of alcohol fell in the series Cd > Hg > Pb > Al > Sn, while the overall yield of the secondary alcohol fell along the sequence Pb > Cd > Al > Hg > Sn. The addition of strychnine to the electrolyser when reducing 2-acetylpyridine in acidic medium causes an appreciable shift in the current–potential curve, which has a quasi-reversible character, to a less negative potential on amalgamated copper and lead cathodes. A small shift in the same direction takes place on bismuth and antimony cathodes while strychnine showed no action on the completely irreversible wave for the reduction of 2-acetylpyridine on cadmium and zinc electrodes.[56] On polarography of 2- and 4-acetylpyridines in strongly acidic medium[55] the shape of the first one-electron reduction wave corresponds to a reversible process with subsequent surface dimerisation of the radicals formed, as observed in the reduction of 2-acetylpyridine in acidic medium at not very low concentrations (see final section of Chapter VIII, Ref. 1 and Ref. 56). All the facts given above indicate persuasively that the critical step of the process of inducing optical activity in the presence of an inducer is the interaction in the adsorbed state of the protonated inducer and the intermediate reduction product of the substrate, a ketyl radical in the present case.

It was recorded even in studies[31,40] that 3-acetylpyridine differs electrochemically from the 2 and 4 isomers. In particular the presence of strychnine does not affect the reduction of the 3 isomer and the product of its reduction is the optically inactive pinacol. With a view to clarifying the reason for the special position of the 3 isomer Koster, Wendt and Lebouc[55] studied the polarographic behaviour of all three isomers of acetylpyridine in DMF in the presence and absence of proton donors. The relative basicities of the ketyl radicals of all three isomers were assessed from the values of the half-wave potentials. It turned out that the basicity of the radical of the 2 isomer exceeded by seven orders of magnitude, and that of the 4 isomer by five orders, the basicity of the ketyl radical of the 3 isomer. The relatively low protonation rate of the 3 isomer ketyl radical is also the reason for the particular electrochemical behaviour of the 3 isomer compared with the 2 and 4 isomers. In

view of the low basicity of the 3-acetylpyridine ketyl radical the comparatively strong camphoric acid was very wisely used as inducer and proton donor.[55] In its presence a small shift was observed in the reduction wave of 3-acetylpyridine to a less negative potential which seemingly must lead to the formation of an optically active product in preparative electrolysis. In fact in a subsequent study an optically active product, though in low optical yield (7%), was successfully obtained by the same authors[57] in the preparative electrolysis of 3-acetylpyridine in the presence of camphoric acid. Data are given in the same study on the preparative electrolysis of 2- and 4-acetylpyridines on the mercury and some solid electrodes in the presence of strychnine. Confirmation was obtained of the high optical yields of alcohol, particularly on a lead cathode, which had previously been observed by Kariv and collaborators.[16]

In a detailed review[58] Wendt showed, with numerous examples, the nature of the three main types of electrocatalysis in organic electrochemistry and considered in particular the catalysis with asymmetric inducers – proton donors.

Highly interesting experimental data and extremely valuable correlations and conclusions related to the mechanism of inducing optical activity when reducing organic compounds in the presence of chiral inducers are contained in the study by Hazard and collaborators.[59] The action of several alkaloids, viz. strychnine, strychnine methiodide, brucine, emetine, yohimbine, narcotine and sparteine, on the reduction of 1-mono and 1,1-dibromo derivatives of 2,2-diphenylcyclopropane was studied under various conditions. The highest optical yields of products (up to 44.3% in the reduction of dibromodiphenylcyclopropane) were obtained in the presence of emetine and the lowest in the presence of narcotine and sparteine. It is interesting that in the presence of emetine the optical yield did not depend on the electrode potential nor on the pH of the medium. While noting the importance of the adsorption of the inducer, the authors[59] nevertheless stressed the absence, discovered previously,[22] of a correlation between the optical yield and the adsorbability of the inducer. The main factor determining the development of asymmetry in the reduction product was considered to be the formation of an adduct between the substrate and the inducer,[32,42] which is protonated after receiving an electron. This protonation of the anion-radical in the adduct by the asymmetric inducer (and most frequently with transfer of a proton from it[31]) determines the formation of the enantiomer. As was indicated, the shift of $E_{1/2}$ for the reduction wave of the bromocyclopropanes to a less negative potential, on adding an inducer to the solution being polarographed, points to the formation of an adduct. It must, however, be mentioned that in this case the shift of $E_{1/2}$ for the wave of the irreversible fission of the C–Br bond is determined to a known extent by the change in structure of the double layer on introducing into the solution cationic inducers adsorbing strongly to the electrode. Nevertheless, as follows from the Tables presented in that study,[59] in the presence of strychnine in fairly acid solution (so that strychnine is in the protonated form) the shift of $E_{1/2}$ for the reduction wave of the bromocyclopropanes to a less negative potential was appreciably greater than in the presence of methylstrychnine. This confirms the correctness of the conclusion[59] that an adduct is formed and a proton is transferred to it from the protonated inducer.

The appreciable increase in optical yield on going from a mono to a dibromo derivative of diphenylcyclopropane is extremely interesting.[50] This is seemingly due to the presence of two stereotopic positions in the molecule being reduced.[50] It has also been considered[59] that ion-pairs are generated in addition to the adduct formed by the inducer and the anion-radical (the intermediate reduction product). The preparation in certain cases of an optically active product (though in low optical yield) in the presence of methylstrychnine is explained by this.[59] It is noteworthy that the sign of the rotation of the product is in this case opposite to that of the reduction product in the presence of strychnine, other conditions being equal. This is due to protonation of the anion-radical in the presence of strychnine occurring with a proton from strychnine while in the presence of methylstrychnine the proton donor is in the solution and the proton approaches the anion-radical from the opposite side.[59]

1-Bromo-2,2-diphenylcyclopropane-1-carboxylic acid was one of the subjects of investigation.[59] This compound gives two waves on the polarogram and the second wave, having a kinetic nature in weakly acidic media, increases in the presence of inducers due to acceleration of protonation. It is interesting that in ammonium acetate solution the shift of $E_{1/2}$ for the waves of the bromides studied[59] is reduced on addition of inducers. Evidently this is caused by competition between ammonium and inducer ions both when forming adducts with the substrate and when building up the outer covering of the electrical double layer on the electrode.

The considerable experimental data contained in study[59] confirm the series of observations and conclusions made previously. The relationships of optical yield to the electrode potential and to the solution pH are, as a rule, described by bell-shaped curves (although in the presence of strychnine and brucine the yield grows with an increase in cathode potential). The highest yields were reached at comparatively low inducer concentrations and by reducing the temperature of electrolysis. The inversion occasionally observed of the sign of the rotation of the enantiomer on increasing the cathode potential is linked with the effect of the electric field on the anion-radical.[36]

It is interesting that the electroreduction of 2,2-disubstituted 1,1-dibromocyclopropanes in the absence of inducers in aqueous alcoholic medium on a mercury cathode with a two-electron fission of one C–Br bond occurs stereoselectively with the formation of the *cis* isomer, particularly if one of the substituents at the 2 position is hydrogen and the second $-CO_2H$ (or CO_2Me, CO_2Et). The yield of *cis* isomer exceeds 90% in the presence of tetraalkylammonium salts.[60]

Somewhat earlier Nonaka and collaborators[61] considered in detail the problem of the preferential formation of one diastereoisomer on electroreduction of ketones, having a chiral carbon atom and substituents of various size in the position α to the carbonyl group, in relation to the orientation of the initial ketone on its adsorption on the electrode.

Horner has analysed the mutual disposition of methylephedrine and acetophenone on the electrode in order to explain the induced asymmetric electroreduction. In the opinion of the authors a particular orientation of acetophenone on the electrode causes the formation of a chiral anion-radical on transfer of an electron from the electrode to the acetophenone molecule.[62]

On electroreduction of 4-carbethoxycoumarin in the presence of small quantities of alkaloids the 3,4-dihydro derivative is formed in almost quantitative yield and up to 20% optical yield. However dextrorotatory *o*-hydroxyphenyl monoethyl succinate is formed as a result of the reversible hydrolysis of the obtained laevorotatory lactone,[63] i.e. in time a change occurs in the direction of rotation of the plane of polarised light in the solution after electrolysis.

According to Klabunovskii (see Ref. 64, p. 4), the presence of a disymmetric component, which controls the process stereochemically,

in the transition state is necessary in order to obtain an asymmetric product. Such a component may be an optically active solvent or one of the components of a mixed solvent. Processes have been described for obtaining enantiomeric products when carrying out electrolysis in an optically active solvent. In the studies of Seebach and collaborators (for example Ref. 65) (*S, S*)-1,4-bisdimethylamido-2,3-dimethoxybutane (i.e. the tetramethylamide of dimethoxysuccinic acid) was used mixed with methanol as the optically active component of the solvent. The pinacol, enriched with the (*R,R*)-conformer, was obtained on electroreduction of acetophenone in this medium with lithium bromide as based electrolyte. It was shown[65] by special experiments by photolysis of the solution being electrolysed that the formation of the pinacol occurs at a certain distance from the electrode surface. The shape of the polarographic wave of acetophenone is described, as a rule, by an equation for the reversible transfer of an electron with subsequent dimerisation of the intermediates in the solution.[66] This indicates that the dimerisation of the intermediates of the reduction of acetophenone occurs within a certain volume of the reaction layer. In the opinion of Seebach and collaborators[65] complexes of anion-radicals (or radicals) with dimethoxysuccinic acid tetramethylamide (or its cationic form in acidic media) may emerge as such intermediates. The adsorption of the starting materials or intermediates accelerates the process significantly and aids the increase in optical yield of enantiomers but is not strictly obligatory. This is also indicated by the accelerating effect of pyridine, creating the volume catalytic hydrogen wave, in the electroreduction of aromatic carbonyl-containing compounds.[4]

The enantiomeric alcohol, albeit in very small optical yield (about 2%), was obtained on electroreduction of acetophenone in the presence of the potassium complexes of chiral crown ethers.[67] It is known that a crown ether may give complexes of the 'guest–host' type with organic molecules having an acidic hydrogen atom[68] as a result of the formation of hydrogen bonds between this atom and the oxygen positions of the cavity of the crown ether. However there are no sufficiently acidic hydrogen atoms in acetophenone for it to form a similar complex. The effect of the crown ether in this case may be explained by the fact that it is adsorbed on the electrode surface,[69] creating by its chirality a local asymmetric field near to which the asymmetric reduction of acetophenone occurs. It may also be proposed that the proton donors existing in the solution form a complex with the crown ether and thereby show an asymmetric action on the protonation of the anion-radical or radical. A water molecule, which often enters the cavity of a crown ether, may serve as such a proton donor.[70]

When reducing methyl acetoacetate in the presence of L-cysteine or cystine at a mercury cathode Nonaka and collaborators[71] obtained an enantiomer of 3-hydroxybutyric acid ester with an optical yield of about 1%. From citraconic acid under the same conditions (*R*)-(+)-methylsuccinic acid was successfully obtained with an optical yield of 2.4%. The use of (*R*)-(−)-benzylmethylphenylpropylphosphonium bromide as inducer in the reduction of phenylglyoxylic acid oxime in anhydrous and in aqueous methanol gave (*S*)-(+)- and (*R*)-(−)-phenylglycine respectively in optical yields in each case of about 1.9%.[71]

VII. The use of electrodes with a modified surface

The electroreduction of hexan-2-one on a powdery electrode, Raney nickel, occurs at −1.0 V (vs. SCE) with a yield on current of over 67% (on the mercury cathode reduction begins at a potential greater than −2.0 V).[72] On modifying such an electrode with optically active tartaric acid an enantiomer of hexan-2-ol was obtained in 2–6% optical yield. Heptan-2-one and octan-2-one were also reduced in a similar manner.[72]

The action of the chiral inducer must evidently be significantly enhanced if it is not adsorbed on the electrode surface but is chemically bound to it.[73] This fruitful concept was investigated for the first time by Watkins, Behling, Kariv and Miller.[73] They oxidised graphite rods (by heating in air to 160 °C), so that carboxyl groups were formed on their surface which could be titrated with alkali. By treatment with thionyl chloride in dry benzene these surface carboxyl groups were converted into acid chlorides, which were then converted into substituted amides of carboxylic acids by reaction with chiral phenylalanine ester in dichloromethane. Such electrodes, both in outward appearance and according to current–potential curves taken on them (on polarisation from −0.5 to −1.5 V), did not differ in any respect from unmodified graphite electrodes. Reduction of 4-acetylpyridine in aqueous-alcoholic acetate buffer solution on a modified electrode afforded the corresponding enantiomeric alcohol, albeit in small optical yield. On electrolysis of a solution of phenylalanine in acetate buffer on an unmodified graphite cathode, catalytic evolution of hydrogen was observed which was suppressed on introducing 4-acetylpyridine into the solution. On reducing the latter in this system the preparation of optically active alcohol was unsuccessful. On reducing phenylglyoxylic acid ester on a graphite electrode modified with phenylalanine, a diastereomer of mandelic acid ester was formed in 94% yield and an optical purity of 9.7%.[73] Although reproduction of these results was unsuccessful,[74] after publication of the paper[73] several studies appeared in which electrodes modified with chiral compounds were used for carrying out asymmetric electrosyntheses.

It has been established[75] which of the faces of crystalline graphite (two types of face exist) acquires on treatment the property to induce asymmetry in a product of an electrode reaction. Separate faces were clearly distinguishable in a sample of highly ordered pyrolytic graphite (Union Carbide Corporation, Parma, Ohio). On sealing first one and then the other face with silicone rubber and modifying them with amino acids both on the face of 'edge' atoms and on the face corresponding to the basal layer, the total yield of alcohol was 90% on reduction of 4-acetylpyridine. An enantiomeric excess (2%) was observed only on the 'edge' carbon atoms which, as is known, are readily oxidised with the formation of carboxyl groups.

It was also established[75] that a graphite electrode modified with amino acids may operate at high anode potentials. A graphite electrode modified with phenylalanine methyl ester was used for the oxidation of methyl *p*-tolyl sulphide to the sulphoxide. The yield of sulphoxide reached 90% and the enantiomeric excess of (−)-sulphoxide was 2.5%.

Instead of modifying electrodes with chiral substances, which provide only a comparatively small surface coverage, Abe, Nonaka and Fuchigami[76] proposed the use of electrodes coated with polymeric films obtained from chiral monomers.

An example has already been described of the electrochemical polymerisation of a pyrrole on a platinum electrode and the properties of the electrode modified in this way have been reported.[77] It turned out[78] that on changing the structure of the monomer (*N*-phenyl substituted pyrrolium cations having various substituents in the *para* position of the phenyl ring) used to obtain the polymeric films, the rate constants for electron transfer from a ferrocene molecule in acetonitrile solution to a platinum electrode coated with polymer varied appreciably.

An electrode, coated with a polymeric film obtained from chiral monomers, was used for the first time[76] for the electrochemical preparation of optically active compounds. On reduction of citraconic acid, on a graphite electrode coated with a film of poly-L-valine, in pH 6.0 phosphate buffer solution, an enantiomeric methylsuccinic acid was obtained with an optical yield of 25%, which is approximately 10 times greater than on the usual electrode in the presence of inducers adsorbed on it.[71]

The use has been described of a graphite electrode coated with poly-L-valine for the electroreduction of prochiral ketones, oxides and *gem*-dihalides.[79] The greatest optical yield (16.6%) was obtained on reducing 1,1,-dibromo-2,2-diphenylcyclopropane to the corresponding monobromo derivative.

There are procedures involving the formation of covalent binding of amino acids to graphite which enable the preparation of more stable polymeric films and multiple use of electrodes.[80]

Nonaka, Abe and Fuchigami[81] have used graphite electrodes modified with chiral polyamino acid films for the asymmetric reduction of citraconic acid, its dimethyl ester and of mesaconic acid.[81] The reduction of citraconic acid was carried out on electrodes coated with six different polyamides. The best yield, 26% methylsuccinic acid, was obtained with a poly-L-valine coating. Coating of lead and especially zinc electrodes with the same film did not enable such high optical yields to be reached as on a graphite electrode. This is apparently linked with the lower adhesion of the polymeric film to a metal electrode.[81] The optical yield when reducing dimethyl citraconate under optimum conditions (pH 6.0, 0 °C, $E = -1.0$ V) was far less than when reducing the acid itself (2.3%). This evidently indicates the important role of hydrogen bonds on inducing chirality.[81] The reduction of mesaconic acid occurred with an appreciably lower optical yield (10%) than did the reduction of citraconic acid, but they both gave predominantly enantiomers with the (*S*) configuration. Since the polymeric film is not conducting but is permeable to protons and substrate molecules (the film does not increase the voltage), the process, in the opinion of the authors,[81] proceeds at the graphite/film boundary and induction is effected on transfer of an electron and not a proton.

Komori and Nonaka[82] have described a method of modifying electrode surfaces, by coating the surface of a platinum electrode a polyamide film. It was established that such an electrode is stable to high anode potentials which enables its use for chiral electrooxidation.[82] On a platinum electrode coated with a poly-L-valine film, cyclohexyl phenyl sulphide is oxidised to the sulphoxide in up to 54% yield.[82]

In a subsequent study,[83] the same authors described the oxidation on platinum anodes, coated with films of polymeric chiral compounds, of seven different unsymmetrical alkyl phenyl and cyclohexyl phenyl sulphides to the corresponding sulphoxides. The highest optical yield (93%) was obtained on oxidising t-butyl phenyl sulphide on a platinum electrode coated with a double layer of polypyrrole and poly-L-valine.

It is interesting that such a modified electrode was used by Komori and Nonaka[84] for the enantiomerically differentiating oxidation of racemic 2,2-dimethyl-1-phenylpropan-1-ol to the ketone.[84] After oxidising half of this alcohol on a lead-lead oxide anode, twice coated with polypyrrole and poly-L-valine, 43% of optically pure (*S*)-(−)-enantiomer of the alcohol was in the unreacted state. This is the first example of the kinetic enantiomeric electrochemical resolution of a racemic alcohol.

The high optical yields of products on electrooxidation of sulphides on modified anodes have attracted attention.

There is considerable interest in an electrode coated with a thin film of clay. Certain racemic tris-complexes of metal ions with organic ligands, such as the trisphenanthroline complexes of iron(II), adsorb on the clay surface in such a manner that their enantiomers alternate in a staggered order.[85] An enantiomeric tris-complex occupies only half the area of the electrode, i.e. only its own space. This enabled a tin-tin oxide electrode coated with clay and an enantiomeric tris-complex $Ru(phen)_3^{+}$ to be used for the selective electrooxidation of racemic $Co(phen)_3^{2+}$.[86]

A review[87] has been devoted to the preparation and use of electrodes, the surface of which is modified by films of organic substances and polymers, and to the effect of such electrodes on electrochemical processes.

VIII. Intramolecular induction

The presence in a molecule of an asymmetric atom and a prochiral centre near to it, as already indicated,[61] enable diastereomers to be prepared by electrode processes. Intramolecular induction is observed in the case of prochiral ketones having an asymmetric centre in the positions α or β to the keto group.[88] On reduction of 2,2,3-trimethylindan-1-one on a mercury cathode in aqueous methanolic alkaline solution a diastereomer is formed with an optical yield up to 82%.

An asymmetric centre may be introduced into the molecule of an acid to be reduced by esterification with L-menthol or D-neomenthol.[89] A chiral product was successfully obtained in optical yield up to 5% by the esterification of itaconic, mesaconic, citraconic and phenylmaleic acids and subsequent reduction.

The electroreductive alkylation of phenylacetates of L-menthol and L-borneol in the presence of dimethyl sulphate (and also methylethyl and methylisopropyl sulphate) at −20 to −40 °C on a platinum cathode leads to replacement of the α-hydrogen atom (relative to the carboxyl group) by alkyl in an overall yield of 78% and an optical yield of up to 22%.[90]

On treating the products of deprotonation of the cyclopentadienyl-tetralin-iron cation with menthyl nitrite, a chiral oxime is formed giving a chiral ketone on hydrolysis. On electroreduction in acidic medium the oxime gives an optically active *endo*-amine and the ketone gives an *endo*-alcohol.[91] The small optical yields of products are caused by the very low optical yield on nitrosation (4−7%). On two-electron electroreduction of (*S*)-(+)-1-bromo-1-carboxy-2,2-diphenylcyclopropane and its ester on a mercury electrode in aqueous acetate buffer solution containing ammonium ions, the debromination product retains the initial configuration (up to 70%) for the ester. The configuration is inverted in the presence of tetraalkylammonium, the extent of inversion did not depend on the electrode potential but was increased on increasing the length of the group in the tetraalkylammonium cation.[92] When reducing the ester in the presence of tetrabutylammonium the inversion reached 60%. Similar results were obtained in ammonia buffer but inversion in the presence of tetraalkylammonium salts depended on the potential in this case.[92]

Mandelic acid amide is formed almost quantitatively on electroreduction of aqueous alcoholic buffer solutions of (*S*)-(−)-*N*-(α-methylbenzyl)benzoylformamide on a mercury cathode. In strongly acidic medium the (*R*,*S*) isomer is mainly formed (maximum optical yield 12.5%) and in ammonia buffer the (*S*,*S*)

isomer (optical yield 8.5%).[93] However at a more negative potential the (*R,S*) isomer is formed in the presence of tetrabutylammonium salt.

Some years earlier A Tallec published a fairly detailed review[94] on electrochemical synthesis of chiral compounds, describing the conditions of electrolysis capable of increasing optical yields. The mechanism of inducing optical activity was almost not touched upon, however the author rejected the hypothesis of Grimshaw[2,7] on hydrogen atom transfer from the uncharged form of the protonated inducer to the substrate molecule, within the confines of an adduct between them, as the step at which asymmetry of the product is provided, citing the paper of Kariv and collaborators.[16] The review indicated[94] may serve as a good information manual on work in the area of asymmetric electrosynthesis. There is much factual material in it on the conditions of electrolysis and yields of products.

IX. The use of electrode–catalysts

E I Klabunovskii and collaborators[95] discovered high enantioselectivity when hydrogenating esters on nickel black modified with (*R,R*)-tartaric acid. In subsequent work[96] this catalyst was used for the electrohydrogenation of ethyl acetoacetate. Finely dispersed catalyst was applied in a uniform layer on a horizontal platinum plate (7 cm^2) serving as a cathode. When hydrogenating ethyl acetoacetate in 0.1 M aqueous NaOH solution or 50% aqueous ethanolic 0.3 M KCl both at the potential of the hydrogen region of the electrode (i.e. in the layer of hydrogen adsorbed on the electrode) and in the region of hydrogen overvoltage potentials, ethyl β-hydroxybutyrate was obtained in practically quantitative yield and the optical yield of the (*R*) isomer was in all cases close to 10%.

Slemcu[97] has described the use of the dielectric Electret applied as a 1 mm layer to a metallic foundation as an electrode for the reduction of fumaric acid from aqueous alkaline solution. At 500 V and a current strength of about 1 mA for 150 h at 100 °C, an 18% excess of laevorotatory enantiomer of malic acid was achieved. Electret consists of mica plates and barium titanate, fused in carnauba wax. The latter, evidently, provides chirality to the electrode surface. It remains unclear why malic and not succinic acid was formed. It is possible that the electric current stimulated the hydration of fumaric acid without electroreduction.

Finally it has been shown[98] very recently by a conductiometric method that phenylglyoxylic acid forms an adduct in water with strychnine of composition 1:1 within which optical activity is induced in the mandelic acid formed on electroreduction.

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Translated from *Uspekhi Khimii* **60** 2143–2166 (1991) U.D.C. 547.741

Mass spectrometry of halogen-containing organic compounds

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ABSTRACT. The mechanisms involved in the formation of the mass spectra of halogen-containing compounds are correlated. All types of processes involving halogens are examined, the material being presented according to the type of fragmentation.

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I. Introduction

Halogen-containing compounds (with the exception of purely synthetic laboratory chemicals) frequently form part of complex mixtures, so their identification and structural determination are mainly carried out by mass spectrometric methods, which are the most informative and particularly effective when combined with chromatographic separation methods. Hence there is an obvious need to elucidate the general mechanisms involved in the formation of the mass spectra of halogen-containing compounds. As a rule, this information is dispersed amongst a large number of articles in which, with the exception of a number of publications,[1–7] only a small proportion of the problems relating to the interpretation of the mass spectra of halogen-containing organic compounds are reviewed.

In this review, in contrast to the traditional approaches, all types of processes involving halogens rather than classes of halogen-containing compounds are reviewed.

By presenting the material according to the type of fragmentation the authors have been able to adopt a thermochemical approach to the interpretation of the mass spectra. This approach is used throughout the whole article both in examining simple bond cleavage and in analysing the peak intensities of the molecular ions, including ways of stabilising a molecular ion. The source of organic compounds in environmental materials, as has now been established, is mainly provided by human activity and to a much lesser extent by natural chlorine-, bromine-, and iodine-containing compounds of vegetable (including petroleum) and animal origin. Therefore we consider it necessary to consider the analytical aspects of the mass spectrometry of halogen-containing compounds in a separate section.

II. Electron-impact mass spectrometry

1. Positive ions

One of the pathways of the fragmentation of organic monohalogen-containing compounds RCH_2X from electron impact (EI) leads to ions of the type $\overset{+}{C}H_2-\ddot{X}\longleftrightarrow CH_2-\overset{+}{X}$, in the same way as other electron-donating groups (alkyl, OR, SR, NH_2, $CH=CH_2$, Ph, etc.). A comparison of the exothermicities Q of the isodesmic[4,8] reaction

$$CH_3^+ + CH_3X \rightarrow \overset{+}{C}H_2X + CH_4$$

gives the following series of stability of these ions compared to the CH_3^+ cation (kcal mol^{-1}): CH_3^+ (0), $\overset{+}{C}H_2F$ (25), $\overset{+}{C}H_2Cl$ (31), $\overset{+}{C}H_2Br$ (35), $\overset{+}{C}H_2I$ (35), $\overset{+}{C}H_2CH=CH_2$ (59), $\overset{+}{C}H_2OH$ (65), $\overset{+}{C}H_2SH$ (69), $\overset{+}{C}H_2NH_2$ (96).

This means that in terms of their donor properties halogens are inferior to other groups, and the stabilising ability of halogens increases in the series F < Cl < Br < I. Halogens can be eliminated as free radicals X$^\cdot$, and the exothermicity Q (kcal mol^{-1}) of the isodesmic reaction

$$\dot{C}H_3 + HX \rightarrow CH_4 + X^\cdot,$$

that reflects the relative thermodynamic stability of X$^\cdot$ decreases in the series I$^\cdot$ (33.5) > Br$^\cdot$ (17) > Cl$^\cdot$ (1.6) > F$^\cdot$ (−31.5).[4] Therefore abundant loss of X$^\cdot$ is to be expected only for I$^\cdot$ and Br$^\cdot$. Together with dehalogenation, dehydrohalogenation with elimination of HX is also typical of halogen-containing compounds.

Calculated[4] thermochemical properties of the simple bond cleavage processes and loss of HX for a C_2H_5X molecule are given in Table 1, and the peak intensities of the corresponding ions are given in Table 2.[9] The enthalpies of formation of molecules, ions, and radicals are taken from a monograph[4] while the ionisation potentials (IP) are taken from a reference book[10] (E_{cr} = AP − IP, the critical energy or energy of activation for dissociation of $[C_2H_5X]^+$ molecular ions (AP is the appearance potential of a fragment ion).

Contrary to expectation the critical energies for separation of X were similar for all halogens (0.78 − 1.22 eV). This occurs because, whereas during homolytic cleavage of a bond by the direct process

$$C_2H_5\text{—}X \longrightarrow C_2H_5^\cdot + X^\cdot$$

the strength of the bond with X decreases in the series F, Cl, Br, I because the stability of X$^\cdot$ increases in the same series, on electron impact it is the molecular ion that dissociates rather than the initial molecule. In the latter, (because of the increase in IP in the series RI→RBr→RCl→RF) the value of E_{cr} decreases in this series, although the absolute values of IP increase from I to F in complete

agreement with processes involving homolytic bond cleavage. The competing fragmentation processes for formation of $CH_3\overset{+}{C}HX$ and $\overset{+}{C}H_2X$ can only occur in organofluorine compounds (both processes have a similar (AP), whereas when X = Cl, Br, I its AP and E_{cr} are substantially higher than for processes involving separation of X. Therefore, in the mass spectra of aliphatic monohalogen derivatives intense peaks due to $\overset{+}{C}H_2F$ and $R\overset{+}{C}HF$ ions occur but there are only weak peaks due to the other $\overset{+}{C}H_2X$ and $R\overset{+}{C}HX$ ions. Simple bond cleavage processes involving a single halogen atom are restricted to those considered above, to which can only be added the loss of neutral [XC≡CH from halobenzenes; XCH=CHR; H(X)C=O; XC≡N] or charged ($\overset{+}{X}C=\ddot{O}$ in a number of disubstituted furans) ring fragments from carbocyclic and heterocyclic compounds. They may be extended to all classes of compounds.[1,4]

Table 1. Thermochemical properties (in eV) of fragmentation processes of ethyl halides

C_2H_5X ($C_2H_5^+ + \dot{X}$; $\overset{+}{C}H_2X + \dot{C}H_3$; $CH_3\overset{+}{C}HX + \dot{H}$; $C_2H_4^{\overset{+}{\cdot}} + HX$)

Compound (M)	IP (M)	IP	E_{cr}	AP	E_{cr}	AP	E_{cr}	AP	E_{cr}
		$C_2H_5^+$		$\overset{+}{C}H_2X$		$CH_3\overset{+}{C}HX$		$C_2H_4^{\overset{+}{\cdot}}$	
C_2H_5F	12.0	12.89	0.89	12.84	0.84	11.99	0	10.93	0
C_2H_5Cl	11.0	11.78	0.78	12.51	1.51	11.97	0.97	11.25	0.25
C_2H_5Br	10.3	11.17	0.87	12.40	2.10	11.95	1.65	11.32	1.02
C_2H_5I	9.34	10.56	1.22	12.31	2.97	12.24	2.90	11.42	1.22

Table 2. Peak intensities of characteristic ions in the mass spectra of C_2H_5X at 70 eV (as a percentage of total ion current).[9]

Compound	$M^{\overset{+}{\cdot}}$	$C_2H_5^+$	$CH_3\overset{+}{C}HX$	$\overset{+}{C}H_2X$	$C_2H_4^{\overset{+}{\cdot}}$
C_2H_5F	5.8	1.1	50.8	13.6	3.4
C_2H_5Cl	28.8	15.7	1.7	7.6	21.4
C_2H_5Br	49.6	15.6	0.75	2.5	8.9
C_2H_5I	54.0	19.2	0.32	1.0	1.4

In compounds containing other substituents in addition to halogens, the primary fragmentation processes (they constitute a determining factor in establishing the structure of the initial compound if it is not known) are controlled by these substituents (this relates in particular to fluorine- and chlorine-containing compounds). However, here also—at advanced stages of the fragmentation—the participation of halogens definitely manifests itself, primarily in the elimination of HX and by the presence of peaks of metastable ions corresponding to these processes.

Let us examine the behaviour on electron impact of polyhalogen-containing compounds in simple bond cleavage processes. In systems that have the perhalogen-containing groups CCl_3-, CBr_3-CBr_2-, $-CCl_2-$ (for perfluoroalkyl groups, see below), abundant loss of Cl or Br occurs because of the increase in IP of the molecule and the decrease in bond strength (polyiodine-containing compounds have hardly been studied at all).[4,11] Of perfluoroalkyl ions it is only CF_3^+ ions that are intense, as a rule. While the stability of alkyl cations increases in the series: $CH_3^+ < C_2H_5^+ < CH_3CH_2CH_2^+ < (CH_3)_2CH^+ < (CH_3)_3C^+$, for perfluoroalkyl cations the stability decreases in a similar series: $CF_3^+ > CF_3CF_2^+ > CF_3CF_2CF_2^+ > (CF_3)_2CF^+ > (CF_3)_3C^+$, which is due to the presence of powerful electron-withdrawing CF_3 groups on the cation site. This also follows from a comparison of the IP of the corresponding free radicals R_F (eV): $\dot{C}F_3$ (8.9); $C_2\dot{F}_5$ (9.1); $CF_3CF_2\dot{C}F_2$ (9.2); $(CF_3)_2\dot{C}F$ (9.5) and $(CF_3)_3\dot{C}$ (10.2).[12] Such high values of the IP have the result that in functional compounds such as $RCOCH_2COR_F$ when the $C-R_F$ bond is cleaved, the charge always remains on the residue not containing R_F, and the latter is released as a free radical. In perfluoroalkyl-containing compounds, in particular perfluoroalkanes, perfluoroalkylperfluorocycloalkanes, fluorinated esters, perfluoroalkyl-1,3-diketones, and others, a peak due to the CF_3^+ ion with mass 69 is observed. The other ion homologues as a rule do not give intense peaks. Nevertheless, peaks from 119^+ or 169^+ ions ($C_2F_5^+$ and $C_3F_7^+$ respectively) appear in the mass spectra of certain compounds. We can attribute this formation of R_F^+ at the advanced stages of fragmentation of $M^{\overset{+}{\cdot}}$ to a pair with very stable neutral molecules that compensate the instability of R_F^+:[12]

$$C_2F_5^+ \longleftarrow\!/\!- \underset{M^{\overset{+}{\cdot}}}{CF_3CF_2CF_2COOCH_3^{\overset{+}{\cdot}}} \longrightarrow \underset{[M-OCH_3]^+}{CF_3CF_2-CF_2-C\equiv\overset{+}{O}} \longrightarrow$$

$$\longrightarrow CF_3\overset{+}{C}F_2 + CF_2=C=O,$$

2.5% base. (70 eV)

$$C_3F_7-CF_2-CF_2-CF_2-CO-CH_2-\overset{+}{C}-\ddot{O} \longrightarrow$$

$$\uparrow\ [M-CF_2]^+$$

$$M^{\overset{+}{\cdot}} -\!/\!\longrightarrow C_3F_7^+$$

$$\longrightarrow C_3F_7^+ + C_2F_4 + CF_2=C=O + CH_2=C=O.$$

%Σ: 2.4 (70 eV): 3.5 (20 eV): 3.2 (12 eV).

The stability of the neutral residues in the absence of more favourable fragmentation pathways explains the appearance of intense peaks from ions with acceptor groups—$(CF_3)_2\overset{+}{C}Cl$ (100%) from $(CF_3)_2CClSO_2Cl$ and $(CF_3)_2CH$ (100%) from $(CF_3)_2CHSO_2OH/H_2O$.[13]

Simple bond cleavage processes have the most direct bearing on such an important characteristic of a compound and its mass spectrum as the intensity of the molecular ion peak. It is the value of the critical energy E_{cr} for the most favourable simple bond cleavage that governs the intensity of the $M^{\overset{+}{\cdot}}$ peak (see Table 2). The value of E_{cr} is determined by two quantities—the AP and IP. The absence of peaks due to $M^{\overset{+}{\cdot}}$ ions in the mass spectra of many polyfluorine-, polychlorine-, and polybromine-containing compounds is due primarily to high values of the IP, since halogen-containing groups that include powerful withdrawing halogen atoms (especially F and Cl) increase the IP and, as a result, reduce E_{cr}. If E_{cr} is equal to zero, i.e., the thermochemical threshold for formation of the fragment ion obtained by simple bond cleavage is the same or less than the IP of the molecule, any $M^{\overset{+}{\cdot}}$ immediately decomposes and is therefore not recorded. Examples of compounds, mainly fluorine-containing ones, which do not produce an $M^{\overset{+}{\cdot}}$ peak are

given in Table 3. It follows from Table 3 that identification of the molecule ion is possible from the primary fragment ion (by mass), usually $[M - F]^+$, but this method is not always reliable. It is advisable to change the method of ionisation, and to use chemical ionisation in particular (see below).

Table 3. Halogen-containing compounds not displaying a molecular ion peak.[4,9,11,13–28]

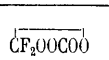
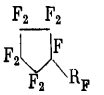
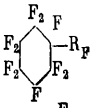
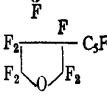
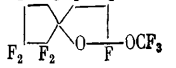
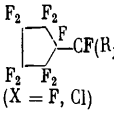
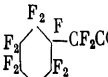
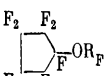
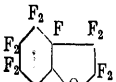
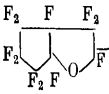
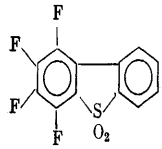
Compound	Ion with greatest *m/z*	Compound	Ion with greatest *m/z*
CF_4	$M-F^+$		$M-CO_2^+$
1, 3, 5, 7-$(CF_3)_4$-adamantane	$M-F^+$	$C(NF_2)_4$	$M-NF_2^+$
$R_F(CF_2CF_2O)_nR'_F$	$M-F^+$	$(CH_3)_2C(NF_2)_2$	$M-NF_2^+$
(R_F, $R'_F = CF_3$, C_2F_5)		$F_2CH_2CH_2CH_2F_2$	$M-NF_2^+$
$CF_3COC_2H_5$	$M-C_2H_5^+$	$F_2NC(F)N=N$	$M-F^+$
$F_2CHCOOC_2H_5$	$M-C_2H_5^+$	$F_2CN(F)NF$	$M-NF^+$
CF_3COOCH_3	$M-F^+$	$H-NCF_2CF_2O$	$C_2F_4^+$
CF_3CF-CF_2 (O)	$M-F^+$	$F-NCF_2CF_2O$	$M-NO^+$
$RCOOCF(CF_3)_2$ (R = F, CF_3, C_2F_5)	$M-F^+$	$R_FR(N_F)COF$	$M-F^+$
$CH_3OCO(CF_2)_nCOCH_3$ ($n = 6-9$)	$M-F^+$	$CF_2CF_2N=N$	$M-N^+$
$FC(O)OC(O)F$	$CF_2=O^+$	$F_2NCF_2NCF(NF_2)NF$	$M-N_2F_4^+$
$(CF_3OO)_2C=O$	$CF_3OOC\equiv O^+$	$F_2NCF_2FC-OCH(CF_3)_2$ (NH)	$M-F^+$
	$M-F^+$	$F_2NC(F)CF(NF_2)NN=CFNF_2$	$M-F^+$
		$F_2CCF_2NFCF_2NF$	$M-CF^+$
	$M-F^+$	SF_6	$M-F^+$
		CF_3SF_3	$M-F^+$
		$(CF_3)_2CHSO_2R$ (R = CH_3, CF_3, $CH(CF_3)_2$)	$(M+H^+)$*
	$M-F^+$		$M-OCF_3^+$
	$M-F^+$	$CF_3COOCH_2CH(CH_3)_2$	$M-H^+$
		$CF_3COOC(CH_3)_3$	$M-CH_3^+$
	$M-F^+$	$CF_3COOSi(CH_3)_3$	$M-CH_3^+$
		$C_2F_5COOC(CH_3)_3$	$M-CH_3^+$
		$C_2F_5COOSi(CH_3)_3$	$M-CH_3^+$
	$M-F^+$	$CHF_2COOSi(CH_3)_3$	$M-CH_3^+$
		cyclo-$C_6F_{11}COOCH_3$	$M-HF-H^+$
		$SF_5N=CFC_2F_5$	$M-F-H^+$
	$M-F^+$	$(CF_3)_2C=NN=S(CF_3)_2$	$M-F^+$
		$FSO_2O(CF_2)_3OSO_2F$	$M-SO_3F^+$
		$CF_3(CF_2)_6OSO_2F$	$M-F^+$
		$Cl(CF_2)_3OSO_2F$	$M-Cl^+$
	$M-OCF_3^+$	$(CF_3)_2NCF_2Cl$	$M-F^+$
		$CF_3N(CHCl_2)_2$	$M-Cl^+$

Table 3 (contd.).

Compound	Ion with greatest *m/z*	Compound	Ion with greatest *m/z*
$(CF_3)_2NCHCl_2$	$M-Cl^+$	$CF_3CON=S(F)CF_3$	$M-F_2^+$
CCl_3CCl_3	$M-Cl^+$	$C_2F_5N=S(F_3)N(CH_3)_2$	$M-F_2^+$
$CCl_3C\equiv N$	$M-Cl^+$	$C_2F_5N=S(Cl)CF_3$	$M-Cl^+$
$C_2H_5CF_2CF_2OCF_2CF_2SO_2F$	$M-F-HF^+$	$(CF_3)_2CFN=S(Cl)CF_3$	$M-F^+$
$R_FSF_2R_F$	$M-F^+$	$Cl(CH_2)_5Cl$	$M-Cl^+$
$CF_3SO_2CF_3$	$M-CF_3^+$	$CFCl_3$	$M-Cl^+$
$R_FSO_2OSO_2R_F$ ($R_F = CF_3$, C_2F_5)	$R_FSO_3^+$	C_2F_5Cl	$M-F^+$
		$ClC(F)N=N$	$M-N^+$
	$M-O^+$	$CCl_3COOC_2H_5$	$M-H^+$
		$ClCH_2COOSi(CH_3)_3$	$M-CH_3^+$
		RSO_2Cl (R-alkyl, CH_3SO_2)	$M-Cl^+$
		$SF_2C(F)ClSF_2CFX$ (X=F, Cl)	$M-F^+$
		3-Br-Ad-$COOCH_3$	$M-Br^+$
$(CF_3)_2CClSO_2Cl$	$M-O^+$	$(CH_3)_3CBr$	$M-Me^+$
$CF_3SN=C(Cl)SSCF_3$	CF_3SS^+	CF_2NCF_2NBr	$M-Br^+$
$R_FS(O)N(CH_3)SCCl_3$	$M-Cl^+$	$CF_2=NCF_2CF_2Br$	$M-CF_2N^+$
$CF_3S(F)=NCF(CF_3)_2$	$M-F_2^+$	$F_5SN=CBr$	$M-F^+$
$(CF_3)_2CFS(F)=NCOCF_3$	$M-CF_3^+$	$TeF_5N=CBr_2$	$M-Br^+$
$CF_3S(F)=NCOCF_3$	$M-F_2^+$	$Ph_2CBrCOCH_2Br$	$M-Br^+$
SF_5CHRSO_2F (R = H, $COOCH_2CF_3$)	$M-F^+$	$(CF_3)_2CFO(CF_2)_4Br$	$M-F^+$

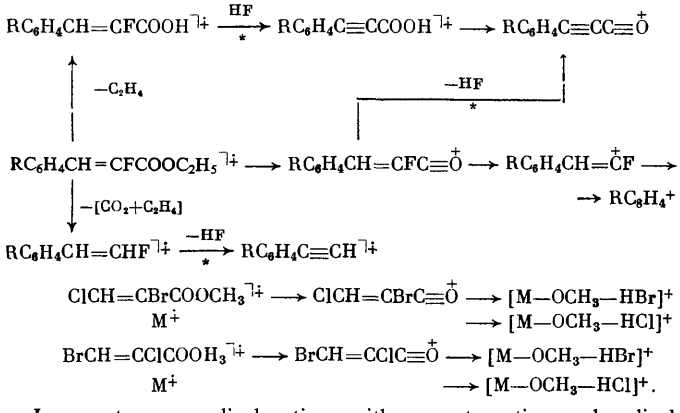
*In the EI mass spectrum.

Another way of obtaining an M^+ peak is chemical modification. The introduction of a group that has a substantially lower IP than an unmodified molecule gives rise to a new fragmentation pathway with E_{cr} not equal to zero, which makes it possible to generate an M^+ peak. This method can only comparatively rarely be applied to halogen derivatives, but nevertheless such examples do exist. In the electrochemical fluorination of acid chlorides, acid fluorides are obtained with a fluorinated chain (more frequently an acid mixture is obtained). Since neither they, nor the methyl esters or trimethylsilyl esters to which it is usual to convert the reaction mixture of acid fluorides give M^+ peaks, it is advisable to react this mixture with phenols or naphthols:[4,11] aryl esters of fluorinated acids give M^+ peaks. For example, the M^+ peak in $C_2F_5COOCH_3$ can only just be detected (0.07% base at 12 eV), the M^+ peak in $C_2F_5COOSi(CH_3)_3$ does not appear, whereas the M^+ peak in $C_2F_5COOC_6H_5$ amounts to 25 and 100% at 70 and 20 eV respectively.[11]

An iodine atom can serve as a group that reduces the IP of a molecule and stabilises M^+, while in compounds with acceptor groups even a bromine atom can be used. Thus, the M^+ peak is absent from the mass spectrum of $RCF_2OCF_2CF_2SO_2F$ (R = C_2H_5) and appears (0.4%) when R = $(CH_2)_4I$.[23] In $CH_2=CHCF_2R$ compounds, where R = $-CF_2CH=CH_2$, $-CF_2CH_2CH_2C_2F_5$, and $-CF_2CHICH_2C_2F_5$, the intensity of the M^+ peak is 0, 2.9, and 33% respectively.[29]

Hydrogen rearrangements for halogen-containing groups are quite similar and they actually comprise a single type of process — loss of

HX. The data in Table 1 (see above) clearly show that loss of HF is extremely favourable; E_{cr} for this process in C_2H_5F is equal to zero, but the actual thermochemical threshold for formation of $[M-HF]^{+\cdot}$ is even lower (by 1.1 eV) than the IP of the molecule. This process is always accompanied by the appearance of a peak of the corresponding metastable ion, which makes it possible (when the $M^{+\cdot}$ peak is absent) to reach the mass number of the molecular ion. In fluorine- and chlorine-containing (to a lesser extent bromine-containing) compounds loss of HX definitely occurs also at the advanced stages of fragmentation, even if the halogen atom is situated in a "strong" position (on the aromatic ring or on a multiple bond). For example:[30,31]



In recent years radical cations with separate cation and radical sites, so-called "distonic" ions[4] such as $CH_3\overset{+}{X}\dot{C}H_2$, $CH_3\overset{+}{X}\dot{C}HX$ (X = Cl, Br),[32] $CH_3\dot{C}H\overset{+}{X}H$ (X = Cl, Br),[33] $\dot{C}H_2\overset{+}{X}H$ (X = F, Cl),[34] have been detected and carefully studied (including a determination of the mechanisms of their formation and thermochemical properties). The appearance of I^+ (together with CH_3^+) in the mass spectrum of CH_3I may also, in our opinion, be due to the involvement of the $\dot{C}H_2\overset{+}{I}H$ ion in the process, without having to resort to assumptions about separate states of $M^{+\cdot}$, as Weber et al. have done.[35] A fluorine shift with formation of the unusual ion $HF\overset{+}{C}\dot{C}HFCl$ was observed by Seibl.[36]

By neutralisation and reionisation (repeated ionisation) of such ions it was possible to prove the existence of the uncharged species

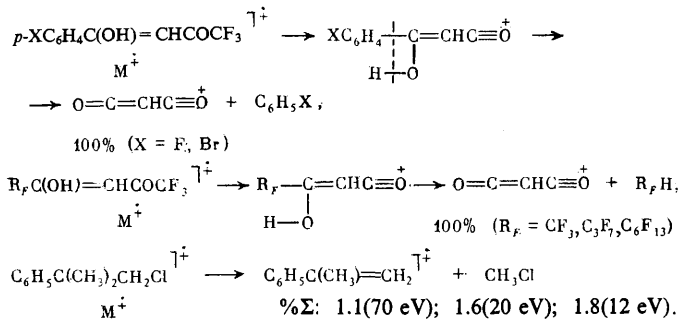
$$CH_3\dot{C}H-Cl-H,\ \dot{C}H_2CH_2ClH,\ \dot{C}H_2-CH_2-Br-H$$

and

$$CH_3CH-Br-H$$

in the mass spectrometer.[37] An attempt to identify neutral CH_2XH (X = F, Cl) was not successful.[34]

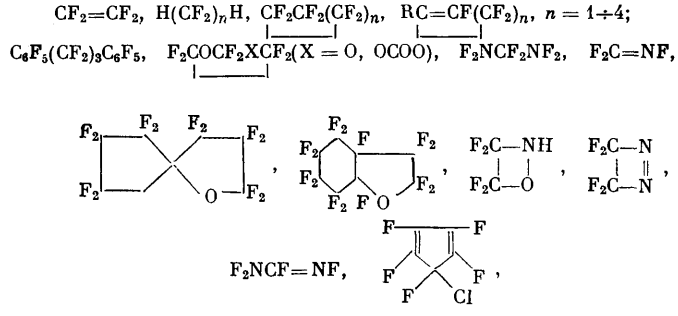
Apart from loss of HX, elimination of RH, where R are halogen-containing groups, occurs in certain cases:[12,3]



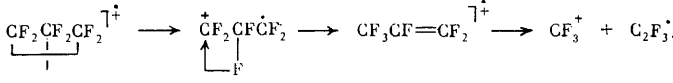
On the whole the role of hydrogen rearrangements in the fragmentation of halogen-containing compounds, with the exception of HX loss, is minor.

2. Skeletal rearrangements

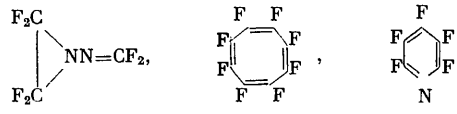
Skeletal rearrangements occur widely in a number of halogen-containing compounds when subjected to electron impact. We shall only examine those rearrangements in which halogens and halogen-containing groups are directly involved. A knowledge of them is necessary for an accurate determination of the structure of a compound if it is unknown. Thus, in the mass spectra of many compounds an intense peak from the CF_3^+ ion occurs when this fragment is not present in the initial molecule.[1,4,9,13–15,18,39,40]



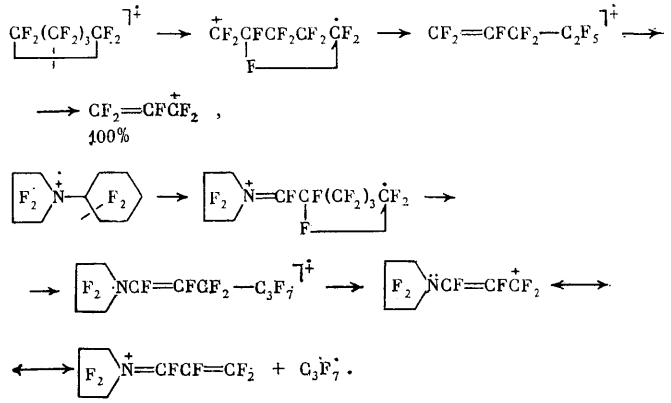
The CF_3^+ ion is formed in cyclic compounds after ring opening (while in aliphatic compounds it is formed in a fragment ion) by migration of an F atom (or atoms) to a cation or radical site. For example:



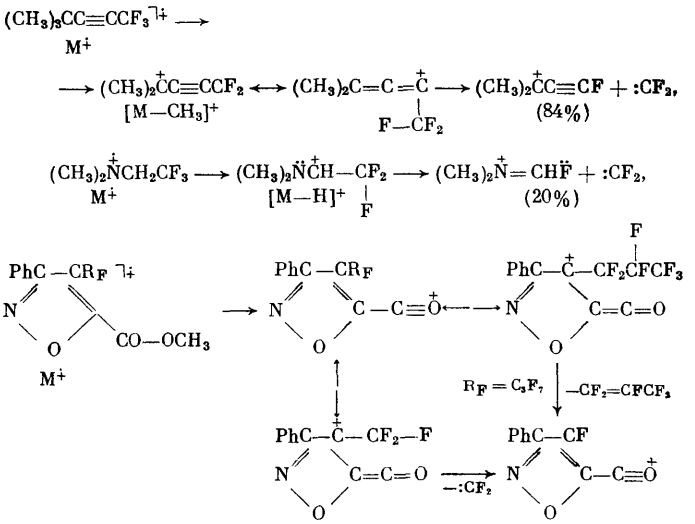
The $M-CF^{+\cdot}$ ion is obtained in a similar manner in the following compounds:[9,14]



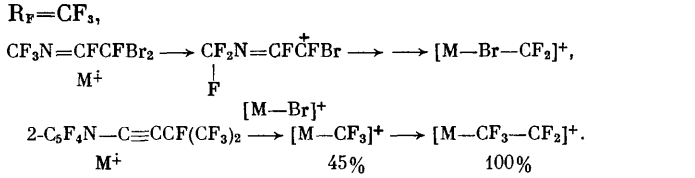
The perfluoroallyl cation is formed by the same route in cyclic compounds:[9,41]



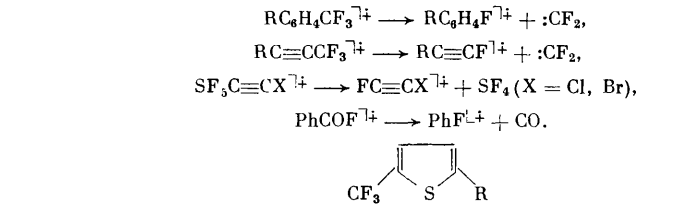
A fluorine atom can migrate to a C atom on which there are no other fluorine atoms:[12,14,18,42,43]



$R_F = CF_3$,



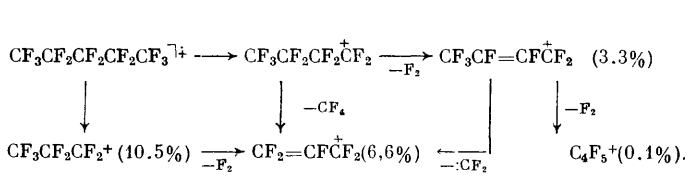
A fluorine atom can migrate to a π-system in a radical cation, particularly in the molecular ion:[9,44,45]



$[M-CF_2]^+$: 50% (R = H); 43% (CF_3); 32% (C≡CH).

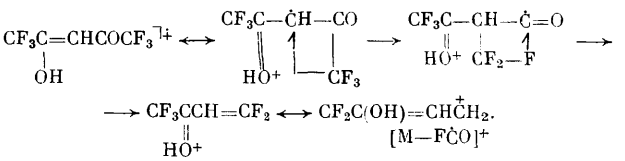
However, this process does not occur with all R groups. For example, in $RC_6H_4CF_3$ (R = $COOCH_3$), OCH_3 rather than CF_2 is eliminated.[46] In $RC{\equiv}CCF_3$ migration of F occurs when R = $C(CH_3)_3$, but not when R = $Si(CH_3)_3$ or $Ge(CH_3)_3$.[42] It is true that elimination of CF_2 takes place in the fragment ions $M-OCH_3^+$ and $M-CH_3^+$ respectively.[42,46]

In perfluorcarbons, since R_F^+ ions are unstable (apart from CF_3^+), stable allylic types of ions are formed. For the latter to be obtained, a skeletal rearrangement occurs in the system with formation of F_2, CF_4, etc.:[9]

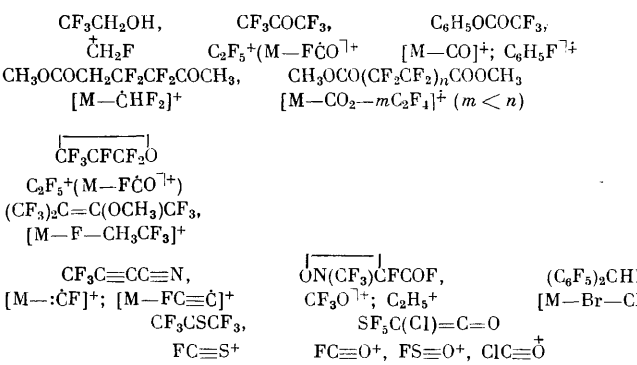


The elimination of other F-containing neutral molecules should be noted:[12,14,18,20,46]

The driving force of all these processes is not only the formation of stable F-containing neutral molecules or difluorocarbene (with low enthalpies of formation) but also the conversion through rearrangment of powerful acceptor substituents (CF_3, R_F, CF_3CO, $-CF_2-$) (destabilising a positively charged system) to donor groups, when the F atom (or atoms) either on a cation site or on a π-system is conjugated with that site. This is shown particularly clearly in aromatic systems with several substituents, when as a result of a very complex rearrangement of the fragment ion (involving ring expansion), F-substituted analogues of the tropylium ion $C_7H_7^+$ are formed at the last stage[12,46] (Table 4). The abundant loss of F from the CF_3 group in a heterocyclic aromatic system most likely also occurs with ring expansion as in its CH_3 analogue.[47] Thus, it is difficult to explain the high intensity of the peak from the $M-CF_3^+$ ion or possibly $M-F-CF_2^+$ ion (87%) in the fragmentation of 2,5-di(trifluoromethyl)thiophene.[45] We can give an example of a complex skeletal rearrangement with a rare case of the migration of CF_3 to a radical site:[39,48]



We can give examples of complex skeletal rearrangements involving F atoms or fluorinated groups with a mechanism that is unclear. A knowledge of these together with the rearrangements examined above is useful for an interpretation of the mass spectrum of both a known and an unknown structure in order to rule out possible suspicions of impurities being present. This doubt always arises if it is not possible to explain the appearance of a given unusual ion:[1,9,11,14,49]



The formation of peaks from $M-COX^+$ ions as well as $M-2COX^+$ (dioxins) and $M-COX-X_2^+$ (furans), where X = Cl, Br, in the mass spectra of polychloropolybromodibenzo-dioxins and

Table 4. Peak intensities of ions with the postulated structure of substituted tropylium ions at 70, 20, and 12 eV (as % Σ_{29}).

Compound	Neutral species	Ion	70 eV	20 eV	12 eV
p-$CF_3C_6H_4COOCH_3$	OCH_3+CO	$C_7H_4F_3^+$	19	8,2	0.31
	COOH	$C_8H_6F_3^+$	0.23	0.51	1.2
m-$CF_3C_6H_4COOCH_3$	OCH_3+CO	$C_7H_4F_3^+$	20	13	12
	F	$CH_3OOC-C_7H_4F_2^+$	1.6	1,0	–
p-$C_2F_5C_6H_4COOCH_3$	OCH_3+CO	$C_8H_4F_5^+$	4.6	5,2	–
	OCH_3+CO+CF_2	$C_7H_4F_3^+$	17	4.9	0,55
	CF_3	$CH_3OOC-C_7H_4F_2^+$	2.9	2,6	1,1
p-$C_3F_7C_6H_4COOCH_3$	OCH_3+CO	$C_9H_4F_7^+$	3.8	2.2	4.9
	C_2F_5	$CH_3OOC-C_7H_4F_2^+$	11	24	15
	OCH_3+CO+C_2F_4	$C_7H_4F_3^+$	11	1,5	0,49
	OCH_3+CO+CF_2	$C_8H_4F_5^+$	2.4	0.78	–
p-$(CF_3)_3CC_6H_4COOH$	CF_3+C_2F_4	$HOOC-C_7H_4F_2^+$	2,0	0,53	–
	COOH+CF_4	CF_2=$CF-C_7H_4F_2^+$	6,3	5,3	0,46
	CF_3+CF_2	$HOOC-C_8H_4F_4^+$	2,0	0,53	–
m-$CF_3CH_2C_6H_4Br$	Br	$C_8H_6F_3^+$	2,4	2,0	2,1
	Br+CF_2	$C_7H_6F^+$	5,3	2,4	–
m-$CF_3CH_2C_6H_4COOH$	CO+OH	$C_8H_6F_3^+$	2,1	0,39	–
	CO+OH+CF_2	$C_7H_6F^+$	7,0	–	–
p-$(CF_3)_3CCH_2C_6H_4COOCH_3$	OCH_3+C_4F_8+CO	$C_7H_6F^+$	16	13	0,10

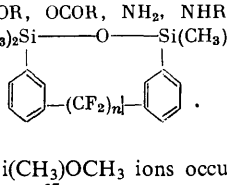
-furans[50] must be accompanied by complex skeletal rearrangements. The unusual ions $M-C_2H_5^+$ occur during fragmentation of $I(CH_2)_4CF_2CF_2OCF_2CF_2SO_2F$[23] and $TeBr_2^+$ is formed from F_5TeN = CBr_2.[21] We can attribute the high intensities of the $M-CF_3^+$ and $M-I^+$ peaks (100% at 12 eV) in the mass spectra of $(CH_3)_3CC{\equiv}CCF_3$ and $(CH_3)_3CC{\equiv}CI$ [42] respectively to isomerisation of their molecular ions to the isomeric cyclopropenyl radical cations,[51] since simple bond cleavage to form ethynyl cations is evidently unfavourable. The loss of CH_3Cl in the fragmentation of the molecular ions of *o*-$CH_3OC_6Cl_4OC_6Cl_5$ [52] and the elimination of Cl_2 in the fragmentation of $(C_6Cl_5)_2$ [53] and $C_{10}Cl_8$ [54] have been recorded.

The migration of F in organoelemental and organometallic compounds is particularly marked. The driving force of these processes is the formation of an element–fluorine or metal–fluorine bond, since radical cations, fragment cations, radicals, and neutral molecules that are isomeric with the initial molecular ions and which contain F on the element or metal have extremely low enthalpies of formation. Thus, while replacement of CH_3 by F in neopentane, i.e., $(CH_3)_4C{\rightarrow}(CH_3)_3CF$, reduces the enthalpy of formation of the molecule by only 8 kcal mol^{-1}, a similar replacement in the Si analogue, i.e., $(CH_3)_4Si{\rightarrow}(CH_3)_3SiF$, leads to a reduction of 56 (!) kcal mol^{-1}. A similar replacement of CH_3 by other halogens, i.e., $(CH_3)_4Si{\rightarrow}(CH_3)_3SiX$ reduces the enthalpy of formation by 42 (Cl), 40 (Br) and 35 (I) kcal mol^{-1} respectively.[4,12] Several conclusions can be drawn from these observations: 1) the driving force of rearrangement is formation of a much more stable shell of the ion (radical, neutral molecule) rather than a better charge stabilisation on the element atom compared to a C atom; 2) migration of a halogen to an element (metal) will occur in both a radical cation (primarily in the molecular ion) and a cation; 3) the migrating ability of the F atom is higher than that of the other halogens.

It is interesting to note that the size of the transition state for migration of halogens in both a cation and the radical part of a radical cation has no fundamental significance. Thus, on the one hand, a halogen atom "finds" an element atom at any distance between them. For example, the $(CH_3)_2SiX^+$ ion (X = F, Cl, Br, I) in $X-(CH_2)_nOSi(CH_3)_3$ is formed when n = 2–11, although with different intensities for different X at different values of n.[55] The $(CH_3)_2SiX^+$ ion (*m*/*z* 77) is formed in the fragmentation of compounds of virtually any structure:[1,11,14,42,44,56]

$(CH_3)_3SiCF_2CF_2CHF_2$; $(CH_3)_3SiC{\equiv}CCF_3$; $R_FCOOSi(CH_3)_3$, (R_F=CF_3, C_2F_5); $F(CH_2)_nSi(CH_3)_3$; $(CH_3)_3SiC{\equiv}CSF_5$;

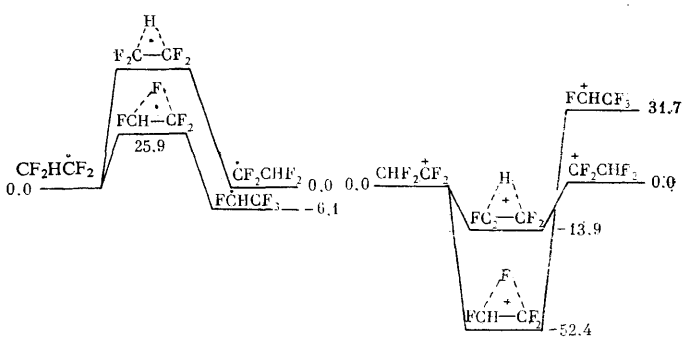
m-$(CH_3)_2Si(H)C_6H_4(CF_2)_nC_6H_4Si(H)(CH_3)_2$; $C_6F_5Si(CH_3)_2X$, (X = CH_3, OR, OCOR, NH_2, NHR); $(CH_3)_3SiN{=}C{=}NCOCF_3$;



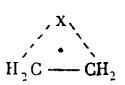
Peaks from $FSi^+(CH_3)OCH_3$ ions occur in the mass spectrum of $C_6F_5Si(OCH_3)(CH_3)_2$ [57] while peaks from $[M-SiF_3]^+$ and SiF_3^+ ions are present in the mass spectrum of $(C_6F_5)_3SiH$.[58]

On the other hand, migration of F via a three-membered transition state (1,2-shift) is more favourable than the analogous H

shift, as follows from quantum-chemical calculations[59] for carbon analogues (enthalpy of formation in kcal mol^{-1}):



The evidently favourable nature of a three-membered transition state for an F shift in a cation should be noted, although in our view the values quoted are too optimistic (especially -52.4 kcal mol^{-1}). According to other data[60] the cyclic isomer



is more stable for X = Cl, Br, I and slightly less stable for X = F than its open isomer $XCH_2\dot{C}H_2$.

In the mass spectra of compounds containing both Si and F atoms, peaks from other types of rearranged ions also occur:[1,11,14,42,61]

$CH_3C{=}CH$, $(CF_3C{\equiv}C)_4Si$, $C_6F_5Si(OCH_3)(CH_3)_2$, $(CH_3)_3EC{\equiv}CCF_3$,
$F_2Si{-}SiF_2$ $E = Si, Ge$
$\overset{+}{S}iF_3$ $[M{-}SiF_3]^+$ $F\overset{+}{S}i(O)$ $(CH_3)_2\overset{+}{E}F$; $CH_3\overset{+}{E}F_2$
$(CH_3)_3SiN{=}C{=}NCOCF_3$, $(CF_3)_2NSi(CH_3)_3$, $ArSiF_2Ar'$,
$F\overset{+}{S}i{=}O$ $F_2\overset{+}{S}i$ $[M{-}SiF_2]^+$
$RCH(NHCOCF_3)COOSi(CH_3)_3$, $F_2CHCOOSi(CH_3)_3$
$[M{-}CO_2{-}(CH_3)_3SiF]^+$ $[M{-}CH_3{-}CO]^+$, $(CH_3)_2\overset{+}{S}iF$

Numerous examples of the migration of F (including repeated migration) to atoms of elements and metals containing fluorine groups or ligands are given in two monographs.[1,62] As there has been no slackening of interest in research into these compounds, new studies on their mass spectra continue to appear, as for example those of the chelates of fluorinated diketones ZrR_4 (R = R′COCH$_2$COR″, where R′ = Ar, CH$_3$; R″ = CHF$_2$, CF$_3$, C$_2$F$_5$, C$_3$F$_7$),[63] in which are observed peaks from ions obtained by an F shift to the metal. The migration of other halogen atoms to elements and metals also occurs on electron impact[1,62] (see also above for the Si atom). In addition to the processes common to F-containing compounds, the migration of CH_2Br can occur for Br-containing compounds (because of the lower electronegativity of Br).[12] We should mention those studies in which migration of chlorine to a Si atom was recorded: trimethylsilyl esters of chlorine-containing acids;[1,10] trimethyl- and t-butyldimethyl-silyl ethers of chlorine-containing alcohols;[61] and the loss of $SiCl_2$ in $ArSiCl_2Ar'$ compounds.[61]

III. Negative-ion mass spectrometry

The fragmentation mechanisms of organic compounds in dissociative electron capture (DEC) with the formation of negative ions has been studied in detail in three monographs,[4,66,67] in which considerable attention is given to halogen-containing compounds. An atlas of mass spectra has been published, but unfortunately it is in a deposited version.[68] We shall therefore only examine the general fragmentation mechanisms of anions and radical anions. The large values of the electron affinity (EA) of halogen atoms—3.448 (F), 3.614 (Cl), 3.37 (Br), and 3.059 (I)—give rise to the appearance of intense peaks from X^{-1} ions, and the formation of other stable anions is suppressed:[11]

$$CH_3O^- \leftarrow XCH_2COOCH_3{}^{\dagger\ddagger} \rightarrow X^-$$

X=Cl	0.38% Σ (6.6 eV)†	M—none	Cl^- 99.2% Σ (0.3 eV)
X=Br	3.50% Σ (5.5 eV)	XCH_2COO^-	Br^- 92.4% Σ (0 eV)
X=I	0.0004% (4.0 eV)	Cl 0.18% Σ (1.6 eV)	I^- 84.7% Σ (0.2 eV)
		Br 0.04% Σ (1.5 eV)	
		I 0%	

Of the other halogen-containing ions that give intense peaks, we should mention $(CF_3)_3C^-$, $(CF_3)_2\bar{C}R$, $C_6F_5^-$, CF_3O^-, CF_3S^- [46,67,69] (EA = 4.1, 3.3, and 2.9 eV for $(CF_3)_3\dot{C}$, $(CF_3)_2\dot{C}H$, and $(CF_3)_2\dot{C}F$ respectively):[4,67]

$(CF_3)_2\bar{C}CH_2C_6H_4COOCH_3 \leftarrow$ *m*-$(CF_3)_3CCH_2C_6H_4COCCH_3 \rightarrow (CF_3)_3C^-$
5.7% Σ (3.2 эВ) M$^-$ 90% Σ (0.5 eV)
3.1% Σ (3.1 eV)

$F^-(0.3\%) \leftarrow CF_3SCF_3{}^{\dagger\ddagger} \rightarrow CF_3S^-$ (100%).

However, the high electronegativity values of the radicals and hence the high thermodynamic stability of their corresponding anions do not always determine the fragmentation pathway. Thus, even though the EA for F is similar to the EA of other halogens, the intensities of the peaks due to F^- ions are small in comparison with those of other halogens. For example, the contribution of the F^- ion to the spectrum of XCH_2COOCH_3 is 15% Σ compared to 99.92, and 85% Σ for Cl^-, Br^-, and I^- respectively. Similarly, despite the presence of many F atoms and the many ways of forming F^- in C_2F_5CN and n-C_3F_7CN, the intensity of its peaks at several resonance states is less than 0.5%, whereas the main ion is $^-C{\equiv}N$,[70] although the EA values for F$^\cdot$ and $^\cdot C{\equiv}N$ are similar (3.45 and 3.82 eV respectively).[4] Another phenomenon that is currently still hard to explain is that the intensities of the peaks due to $XC_6H_4COO^-$ ions are unusually small or these ions are not formed at all,[46] despite the high EA (3.4 eV) [4] for $C_6H_5COO^\cdot$ and the evidently even higher EA for $XC_6H_4COO^\cdot$ with electron-withdrawing groups X:

n-$XC_6H_4COOCH_3{}^{\dagger\ddagger}$ (M$^{\pm}$) $\rightarrow$ $XC_6H_4COO^-$ (X = CCl_3, FCH_2, $(CF_3)_3CCH_2$, C_2F_5, $(CF_3)_2CF$)
$\rightarrow$ $XC_6H_4COO^-$
0.22% (CF_3); 0.007% $(CF_3)_3C$.

It is true that in the aliphatic series the intensities of the peaks due to haloalkanecarboxylate ions are high[6] (EA = 4.5 eV for $CF_3COO^\cdot$):[4]

$CF_3COOR^{\dagger\ddagger}$ (M$^{\pm}$) $\rightarrow$ CF_3COO^-, 100%
R = CH_3, $C(CH_3)_3$, iso-C_4H_9, $CH_2CH{=}CH_2$,
$C_2F_5COOR^{\dagger\ddagger}$ (M$^{\pm}$) $\rightarrow$ $C_2F_5COO^-$, 100% ($C(CH_3)_3$); 30% (CH_3)
n-$C_3F_7COOCO_3{}^{\dagger\ddagger}$ (M$^{\pm}$) $\rightarrow$ $C_3F_7COO^-$, 28%

† Here and subsequently the position of the resonance maximum (i.e., the maximum on the ionisation efficiency curve) is given in brackets in eV; the intensity is recorded at this maximum.

We should note that halogen atoms directly situated on an anion site stabilise the latter by the inductive effect and destabilise it by a conjugation mechanism with the result that the intensities of the $C_2F_5^-$, CF_3^-, F_2CH^-, FCH_2^- are low—the EA of their corresponding radicals are 1.92, 1.74, 0.7, and 0.11 eV.[4] Because the polarisability of other halogens is greater than for F, the EA in $\dot{C}H_2X$, $\dot{C}HX_2$, and $\dot{C}X_3$ (X = Cl, Br, I) increases and the peak intensities of their corresponding ions are greater.[1,10] Amongst simple bond cleavage processes we should mention the loss of the ring fragment $CF_2=O$ in the fragmentation of perfluoro-2-propyltetrahydropyran and perfluoro-2-butyltetrahydrofuran.[71]

In contrast to the previously expressed view[66] that rearrangement processes are not very typical of DEC mass spectra, in recent years in studies on negative ions formed from esters of haloalkanecarboxylic and haloalkylbenzoic acids[4,11,12,46] it has been shown that various rearrangement processes frequently predominate in the fragmentation of anions. In these studies there are numerous examples of rearrangements that are both similar to those of positive ions and characteristic only of anions and radical anions. For example, in the mass spectra of $RCOOCH_3$ compounds, instead a peak due to the $RCOO^-$ ion (which is of low or medium intensity) an intense peak due to the $M-HF^{\dagger\cdot-}$ ion appears: 100% [R = FCH_2, C_2F_5, n-C_4F_9, p-$FCH_2C_6H_4$, p-$(CF_3)_2CFC_6H_4$]. The analogous ion $M-RF^{\dagger\cdot-}$ occurs in the fragmentation of CF_3COOR': 3.3% (R' = CH_3), 3.2% [R' = $CH_2CH(CH_3)_2$], 12% [R' = $C(CH_3)_3$], 16% (R' = $CH_2C\equiv CH$), 44% (R' = C_6H_5), 100% [R' = $Si(CH_3)_3$]. In these studies it was established for the first time that there are many hidden rearrangements. For example, in $R_FC(R_F')FCOOCH_3$ compounds there is a peak from the $M-OCH_3^{\dagger-}$ ion, which is attributed to the structure of the stable rearranged ion $R_F\bar{C}(R_F')-CFO$ rather than its unstable isomer $R_FC(R_F')(F)-\bar{C}=\ddot{O}$.[4,11,12]

We should mention the formation of the rearranged ions CF_3^- and $F_2^{\dagger\cdot-}$ in the fragmentation of perfluorocyclobutane,[72] CF_3O^- from perfluoro-2-propyltetrahydropyran and perfluoro-2-butyltetrahydrofuran,[71] and $Cl_2^{\dagger\cdot-}$ from cyclic perchlorocarbons.[73]

Thus, in studying new halogen-containing compounds, the appearance of peaks from rearranged ions involving halogens in their DEC mass spectra is to be expected.

A further important conclusion follows from the studies considered here.[4,11,46] While for the majority of organic compounds containing functional groups or multiple C—C bonds (including aromatic systems) but not containing halogens the presence of a fairly intense peak from the $M-H^{\dagger-}$ ion is typical, which makes it possible to determine the molecular ion of the compound and its empirical formula (from the isotope peaks), there is quite a different pattern for halogen-containing compounds. It is a common occurrence for the $M^{\dagger\cdot-}$ peak to be absent in $RCOOCH_3$ compounds (where R = haloalkyl). However, an unusual feature is the absence of the $M-H^{\dagger-}$ peak (particularly strange if a mobile H is present) when R = FCH_2, ICH_2, $CHCl_2$, CCl_3, C_2F_5, cyclo-C_6F_{11}, CF_3CH_2, CF_3CHF, $(CF_3)_3CCH_2$, $(CF_3)_2CF$, n-C_3F_7, n-C_4F_9, $(CF_3)_3C$, while at the same time it occurs in compounds that are not very different from the above—when R = $ClCH_2$, $BrCH_2$, $(CF_3)_2CH$. In aromatic compounds with acceptor groups, molecular ion peaks usually occur,[4,66] but halogen-containing substituents introduce a modification here also. Thus, the intensity of the $M^{\dagger\cdot-}$ peak in p-$CF_3CF_2CF_2C_6H_4COOCH_3$ is 100% while that in its isomer p-$(CF_3)_2CFC_6H_4COOCH_3$ is 0.03% (i.e., the latter simply cannot be detected, being indistinguishable from a background peak).[46] This example indicates the highly specific nature of DEC mass spectra, which is certainly difficult to predict. There are no $M^{\dagger\cdot-}$ and $M-H^{\dagger-}$ peaks in the mass spectra of $RC_6H_4COOCH_3$ (R = p- and m-$(CF_3)_3CCH_2$), the $M^{\dagger\cdot-}$ peak is weak (0.7%) in the mass spectrum of p-$(CF_3)_3CC_6H_4COOCH_3$ and the $M-H^{\dagger-}$ peak is absent.[46] These facts should be borne in mind when the DEC mass spectra of unknown compounds are analysed.

IV. Chemical ionisation and other ionisation mass spectrometry

In continuing the previous section, let us start our examination of chemical ionisation (CI) spectra with negative ions. Under CI conditions aromatic compounds give intense peaks from $M^{\dagger\cdot-}$ molecular ions when there is a low degree of fragmentation, while peaks due to $M-H^{\dagger-}$ ions occur for compounds that do not have a system of conjugated bonds. Methane is often used as a working gas for CI, but in certain cases mixtures with halogen-containing compounds such as $CH_3OH + CHCl_3$,[74] $CH_4 + CH_2Cl_2$,[75] NF_3, CF_2Cl_2, CF_3Br [76] are used. Under these ionisation conditions studies have been made of the mass spectra and optimum detection conditions for a series of pentafluorophenyl compounds C_6F_5R (R = CH_3, F, OH, OCH_3, NH_2, SH, $OCOCH_3$, CHO, NO_2, CN),[77] pentafluorobenzoyl derivatives of amino acids,[78] chloro- and fluoro-ethylenes,[79,80] pentafluoropropionates of hydroxylamine derivatives,[81] trifluoroacetyl derivatives of polyhydric alcohols,[82] chloroglucuronides,[83] halogen-containing derivatives of dipeptides and their metabolites,[84] and α,β-difluorocinnamic acid derivatives.[85] Chemical ionisation with negative ions achieves high selectivity (for isomers) and very high sensitivity for polyhalogen-containing compounds. This is used, for example, for quantitative determinations (after GLC separation) of polychloropolybromo-dibenzo-dioxins and -furans from their $M^{\dagger\cdot-}$ and Br^- ions.[48]

Positive-ion chemical ionisation mass spectra are used to establish the molecular formula of a compound being analysed that does not give an $M^{\dagger+}$ peak in its EI mass spectrum. The $M + H^{\dagger+}$ ion, which is formed in compounds containing groups to which the proton of a π-system can be added (aromatic compounds, alkenes, alkynes), carbonyl-containing groups (ketones, aldehydes, acids and their derivatives), groups with coordinate bonds

$(NO_2, -C\equiv\overset{+}{N}\rightarrow\bar{O}, -S(O)-, -SO_2-, SO_2OR, N_3, -P(O)_2OR)$.

is used for this purpose. Thus, while the $M^{\dagger\cdot-}$ peak is absent during EI, an $M + H^{\dagger+}$ peak occurs in CI of the compounds $CF_3(CF_2)_2CF(CF_3)COOC_2H_5$,[86] $SF_5N(Cl)C_2F_5$ and $SF_5N=CFC_2F_5$,[27] $FO_2S(CF_2)_2O(CF_2)_2R$,[87] $F_5EN=CBr_2$ (E = S, Te),[21] and $CF_3O(CF_2)_2O(CF_2)_2SO_2F$.[88] The mass spectra of RSF_5 (R are fluorinated groups with an $-SO_2$ residue) obtained under CI conditions have been studied by Terjeson et al.[19] In the CI of the compound $C_2H_5(CF_2)_2O(CF_2)_2SO_2F$ the $[M + H]^+$ ion does not appear but the $M-F^{\dagger+}$ ion is recorded instead.[23] In the fragmentation of $(CF_3)_3COH$ and $C_4F_9\overset{\frown}{CF(CF_2)_3O}$, $M + F^{\dagger+}$ ions are recorded together with the formation of $M + H^{\dagger+}$.[28]

The fact that a determination of structural elements under CI conditions (if the compound is unknown) is either not feasible or only insignificant information about the structure is contained in the CI spectra is a disadvantage. The reason for this is that the general fragmentation mechanisms of the so-called pseudomolecular ions, such as $M + H^{\dagger+}$ and even more so for $M + X^{\dagger+}$ (or $M + X^{\dagger-}$), have not yet been established and only empirical rules for the formation of positive ions of the individual yet numerous classes of

organic chemicals generated during CI have been put forward.[89] Moreover, in the protonation of compounds with several "sites" for the possible addition of a proton (or other ion), it is as though a mixture of products is obtained (with an unknown relative content of each of them), each of which fragments by its own pathways. Therefore a structural analysis of halogen-containing compounds can be conducted as before (despite the development of new ionisation methods and techniques) by means of the traditional electron impact. In this respect we should mention other methods and techniques. Thus, detection of negative ions is possible during thermal spray ionisation in liquid chromatograph–mass spectrometers used for the analysis of nonvolatile or thermally unstable compounds such as certain pesticides.[90–92] The formation of anions is controlled by the addition of halogen-containing compounds to the eluent. For example, introduction of only 0.1–1% chloroacetonitrile substantially increases the sensitivity of detection of phenols through the formation of $M + Cl^{-}$ ions.

For an analysis of compounds that are nonvolatile under normal EI conditions, such as organic hydrohalide salts[92] or certain pesticides,[94] desorption from the surface in a strong electric field can be used, including that combined with separation of mixtures on a liquid chromatograph.[95] A widely used method for the analysis of unstable compounds with low volatility is fast atom bombardment, which has been used, in particular, to study fluoroalkylsulphonates,[96] metabolites of 2-chloro-*N*-isopropylacetanilide,[97] iodoxamic acid and its dimethyl ester,[98] halides of certain Group IV elements,[99] and complexes with tetrabutylammonium fluoride.[100] The mass spectra of dihalomethanes[101] have been obtained under conditions of collision-activated positive ions, and the mass spectra of chlorodibenzodioxins[102] have been obtained with negative ions. In the latter study[102] both low-energy and high-energy processes during collision with oxygen have been investigated.

The mass spectra of halomethanes,[103] 1,1-difluoroethane,[104] 1,1-dichlorodifluoroethylene,[105] fluoroethylenes,[106] and 5-fluorouracil derivatives[107] have been obtained under photoionisation conditions and interpreted. Photoionisation mass spectrometry is mainly used to obtain thermochemical characteristics of the molecules (including halogen derivatives), ionisation potentials (IP), and, what is particularly valuable, the appearance potentials (AP) of the fragment ions. The enthalpies of formation of halogen-containing ions, radicals (carbenes), and neutral molecules are calculated from the AP. In recent years various reactions involving the transfer of particles, principally H^{+} as well as CH_3^{+}, Cl, and others, have been studied in the gas phase by high-pressure mass spectrometry[108] and ion cyclotron resonance.[109] Together with photoionisation mass spectrometry, these are valuable methods for a determination of the enthalpies of formation of ions, radicals, carbenes, and neutral molecules. Without a knowledge of the latter it is impossible to represent thermochemically the ionisation, isomerisation, and fragmentation processes of halogen-containing compounds on electron impact, under chemical ionisation conditions, etc. Without them a rational interpretation of the mass spectrum and representation of the decomposition pathways and mechanisms are made difficult. By having a knowledge of the thermochemical values, it is possible to predict the direction of isomerisation and fragmentation of molecular and fragment ions. We shall give a brief summary of the sources of information on the thermochemical properties of halogen-containing compounds and their fragments. Enthalpy of formation values of halogen-containing molecules appear in two reference books,[110,111] a review,[112] and two monographs.[4,113] IP values of molecules containing halogens are included in three reference books,[10,114,115] two reviews,[116,117] and individual publications.[12,118,119] Calculated values of the IP, EA, and enthalpies of formation of all the isomeric compounds ranging from tetra- to octa-chlorodibenzo-dioxins and -furans are given by Koester and Hites.[120] Experimental values of the energies of formation (IP_2) of the doubly charged ions of 9 halomethanes and 6 haloethanes that can be obtained not only in a mass spectrometer but also above the earth's ozone layer were derived in two studies.[121,122] In the monograph by Takhistov[4] information is given on the enthalpies of formation of halogen-containing ions and the electron affinity values for 24 halogen-containing radicals. In several studies data are given on the enthalpies of formation of halogen-containing ions—haloacyl ions,[123] 20 novel fluorine-containing ions,[124] trifluoroallyl ions,[125] trifluorobenzenium ions.[126] The proton affinity (PA) values for many halogen-containing molecules and the heats of formation of $M + H^{+}$ ions calculated from the PA values are given by Lias et al.[127] Correlations between the PA of molecules and their adiabatic IP have been derived,[119] which makes it possible to obtain values for the enthalpies of formation of $M + H^{+}$ ions from the IP of halogen-containing molecules. The acidity values of halogen-containing molecules, from which in combination with the heats of formation of the corresponding radicals (see below) it is possible to calculate the heats of formation of anions, are given in several studies.[128–134] The electron affinity values of halogen-containing molecules which are needed to calculate the enthalpies of formation of radical anions are given in two studies.[131,135] We should mention the study of Lias et al.,[136] in which the reaction

$$HCXY + B: \rightarrow :CXY + BH,$$

where B is a base, X and Y = F and Cl, has been investigated; and the study of Mishima et al.,[137] in which Cl^{-} transfer was used to determine the enthalpy of formation of $XC_6H_4\dot{C}H_2$. In two further studies by Mishima et al.[138,139] the proton affinity values of 10 halogen-containing (F, Cl, CF_3) styrenes and α-methylstyrenes respectively have been obtained. In a study by McMahon et al.[140] the values of affinity towards CH_3^{+} have been obtained for a number of halogen-containing molecules.

The enthalpy of formation values of halogen-containing free radicals (formed as pairs with cations and anions in the mass spectrometer) are given in five studies.[4,141–144] In three publications[4,141,142] the energy values for homolytic bond cleavage are given, from which additional information about the enthalpies of formation of free radicals may be obtained. Takhistov[4] provides information about the enthalpies of formation of all the halogen-containing carbenes (:CXY and :CHX) as well as small molecules and radicals that are expressly of interest for mass spectrometry.

V. Analytical aspects of the mass spectrometry of halogen-containing compounds

The prevalence of halogen-containing compounds is steadily increasing. Halogen-containing compounds (freons, pesticides, polyhalobiphenyls, polyhalodibenzodioxins, polyhalodibenzofurans) head the list of those compounds whose contaminating effect has already assumed a global (worldwide) character. Of the 230 volatile organic compounds detected in the atmosphere above a large forest, 18 were halogen-containing compounds.[145] They are found in virtually any living organism in any corner of the earth. Hence there is an urgent need to identify or establish the structure of novel compounds containing halogens. It is therefore useful to summarise

the literature of recent years in which mass spectra are examined (we shall not deal with questions concerning the determination of aromatic chlorine-containing compounds by mass spectrometric methods which were considered in detail in two reviews).[148,149]

For benzene compounds, mass spectra have been obtained for benzenes polysubstituted by Br, CF_3, $CF=CCl_2$,[150] halogen-substituted stilbenes,[151] aromatic sulphones with $-CHF$ and $-CF_2-$ chain residues,[152] benzenes with CF_3CH_2X, O, or NR groups,[153] 10 phenyl-containing β−F-amines,[154] tris(*p*-chlorophenyl)methanol found in biological products,[155] novel natural hexasubstituted dichlorobenzenes,[156] S- and Cl-containing products from the bioconversion of hexachlorobenzene,[157] metabolites of chloropropham (3-chloroaniline and 3,3′-dichloroazobenzene),[158] 86 methyl polychlorobiphenyl sulphones,[159] *p*-methylthioperchlorostyrene (a product of the mussel metabolism of perchlorostyrene),[160] novel chlorine-containing aromatic compounds (anilines, benzonitriles, benzophenones, fluoroenones, xanthen-9-ones) detected during the combustion of domestic waste products,[161] methyl polychlorophenyl sulphones (products of the metabolism of polychloro- and polychloronitro-benzenes by garden plants),[162] polychlorocumenes,[163,164] α-methylstyrenes,[163] the ethylesters of isomeric chlorophenylpropionates and chlorophenylbutyrates,[165] and fluorobromobenzocyclanones.[166]

For heterocyclic compounds mention should be made of mass spectrometric studies on 2-R-substituted furans, thiophenes, pyrroles, and also benzenes [R = $-(CF_2)_nCl$, *n* = 4,6,8],[167] and furans and thiophenes containing CF_3 and $CF=CCl_2$ groups,[45] 2,5-difluoro-2,5-bis(trifluoromethyl)-2,5-dihydro-furan and -thiophene,[45] 3-chloro-4-dichloromethyl-6-hydroxy-2(5*H*)-furan and 2-chloro-3-dichloro-methyl-4-keto-butene-2-oic acid obtained in the chlorination of natural and waste water,[168] 18 mixed chloro- and bromo-dibenzodioxins and 18 mixed chloro- and bromo-dibenzofurans,[50] 3-methoxy-2,6-dichlorodibenzodioxin (a methylated product of the metabolism of 2,5-dichlorodibenzodioxin by goldfish),[169] bromosubstituted nitropyridines and their oxides,[170] imidazoles with RC_6F_4 groups,[171] quinoxalines with $(CH_3)_2CF$ and $C_2H_5(CH_3)C(F)$ groups,[172] F- and CF_3-containing *spiro*-3-indolines,[173] perfluoroalkyl-sorbitan, -isosorbide, and -isomannide (EI and CI mass spectra),[174] products of the electrochemical fluorination of *N*-cycloalkylpyrrolidines and *N*-cycloalkylpiperidines,[175] perfluorobicyclic amines and amino acids,[176] and 1,2-diazacyclopentadienes with isomeric fluorobutyl groups.[177] In a review[178] on the synthesis of heterocyclic compounds with F and CF_3 groups on the ring, references to their MS studies may also be found.

The mass spectra of aliphatic compounds have been studied in the case of β-ketoesters with perfluoroalkyl groups and F atoms at the 3-position,[179,180] 3-substituted ethyl trifluoromethylacetoacetates,[181] their derivatives and also ketones $CF_3COCH(R)(R')$,[181,182] amines with a CF_3CH_2 group and their Cl and Br derivatives,[183] ω-chloroperfluoroacyl(amino)ethylenes,[184] polynitrogen-containing compounds with an F_2NCF_2 group,[20] telomers of chlorofluoropropionitrile fluorides with hexafluoropropylene oxide,[185] the perfluoroacrylate of 1-adamantol,[186] pentamethyl-5-X-cyclopentadienes (X = Cl, Br, I),[187] and halogen-substituted thioesters.[188]

Two reference books[9,14] remain important as sources of information on the mass spectra of halogen-containing compounds.

In conclusion we shall examine certain aspects of the application of the mass spectrometry of halogen-containing compounds. The majority of high-resolution instruments are equipped with computers that are used to calculate the empirical formulae of the ions. In our view, some of the data obtained in this manner must be treated with caution, since errors are possible. Thus, in analysing the results of Hudlicky and Glass[189] we noticed that the computer set to record F-containing ions in the analysis of the compound cyclo-$C_6F_{11}CF_2COOCH_3$ yielded the formula $C_8F_{13}^+$ for the $M-47]^+$ ion with loss of an impossible CH_3OO fragment instead of $M-F-CO]^+$ (the latter is typical of F- and CO-containing compounds) or $C_8H_3F_{12}O^+$ (the authors did not detect this error). In the mass spectra of diketones with a CF_3 group, such as $XC_6H_4COCH_2COCF_3$, $CH_3COCH_2COCF_3$, and $R_FCOCH_2COCF_3$, an intense peak from an ion with *m*/*z* 69 appears, to which both a computer and operator (after manual determination of the exact value of the mass ion) with a good resolution of 10−12 000 would undoubtedly assign the formula CF_3^+. In fact, however, this is an ion with empirical formula $C_3HO_2^+$, and a better resolution (about 15−18 000) is required to distinguish it from CF_3^+, while the CF_3 fragment is eliminated in the primary process:[12]

$$\underset{M^+}{XC_6H_4C(OH)=CHCOCF_3]^+} \longrightarrow \underset{[M-CF_3]^+}{XC_6H_4C(OH)=CHC\equiv\overset{+}{O}} \longrightarrow O=C=CHC\equiv\overset{+}{O}$$

$$69^+ : [M-CF_3-XC_6H_5]\,.$$

Hence there is an obvious need for more careful treatment of the data supplied by a computer.

Some aspects of the analysis of halogen-containing compounds have been considered above. It may be noted in addition that halogens have proved to be elements that can be successfully determined using the empirical formula of compounds and it is possible to establish exactly which halogen occurs in the molecule. The presence of Cl and Br atoms in any quantity and combination is readily established from their characteristic isotope patterns.[4] Since there are several or many F atoms in the majority of F-containing compounds (fluorinated chain, R_F, SF_5, and C_6F_5 groups, several CF_3, NF_2, OCF_3, SCF_3 groups, etc.), the presence of fluorine, which is monoisotopic, can be assessed from the weak intensity of the isotopic (from ^{13}C) peak of the ion next to any peak at large masses. Taking into account its high atomic weight (127), iodine also gives a similar reduced peak. In the literature there are examples of the difficulties and occasionally the impossibility of distinguishing the isomers of fluorinated compounds obtained in a single process (in electrochemical fluorination, for example). Thus, the isomers cyclo-$C_6F_{11}CF_2COOCH_3$ and cyclo-$C_5F_9CF_2CF_2COOCH_3$ or cyclo-$C_5F_9-C_4F_9$ and cyclo-$C_6F_{11}-C_3F_7$ cannot be distinguished in the EI mass spectrum.[189] At the same time it is possible to distinguish positional isomers and the geometric isomers $ClCH=C(Br)COOCH_3$ and $BrCH=C(Cl)COOCH_3$.[24] The isomers *p*-$CF_3CF_2CF_2C_6H_4COOCH_3$ and *p*-$(CF_3)_2CFC_6H_4COOCH_3$ were readily distinguished in DEC mass spectra (in contrast to the EI mass spectra).[46]

Halogens can be used to analyse other compounds. Thus, a fluorine or chlorine "label" in the form of an XC_6H_4 or $X_2C_6H_3$ (3,5-$Cl_2-C_6H_3-$) group is used for a number of aryl (usually phenyl) groups at different positions, since the direction of fragmentation when C_6H_5 is replaced by these groups does not alter and these halogens do not introduce any new pathways for the decomposition of molecular and primary (secondary) ions (their effect only becomes evident at the advanced stages of fragmentation). The $Si(CH_3)_2CH_2Cl$ group is used in mass spectrometry to "protect" hydroxyl-containing groups; it is more successful than the traditional group—$Si(CH_3)_3$. Although the M^+ peak does not appear in the modified compound, as in the initial

HO-containing compound, the $M-CH_2Cl^+$ ion has the highest mass (and is considerably more intense than the $M-CH_3^+$ ion in $(CH_3)_3Si$ derivatives).[4] This group can also be of help in distinguishing stereoisomers.

The groups CF_3CO, C_2F_5CO, and C_3F_7CO serve as valuable protecting groups in complex molecules of biological origin. By replacing hydroxyl groups with them, it is possible to increase substantially the molecular weight of the compound being analysed and to shift the peaks of the characteristic mass ions to higher mass, having thus eliminated the effect of impurities, the solvent, metabolites, if the analysis is conducted from a biological fluid (blood, urine, plasma). Although M^+ naturally does not appear in such systems, the characteristic series $M-R_FCOOH^{+\cdot}$, such as $M-CF_3COOH^{+\cdot}$ (or $M-114^{+\cdot}$), $M-2CF_3COOH^{+\cdot}$ (or $M-228^{+\cdot}$), etc., can be detected.

A review of the methods for introducing the CF_3CO group, including those using the convenient novel reagent 2-trifluoroacetoxypyridine, is presented by Koemi et al.[190] The mass spectra of C_3F_7CO-substituted amines have been reported by Mikaya et al.[191]

Mass spectrometry is a versatile method for detecting an element in a sample even when any other element is present in the latter, owing to the unique nature of the isotopic composition of each of them. The problem is merely that of obtaining volatile forms of the elements. A versatile, synthetically accessible class of organometallic compounds that is suitable for analysis using mass spectrometric methods is made up by complexes of metals with fluorinated ketones, in particular $CF_3COCH_2COCH_3$ and $CF_3COCH_2COC.(CH_3)_3$.[4] Volatile chelates of about 60 elements of the Periodic Table are known, even including those of the "awkward" Group I elements (as double salts with rare earth elements). A series of different halogen-containing diketones and their sulphur-containing analogues are reviewed by Takhistov.[4] Methods of modifying compounds to forms that are convenient for mass spectrometric analysis are described in a monograph by Zaikin and Mikaya,[192] as well as in the above review.[4]

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Translated from *Uspekhi Khimii* **60** 2167–2188 (1991) U.D.C. 547.341 + 547.544.3

Enolisation of the phosphoryl group

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ABSTRACT. **The potential ability of the phosphoryl group to undergo enolisation is demonstrated. The conditions for enolisation of phosphoryl and thiophosphoryl groups are examined. In order to determine the acidifying capacity of groups attached to the α-carbon atom, constants that depend on the number of substituents on this atom have been used. The limiting values of the totals of the constants that are responsible for enolisation of the phosphoryl group have been calculated. It is shown that enolisation of the phosphoryl group obeys the laws comprising the theory of prototropic tautomeric acid–base equilibrium.**

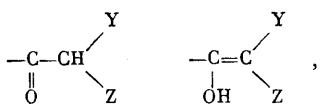
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I. Introduction

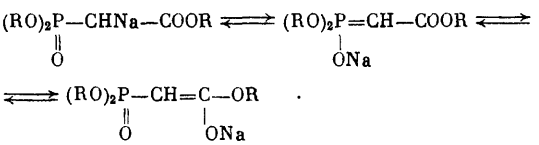
The ability of the carbonyl group to undergo enolisation is well known. It manifests itself most clearly in β-dicarbonyl compounds and in other cases where another electronegative group is situated at the β-position relative to the carbonyl group



(I)

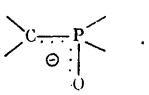
where Y and Z = COR, COOR, CN, SO_2R, etc., while Y can be H, Alk, or Ar. It is also known that simple ketones are only slightly enolised. It was established some time ago that a strong acidifying effect is needed from substituents Y and Z for enolisation to occur. This question was examined at one time by Arndt[1–4] and also Schwarzenbach et al.[5–7] in a series of studies on enolisation and acidity.

In the chemistry of organophosphorus compounds the phosphoryl group P=O is the analogue of the carbonyl group C=O. However, until the end of the 1970s not a single case of enolisation of the phosphoryl group was recorded in the literature. It may merely be mentioned that A E Arbuzov and A I Razumov in 1929 and 1934 proposed that the sodium derivative of phosphonoacetic ester undergoes tautomerism:[8,9]



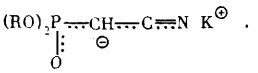
If it is borne in mind that at that time the concept of mesomeric ambident anions had not been widely developed, this report may be regarded as the first suggestion that the phosphoryl group can enolise. It was, of course, purely speculative in nature.

Subsequently lithium derivatives of di- and tri-phosphoryl-methanes were used more than once in organic synthesis.[10–13] In these Li derivatives the negative charge of the anion of the phosphorylated CH acid is undoubtedly delocalised on to the oxygen atoms of the phosphoryl groups in (II):



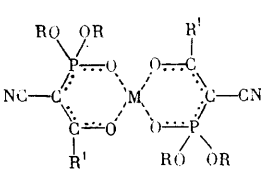
(II)

The same can be said of the metal-containing intermediates of the widely used Horner olefination that is activated by P=O.[14–16] Many examples of the alkylation and acylation of metal derivatives of β-ketophosphonates and other compounds have been reported.[7–29] However, in these cases the authors were dealing with conventional metal enolates on the carbonyl group. Nevertheless, the structure of these metal derivatives has not been studied in detail. In the studies of Kirilov and Petrov[20,22] the potassium derivative of phosphorylacetonitrile was thought to contain the ambident anion (III), whose charge is concentrated to a considerable degree on the phosphoryl oxygen atom:



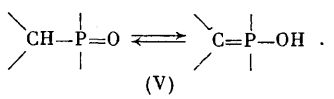
(III)

Finally, mention should be made of the crystalline magnesium and copper complexes of acylated phosphorylacetonitriles whose structure is described by Petrov and Kirilov.[30] These are *cis*-chelates with a P–O–M (IV) bond



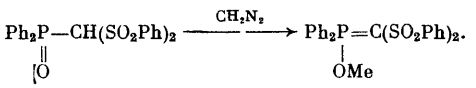
(IV)

Thus, in anions of phosphorylated CH acids the oxygen atoms of the phosphoryl group can carry, if only partially, the anion charge with a corresponding reduction in multiplicity of the P=O bond and in certain cases can form a bond with a metal cation. However, there has been no single recorded case of the tautomerism of phosphoryl and phosphaenol structures (V):



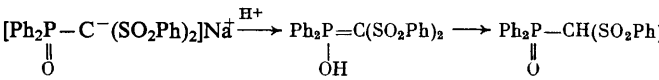
(V)

The enolisation of β-phosphorylated carbonyl compounds has been studied in great detail, but in all cases only the normal enol forms ($=\overset{|}{C}-OH$) rather than phosphaenol forms ($=\overset{|}{P}-OH$) have been observed.[20,22,26–28,31–38] The same occurs for thiophosphoryl compounds.[39] The above does not apply, of course, to the ambident reactivity of phosphoryl compounds, or more accurately their carbanions, towards electrophilic reagents. An example is the reactivity towards methylation of phosphoryl oxygen atom on treatment of diphenylphosphinylbis(phenylsulphonyl)methane with diazomethane:[40]



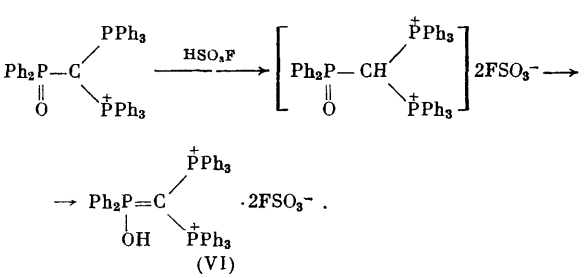
But this is a methylation reaction, rather than the addition of a proton which is needed to produce the phosphaenol form.

The first reports on enolisation of the phosphoryl group appeared in the latter half of the 1970s. Kolodyazhnyi[41] reported the formation of the unstable phosphaenol form of diphenylphosphinylbis(phenylsulphonyl)methane on acidification of a solution of its sodium derivative:



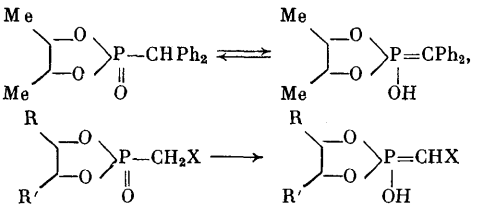
This phosphaenol form is rapidly and irreversibly converted to the CH form.

Mastryukova et al.[42] observed the formation of the stable phosphaenol form of diphenylphosphinylbis(triphenylphosphonio)-methane (VI) on protonation of the corresponding phosphorane-phosphonium salt with fluorosulphonic acid:



(VI)

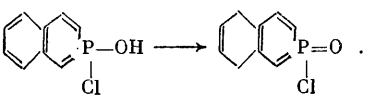
There are two reports by Ovchinnikov et al.[43,44] on the phosphaenolisation of cyclic phosphates:



R=Me, R′=H, Me; X=COOMe, CN.

However, the phosphaenol structure of these compounds was later disputed.[45]

Finally, in 1979 Bickelbaupt et al.[46] synthesised the cyclic phosphaenol (VII), which readily and irreversibly "ketonised":



(VII)

With regard to enolisation of the thiophosphoryl group, the only example of this type (VIII) was found by Mastryukova et al.[47] It fully resembles the enolisation of the corresponding phosphoryl compound:



(VIII)

Thus, up to the beginning of the 1980s there were only isolated reports concerning phosphaenol forms in the literature and information about phosphoryl–phosphaenol (phosphoryl–hydroxy-ylide) tautomerism was absent altogether.

II. Possible enolisation of the phosphoryl group

It has been established that the position of a prototropic tautomeric equilibrium is determined by the ratio of the acidity constants of the forms in the given medium:

$$K_T = K_1/K_2. \qquad (1)$$

Here K_T is the tautomeric equilibrium constant, and K_1 and K_2 are the acidity constants of the tautomeric forms.[48] On enolisation of carbonyl groups, enol OH acids are formed, which, depending on their structure and stereochemical configuration, have an acidity that varies over a wide range—from pK_a = 10–12 for simple ketones and the least acidic β-dicarbonyl compounds to pK_a = 5–9 for normal β-dicarbonyl compounds† (data for aqueous solution).[49] Therefore, in order for enolisation to occur, it is necessary that the CH acidity of the ketone forms are similar to that of enols, i.e., pK_a = 5–10 (in water). In the case of enolisation of phosphoryl groups, the OH acidity of phosphaenols is substantially higher than

† Only when there are certain structural features of a β-dicarbonyl compound (fluorinated β-diketones, *trans*-configured cyclic enols with small rings, etc.) is an OH acidity with pK_a = 2–4 attained.[50]

that for their carbon analogues. Unfortunately, there are no comparative data for aqueous solutions. However, the acidity in water of other OH acids of phosphorus, and carbon (phosphoric and carbonic acid, methylphosphonic and acetic acids, etc.) can be compared. In this case there is very convincing evidence that phosphorus OH acids are stronger by a factor of 10^2-10^4. Therefore, for enolisation of the phosphoryl group to occur, phosphoryl CH acids must have $pK_a = 3-5$. This can only be achieved when there are strongly acidifying electron-withdrawing groups, stronger than in the chemistry of β-dicarbonyl compounds, at the β-position relative to the phosphoryl group.

Because of the need to make an objective determination of the acidifying effect of groups on CH acidity, we have developed a method of σρ correlation analysis of CH acidity based on the familiar Hammett equation:[51] $pK = pK^0 - \rho\sigma$. It was natural to use σ^- constants, which take into account directly polar conjugation of the substituent with the nucleophilic reaction site. However, difficulties related to the existence of the so-called "saturation effect" arose.[52] This means that the effect of an acidifying group attached to the central carbon atom is variable. It depends on the number of those groups that are already attached and decreases as these groups accumulate. This circumstance required the calculation of three σ^- values for each substituent — $\sigma_{CH_3}^-$, $\sigma_{CH_2}^-$, and σ_{CH}^- — depending on whether the substituent is located on a primary, secondary, or tertiary carbon atom. In developing this method of σρ correlation, the values of the $\sigma_{CH_n}^-$ constants were refined from the large quantity of experimental data in the literature on the CH acidity of different compounds and also from our own data on the CH acidity of organophosphorus compounds. Some of the derived values of the $\sigma_{CH_2}^-$ and σ_{CH}^- constants are given in Tables 1 and 2.[53-55] When these constants were used, good and excellent correlations between the pK of a large number of CH acids and the $\sigma_{CH_n}^-$ constants were obtained in different media and under different experimental conditions.

Table 1. $\sigma_{CH_2}^-$ and σ_{CH}^- constants for certain groups X.[53,54]

X	$\sigma_{CH_2}^-$	σ_{CH}^-	X	$\sigma_{CH_2}^-$	σ_{CH}^-
Me	0.12	0.13	$PhSO_2$	0.77	0.71
Ph	0.365	0.26	n-$MeC_6H_4SO_2$	0.75	0.70
MeCO	0.88	0.66	NO_2	1.26	1.12
PhCO	0.98	0.78	COOEt	0.725	0.60
CN	0.80	0.75	$CONEt_2$	0.58 *	0.42

* See study of Matveeva et al.[54]

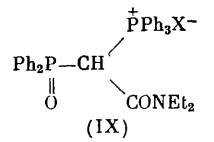
By using the new $\sigma_{CH_n}^-$ constants it proved possible to correlate the CH acidity of β-dicarbonyl compounds with their enolising capacity. Thus, for the completely enolised triacetylmethane, $\Sigma\sigma_{CH}^- = 1.98$; for the strongly enolised benzoylacetone, $\Sigma\sigma_{CH_2}^- = 1.86$; for the slightly less enolising acetylacetone, $\Sigma\sigma_{CH_2}^- = 1.76$; for the weakly enolising acetoacetic ester, $\Sigma\sigma_{CH_2}^- = 1.60$; and for malonic ester, which has a very low tendency to undergo enolisation, $\Sigma\sigma_{CH_2}^- = 1.44$. Thus, a range of values of $\Sigma\sigma_{CH_n}^-$ approximately from 1.6 to 2.0 in β-dicarbonyl compounds governs the strength of CH acidity that assists enolisation. It is of course necessary to take into account the OH acidity of the enol forms [cf. Eqn. (1)]. The acidifying effect of the substituents influences the OH acidity of enols, although to a lesser extent, but to a first approximation we can confine ourselves to the treatment of $\Sigma\sigma_{CH_n}^-$.

Table 2. $\sigma_{CH_2}^-$ and σ_{CH}^- constants for certain phosphorus groups X.[55]

X	$\sigma_{CH_2}^-$	σ_{CH}^-	X	$\sigma_{CH_2}^-$	σ_{CH}^-
$Ph_3\overset{+}{P}$	1.22	1.08	$Ph_2P(O)$	0.57	0.44
$(PhO)_2P(O)$	0.60	0.47	$Et_2P(O)$	0.47	0.36
$(EtO)_2P(O)$	0.56	0.44	$Me_2P(O)$	0.47	(0.35) *
$(BuO)_2P(O)$	0.55	(0.43) *	PhEtP(O)	0.51	(0.39) *
Bu(EtO)P(O)	0.50	(0.38) *	$Ph_2P(S)$	0.60	0.46
$Bu_2P(O)$	0.45	0.34	$(EtO)_2P(S)$	0.59	0.50

* Figures in brackets are values obtained by interpolation.

The OH acidity of phosphaenol forms is higher than in β-dicarbonyl compounds. Therefore, their CH acidity must also be substantially higher. We recently discovered that compound (IX) with $\Sigma\sigma_{CH}^- = 1.94$ does not enolise under any conditions,[56] whereas it was found previously that the corresponding diphosphonium derivative (VI) with $\Sigma\sigma_{CH}^- = 2.60$ is completely enolised.[42] Consequently, a value of $\Sigma\sigma_{CH}^-$ ranging from 2.0 to 2.6 is most favourable for enolisation of the phosphoryl group and phosphoryl–hydroxyl-ylide tautomerism:

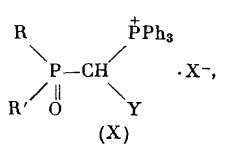


(IX)

Since it is difficult to achieve such high values of $\Sigma\sigma_{CH_n}^-$ without the use of phosphonium substituents, studies were subsequently made on compounds in which a triphenylphosphonium group was located on the central carbon atom together with the phosphoryl group. In this case by varying substituent Y it was possible to obtained cases of $\Sigma\sigma_{CH_n}^-$ ranging from 2.0 to 2.6.

III. Synthesis of phosphoryl compounds

Phosphoryl(triphenylphosphonio)methanes substitueed on the central carbon atom with the general formula (X)



(X)

where Y = $^{+}PPh_3X^{-}$, CN, Ts, COOEt, $CONEt_2$; R and R′ = Et, Bu, Ph, EtO, BuO, PhO in different combinations: X = Cl^{-}, Br^{-}, ClO_4^{-}, BF_4^{-} were synthesised.[57–60] The starting materials used were the respective phosphine-substituted phosphoranes (XII) obtained in accordance with literature data[61,62] from the corresponding monosubstituted triphenylmethylenephosphoranes (XI) and halophosphines or halophosphites in the presence of triethylamine:

$$Ph_3P{=}CHY + RR'PX \xrightarrow{Et_3N} RR'P{-}C(PPh_3)(Y)$$

(XI) (XII)

The phosphinophosphoranes (XII) were then oxidised to the phosphorylphosphoranes (XIII) on treatment with $KMnO_4$ in acetone or H_2O_2 in t-butanol:

$$(XII) \xrightarrow{KMnO_4 \text{ or } H_2O_2} R'P(O)(R)-C(PPh_3)(Y)$$

(XIII)

In many cases, instead of starting from monosubstituted triphenylmethylenephosphoranes (XI), it proved more advantageous to use the corresponding phosphonium salts (XIV), i.e., to treat them with dialkyl- or diaryl-halophosphines (RR′PX) or phosphorohalidites [$(RO)_2PX$] and triethylamine in a solution of dichloromethane under mild conditions (atmosphere of argon, temperature 0–20 °C):

$$\underset{(XIV)}{Ph_3P{-}CH_2{-}Y} + RR'PX + 2Et_3N \rightarrow (XII) + 2Et_3N{\cdot}HX.$$

It subsequently proved possible to carry out the oxidation stage of (XII) → (XIII) without isolation of (XII) from the reaction mixture but to treat it directly with H_2O_2 in t-butanol at 0 °C.

Phosphoranephosphonium salts (XIII), where Y = $^{+}PPh_3X^{-}$, were obtained by addition of diphenyl- or dialkyl-halophosphines to hexaphenylcarbodiphosphorane (XV) with isolation of the intermediate crystalline phosphino derivative (XII), Y = $^{+}PPh_3Cl^{-}$:

$$\underset{(XV)}{Ph_3P{=}C{=}PPh_3} + R_2PCl \longrightarrow (XII) \xrightarrow{KMnO_4} (XIII) .$$

Oxidation of (XII) to (XIII), Y = $^{+}PPh_3Cl^{-}$, was carried out with $KMnO_4$ in acetonitrile. Protonation of phosphoranes (XIII) was carried out in benzene or dichloromethane at 20 °C by treatment with an ethereal solution of halogen halides:

$$(XIII) \xrightarrow{HX} (X) .$$

Crystalline phosphonium salts (X) were generally obtained; their melting points are given below in Table 3.

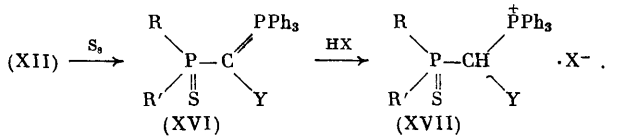
Table 3. Melting points and IR spectra of phosphorylphosphonium salts in the crystalline state.[57–60,65]

$R_2P(O)-CH(Y)-\overset{+}{P}Ph_3X^{-}$ (A) or $R_2P(OH)=C(Y)-\overset{+}{P}Ph_3X^{-}$ (B)

No.	Y	R	X	m.p.	IR spectrum, KBr pellets, ν, cm^{-1}			Other frequencies	Form of compound
					P=O	P–OH	OH...X		
1	COOEt	Ph	Cl	123–125 (decomp.)	–	970 [2*]	1500–2200	1600(CO), 3440(EtOH)	B
2	COOEt	Ph	ClO_4	164–166 (decomp.)	1160, 1180 (shld.)	–	–	1730(CO), 2900(CH)	A
3	COOEt	PhO	ClO_4	113 (decomp.)	1290	–	–	1740(CO), 2880(CH)	A
4	COOEt	Ph	BF_4	117–119 decomp.)	–	–	600–1800	1670(CO)	BHB+
5	$CONEt_2$	Ph	Cl	167–168	1150	–	–	1630(CO), 2500–2800 (CH...Cl)	A
6	CN	Bu	Br	144–146	–	975	1500–3000	2170(CN)	B
7	CN	Ph	Br	160.5–162	–	965	1500–3000	2175(CN)	B
8	CN	Bu	ClO_4	144–145	–	910	1960–3000	2170(CN)	B
8[a]	After crystallisation in air			116–118	–	–	1640–1900	3100–3600(H_2O)	$BHOH_2^{+}$
9	CN	Ph	ClO_4	149–151	–	–	700–1700(OH...O)	2170(CN)	BHB+
10	Ts	Bu	Br	149–150	–	960	1800–2000	1130, 1280 [3*]	B
11	Ts	Ph, Et	Br	179–181	–	940	1700–2800	1125, 1285 [3*]	B
12	Ts	Ph	Br	123–125	–	945	2000–2700	1135, 1280 [3*]	B
13	Ts	BuO	Br	100–102	–	970	2000–3000	1140, 1290 [3*]	B
14	Ts	Bu	ClO_4	154–155	see 4*	–	–	1150, 1330 [3*]	A
15	Ts	Ph, Et	ClO_4	181–184	1195	–	–	1150, 1330 [3*]	A
16	Ts	Ph	ClO_4	173–178	–	–	600–1800	1135, 1282 [3*]	BHB+
17	Ts	Bu, EtO	ClO_4	167–168	1245	–	–	1159, 1330 [3*]	A
18	Ts	BuO	ClO_4	162–163	1275	–	–	1150, 1340 [3*]	A
19	Ts	EtO	ClO_4	184–185	1272	–	–	1155, 1330 [3*]	A
20	+ Ts	BuO	ClO_4	220–222	1290	–	–	1165, 1330 [3*]	A
21	PPh_3Br^{-}	Ph	Br	261–264	–	940 (br.) 980 (br.)	1600–3000	–	B [5*]

With $^1/_2$ M of crystalline EtOH; [2] in petrolatum 960, 980 cm^{-1}; [3*] first figure for symmetric SO_2 vibrations, second figure for antisymmetric SO_2 vibrations; [4*] PO vibration region masked by ClO_4 band; [5*] $B...H...OH_3^{+}$ is possible.

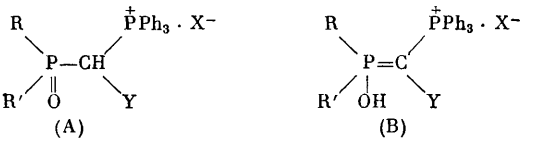
The thiophosphoryl derivatives (XVI) were obtained by addition of sulphur to phosphinophosphoranes (XII) in benzene, acetonitrile, or mixtures of them in the cold for 6–24 h or by boiling for 10–15 min.[63,64]



(XII) (XVI) (XVII)

IV. Phosphaenols (hydroxyl-ylides) in the crystalline state

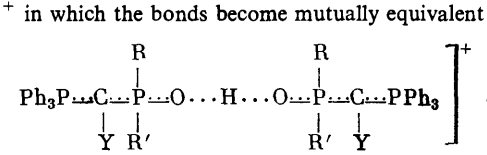
The crystalline phosphorylphosphonium salts that were studied are listed in Table 3. They are stable compounds that can be recrystallised in air without any special precautions. The conclusion about their phosphoryl CH structure (A) or phosphaenol structure (B) is based on an examination of their IR spectra, and in a number of cases X-ray diffraction analysis was used:



(A) (B)

The IR spectra of the compounds with structure (A) contain a very characteristic band due to P=O in the region 1150–1195 cm^{-1} when alkyl or aryl groups are attached to phosphorus and at 1270–1290 cm^{-1} when RO groups are attached. When structure (B) is formed this band disappears and in its place a band appears at 910–975 cm^{-1} that is typical of the protonated P=O group.[66] At the same time very broad absorption bands appear in these spectra at 1500–3000 cm^{-1} which suggest that OH groups with strong hydrogen bonds OH...X^- are present. As far as the vibrations of groups Y are concerned, these groups are attached to an sp^3-hybridised carbon atom in structures (A) and to an sp^2-hybridised carbon atom in structures (B). As a consequence the frequencies in the first case are higher. Thus, the CO vibration of the carbethoxy group for structure (A) is 1730–1740 cm^{-1} while for structure (B) it occurs at 1660 cm^{-1}. The symmetric SO_2 vibrations in structure (A) are at 1150–1165 cm^{-1} while in structure (B) they occur at 1125–1140 cm^{-1}, the antisymmetric vibrations occur at 1330–1340 cm^{-1} (A) and 1280–1290 cm^{-1} (B) respectively. All of these changes are very uniform, which provides sufficient reliability in the assignment of structures to (A) and (B).

In addition to structures of the type (B) with an OH...X^- hydrogen bond, "dimeric" structures in which the conjugate base acts as an H-bond acceptor were detected. A complex of the type BHB^+ in which the bonds become mutually equivalent is formed:



The IR spectra of the BHB^+ structures are characterised by the absence of bands due to P=O and P–OH and the presence of a broad complex band at 600–1800 cm^{-1}. In this case the vibrations of Y conform to structure (B). Such "dimeric" complexes have been confirmed by X-ray diffraction data.

It should be noted that the X-ray diffraction data very clearly characterise both the phosphaenol forms and BHB^+ structures. Thus, in the structure of the tosyl derivative with form (B) (No. 12, Table 3) (Fig. 1), the central carbon atom [C(1)] has only a slightly distorted planar trigonal coordination with a projection of 0.118 Å from the P(1)P(2)S plane. The C(1)–PPh_2OH and C(1)–PPh_3 have virtually the same length—1.751(4) and 1.764(4) Å—and a multiplicity of one and a half.[67] The phosphaenol form is stabilised in the crystalline state by an OH–Br hydrogen bond of length 3.078 Å.

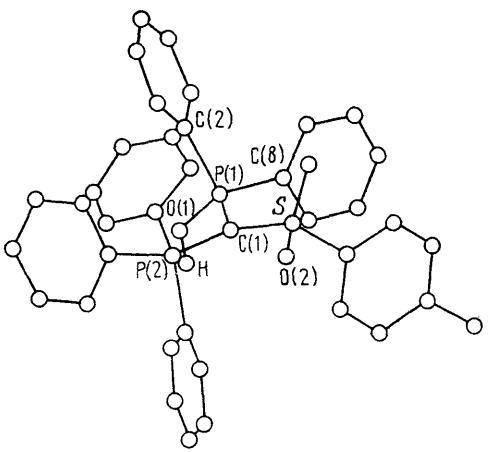


Figure 1. Crystalline structure of the cation component of the bromide salt of (hydroxydiphenylphosphoranylidene)tosyl(triphenylphosphonio)methane $Ph_3P^+C(Ts)=P(Ph_2)O-H...(Br^-)$.[65]

Stabilisation of the phosphaenol structure can, however, be achieved with the assistance of another protophilic species. Thus, in the case of crystals of (dibutylhydroxyphosphoranylidene)cyano-(triphenylphosphonio)methane perchlorate (No. 8, Table 3), structure (B) is unstable, and on recrystallisation from an acetone–ether mixture when air is admitted, it is stabilised by absorption of a single water molecule to form a salt of the type $(BHB')^+$, where B' is the water molecule. In this novel structure the crystal is composed of two crystallographically independent cations. In each of them (Fig. 2) the central carbon atom C(1) is also planar trigonal, the projections from the plane are 0.072 and 0.054 Å, and the sum of the angles about C(1) is 359.4°. The C(1)–PBu_2OH and C(1)–PPh_3 bonds are virtually the same and on average have a length of 1.745(9) Å, which corresponds to a multiplicity of approximately one and a half. The oxygen atoms of the water molecule O(11) act as acceptors of protons from the P–OH group. The O...H...O distances are equal to 2.501(6) and 2.482(7) Å, which corresponds to hydrogen bonds of increased strength.[68] It is interesting to note that in turn the H_2O molecules also participate through their H atoms in the formation of O–H...N bonds with the cyano groups of the neighbouring cations.

The structure of (diphenylhydroxyphosphoranylidene)carbethoxy (triphenylphosphinio)methane borofluoride (No. 4, Table 3) is shown in Fig. 3 as an example of a symmetric BHB^+ complex. The

structure is centrosymmetric. Its two "halves" are identical and joined by a hydrogen bridge. The central C(1) carbon atom is planar trigonal, the sum of the angles is 359.3° and the lengths of the C(1)—PPh_2OH and C(1)—PPh_3 bonds are virtually the same—1.725(8) and 1.735(8) Å—with a multiplicity of about one and a half. The length of the O...H...O hydrogen bond is 2.422(8) Å. The lengths of all the bonds of the "dimer" are mutually equivalent, which suggests that the cation charge is delocalised over both "halves".

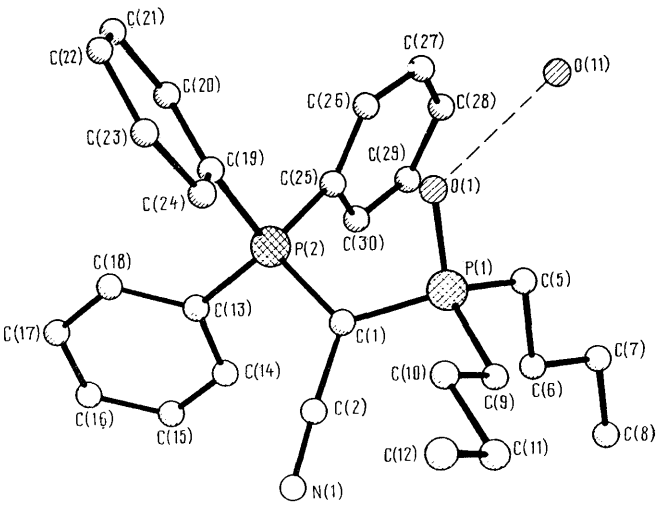


Figure 2. Structure of one of the two crystallographically independent cations of (hydroxydibutylphosphoranylidene)cyano-(triphenylphosphonio)methane perchlorate—a $(BHB')^+$ complex with a molecule of H_2O [the O(11) oxygen atom is shown]; $PH_3P^+C(CN)=(Bu_2)O-H...OH_2(ClO_4^-)$.

It may be concluded from an examination of the data in Table 3 that there are two principal factors that govern the alternative structure. The first is the nature of Y. The phosphaenolising capacity of the Y groups is given by a series that corresponds to the following variation in σ_{CH}^- values:

	$Ph_3\overset{+}{P}$	>CN	>Ts	>COOEt	>$CONEt_2$
σ_{CH}^-	1.08	0.75	0.70	0.60	0.42

The $^+PPh_3$ group has the highest phosphaenolising capacity while $CONEt_2$ has the lowest capacity. The second factor is the nature of the counterion X^-. The OH...X^- hydrogen bond undoubtedly stabilises the phosphaenol. The anions also form the following series of ability to form an H bond: $Cl^- > Br^- > ClO_4^- \approx BF_4^-$. Therefore, with the exception of the compound with a $CONEt_2$ group, all the chlorides and bromides are phosphaenols. The ClO_4^- anion, which has a low tendency to form H bonds, gives rise to the formation of structures (A) or BHB^+ (Table 3). The results can be understood if the combined effect of these two factors is taken into account.

Two phosphonium groups (compound No. 21, Table 3) have such a strong acidifying effect that the proton is not retained on the central carbon atom but is located on the PO group. When Y = CN (bromides Nos. 6 and 7, Table 3), the phosphaenol structure is governed by the fairly strong acidifying effect from the CN group and the stabilising effect from a strong OH...Br hydrogen bond. For the perchlorate this stabilisation is achieved either with a molecule of the conjugate base (No. 9, Table 3) or with a water molecule (No. 8, Table 3)—BHB^+ or $BH-OH_2^+$ complexes are formed. The pattern is quite clear when Y = Ts; the bromides have structure (B) and the perchlorates have structure (A) or BHB^+. As for compounds with the relatively weakly acidifying group Y = COOEt—, although the chloride (No. 1, Table 3) in this case has structure (B), the perchlorates (Nos. 2 and 3, Table 3) have structure (A), and the borofluoride has a BHB^+ structure. Finally, the carbamoyl group (Y = $CONEt_2$, compound No. 5, Table 3) with the weakest effect causes the chloride to have structure (A).

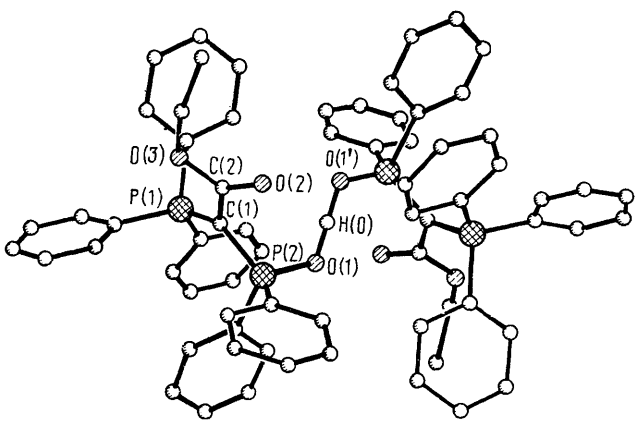


Figure 3. BHB^+ structure of (hydroxydiphenylphosphoranylidene)-carbethoxy(triphenylphosphonio)methane:

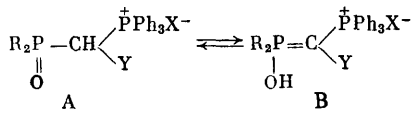
$$Ph_3P^+-C(COOEt)=P(Ph_2)O\cdots H\cdots O=$$
$$=P(Ph_2)P-C(COOEt)=PPh_3(BF_4^-)\ .$$

The relative stability of the phosphaenol forms in the crystalline state naturally depends on the many factors that determine the crystal lattice energy, but it may be assumed that the acidifying effect of groups Y and the strength of the OH...X^- hydrogen bonds are amongst the most important ones.

V. Phosphoryl—phosphaenol tautomerism

Phosphoryl—phosphaenol tautomerism, otherwise known as Phosphoryl—hydroxy-ylide tautomerism, as in (V), is the phosphorus analogue of keto—enol tautomerism, as in (I). Therefore the methods used to study keto—enol systems can be applied to it also.

Table 4. $^{31}P-\{^1H\}$ NMR of phosphorylphosphonium salts (X), CH_2Cl_2.[61,62]

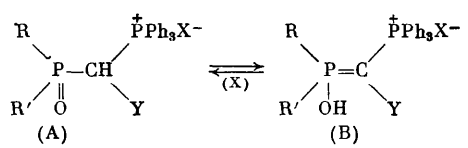


A B

Y	R	X	T, °C	Form	δ_{PO}, ppm	δ_{PPh_3}, ppm	J_{PP}, Hz
$^+PPh_3X^-$	Ph	Br	30	B	40.9 (trip.)	23.5	20
$^+PPh_3X^-$	Ph	ClO_4	20	B	38.3 (trip.)	24.8	21*
$^+PPh_3X^-$	Ph	CF_3COOH	30	B	49.2 (trip.)	22.7	20 [2*]
CN	Ph	Br	30	B	51.5 (br. s.)	22.7	27
CN	Ph	CF_3COOH	−20	A	33.4 (br. s.)	24.3	см [2*]
CN	Ph	ClO_4	30	BHB$^+$	43.6	23.9	26
CN	Bu	Br	30	B	74.8	23.4	20
CN	Bu	ClO_4	30	B	76.9	23.2	20
				A	51.5 (br. s.)	26.0	–
CN	PhO	Cl	−80	A	6.9 (br. s.)	23.7 (br. s.)	–
CN	EtO	Cl	−80	A	0.1 (br. s.)	24.6 (br. s.)	–
COOEt	Bu	Cl	−70	B	79.2; 78.0	19.2; 20.3	24 [3*]
				A	48.8	23.1	7
COOEt	Ph	Cl	−80	B	43.8; 40.6	19.0; 20.0	40, 42 [3*]
				A	28.6	23.8	7
COOEt	Ph	ClO_4	30	A	25.2	24.3	7
COOEt	PhO	Cl	30	A	4.1	22.0	–
COOEt	PhO	ClO_4	30	A	2.6	23.0	5 [4*]
$CONEt_2$	Ph	Cl	30	A	29.4	27.0	10

In $MeNO_2$; [2] in CF_3COOH; [3*] two conformers; [4*] in $CHCl_3$.

In the $^{31}P-\{^1H\}$ NMR spectra in solutions of tautomeric phosphonium salts (X) two pairs of doublet signals are generally observed.



(A) (B)

In this case forms (A) display two doublet signals with chemical shifts that are not very different from the initial phosphorylphosphoranes (XIII) but with much smaller spin-spin coupling constants J_{PP} (from 0 to 10 Hz). For forms (B) the chemical shifts of the phosphorus nucleus in the PPh_3 group hardly differ from the above, but the signals due to the nuclei in the P−OH groups are displaced downfield by 20−30 ppm. On the other hand the values of J_{PP} are similar to those of the initial phosphoranes. We should note that the number of signals from forms (B) can double, especially at low temperatures, because of the presence of two conformers in solution or of two diastereoisomers in other cases. On increasing the temperature a number of changes occur in the ^{31}P NMR spectra. There is a redistribution of intensities of the signals due to a change in position of the tautomeric equilibrium and the signals change because of an acceleration of both conformational transitions and proton exchange between the forms. At first the conformational doublets coalesce—a single pair of doublets remains in the spectrum—and these are then converted to broad singlets or even merge into the background noise.[56−60,63−65]

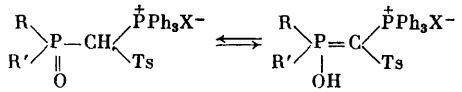
In the PMR spectra, triplet or doublet-doublet signals due to the methine protons of forms (A) with J_{PCH} constants of the order of 13−17 Hz, singlet signals due to the P−OH protons of form (B), and also signals from other groups occur. However, because of rapid proton exchange the signals from CH and OH frequently combine to give a broad singlet. The protons of other groups, such as those from COOEt or $SO_2C_6H_4Me$, on the other hand, appear as separate signals from the tautomeric forms, and they can be used to determine the tautomeric equilibrium constants. However, this is also more suitable to observe at a low temperature.

The tautomeric equilibria are established rapidly and do not change with time. They do not depend on the method of preparing the solution—by dissolving salt (X) or by treatment of phosphorane (XIII) with acid. The results obtained by various methods of studying the tautomeric equilibria are in good agreement. The $^{31}P-\{^1H\}$ NMR data recorded in CH_2Cl_2, the most significant for all of the compounds studied, are given in Table 4 and 5.

It was found that the bis(triphenylphosphonium) salt (X), $Y = {}^+PPh_3$, R and R′ = Ph, exists in solution solely as form (B) (Table 4).[61,62] This applies both to the bromide and perchlorate. Moreover, in trifluoroacetic acid, in which only the (A) forms occur in all other cases, only form (B) occurs in the case of the bis(phosphonium) salt. Evidently because of the strong acidifying capacity of the triphenylphosphonium groups ($\sigma_{CH}^- = 1.08$), the CH acidity of the diphosphonium salt is so high that formation of the CH structure [form (A)] is impossible even in CF_3COOH.

CN-Substituted compounds (X), Y = CN (bromides) with R and R′ = Ph or Bu are in the form of phosphaenols (B), while when R

Table 5. $^{31}P-\{^1H\}$ NMR of phosphorylphosphonium salts (X), Y = Ts, CH_2Cl_2.[58,60,64]



(A) (B)

R	R′	X	T, °C	Form	δ_{PO}, ppm	δ_{PPh_3}, ppm	J_{PP}, Hz
Ph	Ph	Br	30	B	46.4	18.2	29.0 *
Ph	Ph	ClO_4	30	B	45.9	17.5	26.0 *
Ph	Et	Br	30	B	58.1	18.2	24.0
Ph	Et	ClO_4	30	B	60.7	18.3	26.0
				A	44.4 (s.), 43.0 (s.)	20.1 (s.), 21.0 (s.)	см 2*
Bu	Bu	Br	30	B	75.3	16.7	23.0
				A	55.6 (s.)	19.6 (s.)	–
Bu	Bu	ClO_4	30	B	78.0	17.0	23.0
				A	58.4	19.0	–
Bu	EtO	Br	−80	B	72.0	17.0	24.5
				A	45.8 (c)	18.2	–
Bu	EtO	ClO_4	30	B	70.2	17.5	27.0 3*
				A	45.9; 43.6 (s.)	19.5 (s.); 19.7 (s.)	6.0 2*
BuO	BuO	Br	−80	B	22.0	17.7	39.0
				A	7.3 (s.)	20.4 (s.)	–
BuO	BuO	ClO_4	30	A	6.7 (s.)	21.3 (s.)	–
EtO	EtO	Br	−80	B	25.5	17.9	41.5
				A	6.8 (s.)	20.4 (s.)	–
EtO	EtO	ClO_4	30	A	6.5 (s.)	21.2 (s.)	–
PhO	PhO	Br	−80	A	−0.2 (s.)	20.7 (s.)	–
PhO	PhO	ClO_4	30		−0.9 (s.)	22.0 (s.)	–

(98% B); 2 two diastereoisomers; 3* in $CHCl_3$.

and R′ = EtO or PhO (chlorides) at low temperature, they exist as (A). As for perchlorates, both forms occur in solution when R and R′ = Bu, while when R and R′ = Ph a complex of the type BHB^+, in effect form (B), is formed. In contrast to the bis(phosphonium) salt, only for (A) occurs in CF_3COOH.

In the tosyl derivatives (X), Y = Ts (Table 5) when R and R′ = Ph only form (B) occurs in a solution of the bromide and perchlorate. When R = Ph and R′ = ET a tautomeric equilibrium occurs for the perchlorate.‡ There is also a tautomeric equilibrium when R and R′ = Bu (bromide and perchlorate) and when R = Bu and R′ = EtO (X = Br^- and ClO_4^- also), as well as when R and R′ = AlkO (in the bromides). But in solutions of the perchlorates when alkoxy groups are attached to phosphorus, only the (A) forms occur. This also applies, of course, when R and R′ are phenoxy groups.

The carbethoxy derivatives (X), Y = COOEt (Table 4), exhibit a tautomeric equilibrium only when R and R′ = Ph or Bu with X = Cl. In the remaining cases only the (A) forms are present. Finally, if Y = $CONEt_2$, the group that has the lowest acidifying capacity (σ_{CH}^- = 0.42), only form (A) occurs (Table 4). Thus, a decrease in the electron-withdrawing capacity of groups Y leads to a predominance of form (A) and vice versa.

The R and R′ groups attached to phosphorus have a considerable effect on the position of tautomeric equilibrium, as was to be expected. Data on the effect of these groups on the tautomeric equilibrium constants in the series of tosyl derivatives are given in Table 6. These results are correlated with σ^Φ constants, which characterise the effect of the substituents attached to phosphorus on the acidity of phosphorus acids.[69] It can be seen that the content of form (B) increases with a decrease in electronegativity of R and R′. This is quite natural—highly electronegative groups R and R′ increase the strength of P−OH acids, which assists transfer of the proton to carbon.§ A special position is occupied, however, by aromatic derivatives. A phenyl group attached to phosphorus markedly assists phosphaenolisation. The cause of this phenomenon has been discussed more than once in other cases of the "phenyl anomaly". It has been suggested that OH...Ph hydrogen bonds are formed,[70] that there is steric destabilisation of the CH form,[60] that the hydrophoby and rigidity of the benzene rings have an effect, etc. Unfortunately, the origin of this phenomenon is still not clear.

The nature of the anion has a considerable effect on the position of the tautomeric equilibrium (A) ⇄ (B), varying in accordance with its ability to form an H bond that stabilises the phosphaenol: $Cl^- > Br^- < BF_4^- \geqslant ClO_4^-$. The effect of the solvent is also considerable. In aprotic media the percentage content of form (B) decreases with an increase in dielectric constant ε of the solvent.

‡ In this case the signals due to form (A) are split because of diastereomeric anisochronism.

§ This explanation implies that the substituents attached to phosphorus have a greater on effect on the strength of P−OH acids than on P−CH acids, which is very probable.

As an example we can illustrate the effect of solvents on the content of form (B) in $PPh_2(O)CH(\overset{+}{P}Ph_3Cl^-)COOEt$ at −60 °C:

	CH_2Cl_2	CH_2Cl_2+MeCN (4 : 1)	$MeNO_2$
ε	9.14	14.6	38.57
% B	77.0	60.0	<45

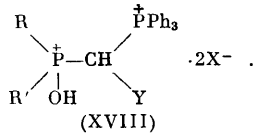
The proton-donating solvent chloroform effectively solvates the P=O group and hence shifts the equilibrium towards from (A). In alcohols, which effectively solvate the OH forms, the equilibrium is shifted towards form (B).

Table 6. Effect of substituents R and R′ on the position of the tautomeric equilibrium A ⇄ B of phosphonium salts (X), Y = Ts, CH_2Cl_2.[58,60,64]

R	R′	$\sum\sigma^{\Phi}$	X=Br⁻ (−80° C)		X=ClO_4 (30° C)	
			% B	K_T	% B	K_T
Bu	Bu	−2.44	75	3.00	29	0.39
Bu	EtO	−1.43	50	1.00	12	0.14
BuO	BuO	−0.82	45	0.82	<2	<0.02
EtO	EtO	−0.42	25	0.33	<2	<0.02
PhO	PhO	−0.12	<2	<0.02	<2	<0.02
Ph	Et	−1.58	95	19.0	60	1.5
Ph	Ph	−1.18	>98	>49	>98	>49

As for the effect of temperature, it depends on the nature of the solvent. In the aprotic solvent CH_2Cl_2 an increase in temperature shifts the equilibrium in favour of the (B) forms, which characterises the (A) forms as more stable. In an alcoholic medium the opposite occurs. The thermodynamic parameters for tautomerism of (X), when Y = COOEt, were calculated from the temperature dependence of the tautomeric equilibrium constants. The tautomers proved to have very similar enthalpies ($\Delta H°$ ranging from −1.5 to +2.5 kcal mol^{-1}). The entropy differences were found to be higher (ΔS ranging from −3.6 to 10.6 E. U.).[59]

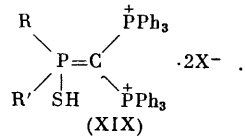
The effect of the acidity of the medium on the position of the equilibrium (A) ⇄ (B) is interesting. An increase in acidity of the medium shifts the equilibrium towards form (A). It would appear that protons from the acid compete with the protons of the P−OH group for hydrogen bonding with the anions and thus decrease the stabilising effect of the latter. With a large increase in acid concentration doubly protonated products (XVIII) are formed:



(XVIII)

In the ^{31}P NMR spectra of these acid salts the chemical shifts of the phosphoryl P nucleus occur at lower field. Thus, when Y = COOEt, X = Cl, and R and R′ = Ph, δ_{PO} = 50.1 ppm (as opposed to 28.6 ppm in the monoprotonated (A) form], while when R and R′ = Bu, δ_{PO} = 82.7 ppm [48.8 ppm in the (A) form].

Enethiolisation of the thiophosphoryl group is markedly different from its oxygen analogue.[63] All the phosphonium salts (XVII) have a CH structure in the crystalline state. The salt with two phosphonium groups (XVII), Y = $\overset{+}{P}Ph_3X^-$, cannot be obtained in the crystalline state because of the extremely low basicity of the corresponding phosphorane (XVI), but in solution of CH_2Cl_2 or FSO_3H it has the mercapto-ylide structure (XIX), which is established with certainty from its ^{31}P-{^1H} NMR spectrum:



(XIX)

All of the remaining (XVII) salts, regardless of the nature of Y, R, R′, and X, have a thiophosphoryl structure and do not exist as tautomers. Only in diphosphonium salt does a low value of J_{PP} occur—from 1 to 8 Hz. In all of the remaining salts the value of J_{PP} is in line with that of the thiophosphorylphosphoranes.

Thus, enethiolisation of the thiophosphoryl group only occurs when Y = $\overset{+}{P}Ph_3$. Even the CN group has an insufficient acidifying effect for the enethiol form to occur, and all derivatives with CN and other groups with lower σ_{CH}^- values have the thiosphosphoryl structure (XVII) and do not exist as tautomers. It may be assumed that the region of thiophosphoryl−mercapto-ylide tautomerism must occur when the $\Sigma\sigma_{CH}^-$ values approximately vary from 2.5 to 2.7. Unfortunately, this region remains inaccessible for the time being (cf. Tables 1 and 2).

VI. Enolisation of the phosphoryl group and acidity

It has been known for a long time that the acidic properties of prototropic tautomeric compounds are related in a complex manner to the position of the tautomeric equilibrium. The latter, as is evident from Eqn. (1), is determined by the ratio of the acidity constants but not by the degree of acidity of both forms. Experimentally the given apparent dissociation constant K_{app} of the equilibrium mixture, which is related to the dissociation constants of the individual forms, is determined by ratio (2):[48]

$$K_{app} = K_1.K_2/(K_1 + K_2), \quad (2)$$

where K_1 and K_2 are the dissociation constants of the forms. By measuring the apparent dissociation constant K_{app} and the tautomeric equilibrium constant K_T, it is possible to calculate the dissociation constants of the individual forms:

$$pK_1 = pK_{app} - \lg(K_T + 1), \quad (3)$$

$$pK_2 = pK_1 + \lg K_T. \quad (4)$$

It was of considerable interest to elucidate the acidic properties of phosphoryl CH acids [(A) forms] and phosphaenols [(B) forms] and their structural dependences. It was also suitable to make use of σρ correlation analysis for this purpose. In addition to that it was necessary to test the applicability of the latter for a quantitative representation of the acidity of compounds with these structures on products that were of the same type but not tautomeric. The

thiophosphorylphosphonium salts (XVII) were used as such compounds. The dissociation constants of these compounds in nitromethane and absolute ethanol were determined potentiometrically with a glass electrode.[71] The results of the measurements are given in Table 7.

Table 7. Acid dissociation constants of thiophosphorylphosphonium salts (XVII) $R_2P(S)CH(Y)\overset{+}{P}Ph_3\cdot X^-$ in $MeNO_2$ and absolute EtOH at 25 °C.

No.	R	Y	$\Sigma\sigma_{CH}^-$	pK_{app}, $MeNO_2$,	pK_{app}, EtOH
1	Bu	COOEt	2.06	9.60	4.56
2	Ph	COOEt	2.14	7.63	4.08
3	Bu	Ts	2.16	6.05	4.05
4	Bu	CN	2.21	4.71	–
5	Ph	Ts	2.24	4.03	3.63
6	EtO	Ts	2.28	3.86	3.61
7	Ph	CN	2.29	3.50	3.36
8	PhO	Ts	2.30	2.55	3.31

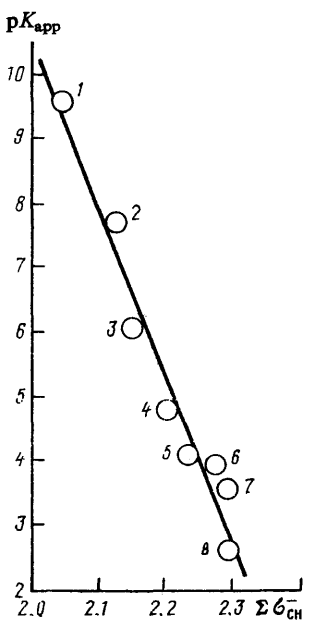


Figure 4. Correlation of pK_{app} with $\Sigma\sigma_{CH}^-$ for $RR'P(S)CH(Y)\overset{+}{P}Ph_3X^-$ in $MeNO_2$; the numbers of the points correspond to the numbers of the compounds in Table 7.

These acids can evidently be classed as fairly strong. We can show for comparison that in $MeNO_2$, pK = 7.05 for CF_3COOH, pK = 11.62 for $ClCH_2COOH$, and pK = 14.41 for CH_3COOH.

On Hammett coordinates with σ_{CH}^- constants they give a good correlation (even an excellent one in absolute ethanol) (Figs. 4 and 5) with the following parameters

In $MeNO_2$: $pK_{app} = 65.82 - 27.410\ \Sigma\sigma_{CH}^-$;

n=8; r=0.980; s=0.52; s_ρ=2.32.

In EtOH: $pK_{app} = 14.94 - 5.052\ \Sigma\sigma_H^-$;

n=7; r=0.998; s=0.03; s_ρ=0.13.

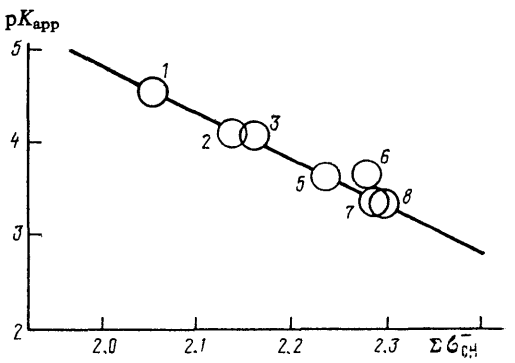


Figure 5. Correlation of pK_{app} with $\Sigma\sigma_{CH}^-$ for $RR'P(S)CH(Y)\overset{+}{P}Ph_3X^-$ in EtOH; the numbers of the points correspond to the numbers of the compounds in Table 7.

In the correlation in $MeNO_2$ two details attract attention. Firstly, the straight line has a very high gradient (ρ = 27.410). This results from the well-known strong differentiating effect of $MeNO_2$; the difference between the strengths of the acids in this case is as high as a factor of 10^7. Secondly, there is a very high value of pK^0 (almost 66). Theoretically this should correspond to the pK of methane in $MeNO_2$. Measurement of this constant is, of course, experimentally impracticable. Ethanol, on the other hand, is a solvent that causes a levelling out; in this case the difference in pK_{app} values does not exceed a factor of $10^{1.25}$. A linear Brønsted relationship occurs between the pK in the two solvents.

$$pK_{MeNO_2} = -15.72 + 5.535 pK_{EtOH},$$

r=0.978; s=0.58; s_ρ=0.52.

The high gradient, which differs markedly from unity, suggests that there are considerable differences in the differentiating capacity of nitromethane and ethanol.

The acid dissociation constants of the tautomeric phosphorylphosphonium salts (X) were determined in a similar manner. The results are listed in Table 8, where the equilibrium content of the phosphaenol forms (B) determined ^{31}P NMR is given for comparison. It can be seen that all the compounds can also be classed as comparatively strong acids. In nitromethane their strength is on average about 0.7 pK units lower than the thiophosphoryl acids (XVII) examined above; in ethanol they are virtually of equal strength. The strong differentiating action of nitromethane occurs here in the same way. The dissociation

constants vary by a factor of 10^{11} in accordance with the substituents attached to phosphorus and carbon, while they vary by a factor of only 10^3 in ethanol, which levels out the differences. With the same substituents on phosphorus the acid strength decreases on changing from Y = CN via compounds with Y = Ts to the carbethoxy and then carbamoyl derivative. These results vary in the same way as the σ_{CH}^{-} constants of the Y groups. Marked variations in the content of the phosphaenol forms occur on changing the substituents in both solvents, and phosphaenolisation does not vary in the same way as acidity. For example, the more acidic compound 2 (Table 8) is only slightly enolised while the less acidic compounds 1 and 4 (Table 8) are almost completely enolised. Relationships of this type are known in the classical chemistry of tautomeric compounds. For example, the more acidic cyclopentanonecarboxylic ester is enolised less than the less acidic cyclohexanonecarboxylic ester. As has already been mentioned, enolisation depends on the acidity ratio of the forms rather than the overall degree of acidity.

Table 8. Dissociation constants of tautomeric phosphorylphosphonium salts

$$\underset{(A)}{RR'P(O)CH(Y)\overset{+}{P}Ph_3X^-} \rightleftarrows \underset{(B)}{RR'P(OH)=C(Y)\overset{+}{P}Ph_3X^-}$$

in $MeNO_2$ and absolute EtOH at 25 °C.

№ п/п	R, R'	Y	$\Sigma\sigma_{CH}^{-}$	$MeNO_2$				EtOH			
				pK_{app}	% B	pK_{CH}	pK_{OH}	pK_{app}	% B	pK_{CH}	pK_{OH}
1	Ph	CN	2.27	4.27	~98	2.57	4.26	3.86	>99	–	~3.86
2	PhO	Ts	2.25	2.44	~2	2.43	0.73	–	–	–	–
3	EtO	Ts	2.22	3.38	~2	3.37	1.68	3.63	>99	–	~3.63
4	Ph	Ts	2.22	6.00	~98	4.30	5.99	3.14	>99	–	~3.14
5	BuO	Ts	2.21	–	–	–	→	3.70	>99	–	~3.70
6	Ph, Et	Ts	2.18	5.27	50	4.97	4.97	–	–	–	–
7	Bu	CN	2.17	5.79	~98	4.09	5.78	3.88	>99	–	~3.88
8	PhO	COOEt	2.15	6.60	~2	6.59	4.90	–	–	–	–
9	Bu	Ts	2.12	6.70	16	6.62	5.90	4.58	97	3.06	4.57
10	Ph	COOEt	2.12	8.82	16	8.74	8.02	3.54	70	3.02	3.39
11	Bu	COOEt	2.02	10.59	33	10.42	10.11	4.73	36	4.54	4.29
12	Ph	$CONEt_2$	1.94	13.84	~1	13.84	11.84	6.22	~2	6.21	4.51

The dissociation constants of the (A) forms (pK_{CH}) and the dissociation constants of the (B) forms (pK_{OH}) were calculated using Eqns. (2)–(4). The results are included in Table 8. It can be seen that the value of pK_{CH} increases as $\Sigma\sigma_{CH}^{-}$ decreases. At the same time the Hammett correlation is perfectly satisfactory in nitromethane and good in ethanol (Fig. 6):

In $MeNO_2$: $pK_{CH} = 81.99 - 35.246\ \Sigma\sigma_{CH}^{-}$;

$n=11$, $r=0.977$, $s=0.80$, $s_\rho=2.55$.

With regard to the pK_{CH} in ethanol, only the last four figures in Table 8 are reliable. There is a good correlation between them and $\Sigma\sigma_{CH}^{-}$.

In EtOH: $pK_{CH} = 39.61 - 17.268\ \Sigma\sigma_{CH}^{-}$;

$n=4$; $r=0.996$; $s=0.16$, $s_\rho=1.06$.

In these correlations also there is an unusually high value of pK^0, especially in nitromethane.

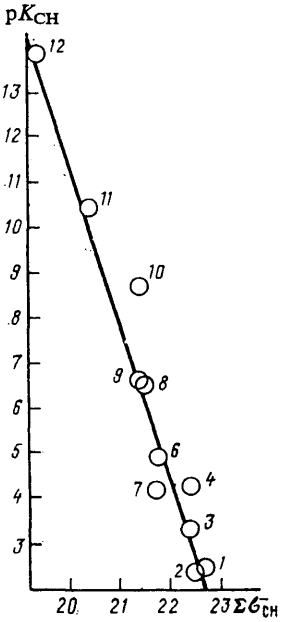


Figure 6. Correlation of pK_{CH} with $\Sigma\sigma_{CH}^{-}$ for $RR'P(O)CH(Y)\overset{+}{P}Ph_3X^-$ in $MeNO_2$; the numbers of the points correspond to the numbers of the compounds in Table 8.

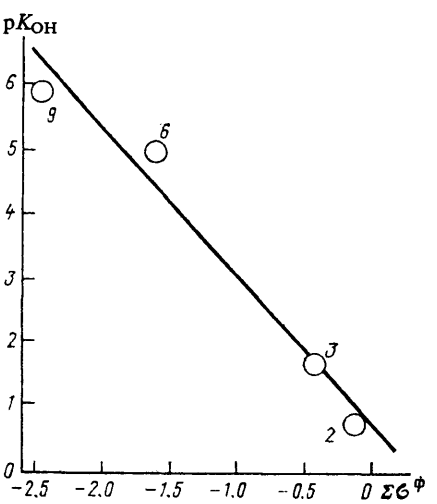


Figure 7. Correlation of pK_{OH} with $\Sigma\sigma^{*}$ for $RR'P(OH)=C(\overset{+}{P}Ph_3X^-)CH(Ts)$ in $MeNO_2$; the numbers of the points correspond to the numbers of the compounds in Table 8.

The dependence of pK_{OH} on structure proves to be quite complex, since in the (B) forms it is not only the substituents on the phosphorus atom that vary but also the nature of the $=C(^{+}PPh_3X)(Y)$ group.

group, which mimics the oxygen atom of the P=O group. When Y is constant, for example, Y = Ts, the pK_{OH} values provide a linear correlation with the σ^{Φ} constants[69] (Fig. 7)

In $MeNO_2$: $pK_{OH} = 0.70 - 2.296\ \Sigma\sigma^{f}$;

$n=4$; $r=0.983$; $s=0.56$; $s_{\rho}=0.30$.

Admittedly in this case the point corresponding to two benzene rings was excluded (see above). With regard to the pK_{OH} values in ethanol, they are virtually equal to pK_{app}, as more than 99% of the (B) form is present in solution. The relationship between pK_{OH} and the nature of the substituents is complex.

Thus, the pK_{app} acidity measurements and calculation of pK_{CH} and pK_{OH} provide a clear definition of the relationship between enolisation of the P=O group and the acidity of phosphoryl compounds.

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The main conclusion to be drawn from the above material is that the phosphoryl group *can* undergo enolisation. A high acidity of the phosphoryl CH form (A) is a necessary condition for this to occur. This condition is of course necessary, but it is not sufficient. It is also necessary that the corresponding enol form (B) has a similar acidity to that of the phosphoryl form; this is readily achieved, however, with sufficiently acidic CH forms. The conditions for enolisation of the thiophosphoryl group are more rigorous. The reason for this is the higher acidity of phosphorus thio acids compared to their oxygen analogues. It can be demonstrated that up to the present time it was not possible to observe enolisation of the P=O group because the $\Sigma\sigma^{-}_{CH}$ values of the groups attached to the central carbon atom did not exceed 2, which was naturally a consequence of the fact that the attached groups had an insufficient acidifying effect. Thus, for example, for the "phosphonoacetic ester" of Arbuzov and Razumov[1-9]—$(EtO)_2P(O)CH_2COOEt$—the $\Sigma\sigma^{-}_{CH_2}$ value is 1.28, which is quite insufficient for phosphaenolisation to occur, while the compound used by Kolodyazhnyi[40,41]—$Ph_2P(O)CH(SO_2C_6H_5)_2$—has $\Sigma\sigma^{-}_{CH}$ = 1.97, which is at the limit of enolisability. On introduction of electronegative substituents into the benzene ring, this limit is exceeded and enolisation becomes quite appreciable.

All in all, enolisation of the phosphoryl group fully obeys the laws comprising the theory of prototropic tautomeric acid–base equilibrium.

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Translated from *Uspekhi Khimii* 60 2189–2219 (1991) U.D.C. 547.26'118

N-Phosphorylated amides and thioamides

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ABSTRACT. The first systematic review is presented on carboxylic and thiocarboxylic acid amides containing a four-coordinated phosphorus atom on the nitrogen atom. The synthesis, structure and certain chemical properties of this compound class have been examined together with their prototropic and phosphorylotropic tautomerism, their dual reactivity, and the structure and properties of some of their metallic and organic derivatives. Particular attention has been paid to the practical application of these compounds.

The bibliography contains 223 references.

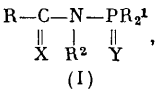
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I. Introduction

Carboxylic acid amides have been studied thoroughly and are widely used in industry, agriculture, and in various fields of science and technology.[1] Thioamides, however, have become a focus of attention only in the last decade in view of recently discovered practical applications, their diverse reactivity, and their potential value in organic synthesis.[2–5] *N*-Functionalised (including *N*-acylated) amides and thioamides, such as phthalimide, succinimide, and a large number of derivatives, have also proved to be very effective reagents in organic synthesis. Phosphorylated analogues of these polyfunctionalised compounds have also received much attention during the last two decades as a result of the discovery of a broad spectrum of properties of practical value.

The chemistry of *N*-phosphorylated amides and thioamides of type (I) has developed in three stages. After the initial



(I)

R = Alk, Ar; R^1 = Alk, Ar, AlkO, ArO, AlkS, ArS, Alk_2N, Ar_2N, etc.,

R^2 = H, Alk, Ar; X, Y = O, or S,

syntheses at the beginning of the 20th century,[6–8] there was a gap of some fifty years during which there was practically no research in this field. Then, during the fifties, A V Kirsanov's "phosphazo reaction" provided a new and simple methodology for preparing this class of compound.[9] Finally, in the 'seventies, with the discovery of their pesticidal activity, *N*-phosphorylated amides again became a focus of renewed interest, specifically with regard to (I, X = Y = O), the *N*-thiophorylated analogues (I, X = O, Y = S), *N*-phosphorylated thioamides (I, X = S, Y = O), and *N*-thiophosphorylated thioamides (I, X = Y = S). In this period, the broad spectrum insecticide, acephate (*O,S*-dimethyl *N*-acetylthiophosphoromonoamidate), was discovered and became commercially available.

In recent years, certain organophosphorus compounds of general formula (I) have proved to be highly effective complexing agents, extractants, and anti-microbial and -tumour agents, etc. This has stimulated the search for simple, convenient, and industrially viable routes to this class of compound, as well as the study of their chemical properties and structure.

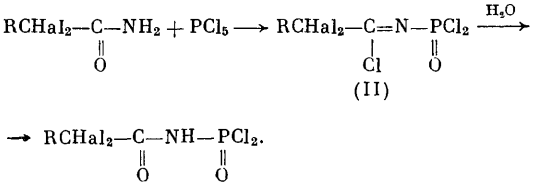
This is the first systematic review on the synthesis, structure and properties of *N*-phosphorylated amides and thioamides. Where possible, analyses have been made of the influence of the structure of these compounds on their reactivity and on other properties.

II. Methods of synthesis

1. Synthesis of *N*-phosphorylated amides

The first *N*-phosphorylated amides of type (I) were obtained by phosphorylation of α-halogeno- and α-nitrocarboxylic acid amides with phosphorus pentachloride.[6–8]

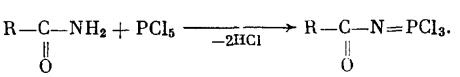
The authors suggested that reaction proceeds via *N*-phosphoryliminochlorides (II) which were converted to the corresponding amides (I, R = Hal, H, NO_2) on exposure to moist air.



(II)

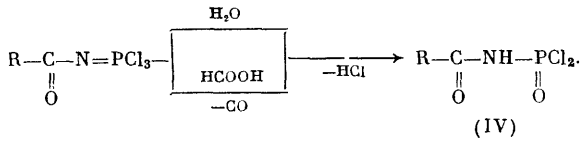
(Ia)

In 1954, A V Kirsanov renewed the study of the reaction between carboxylic acid amides and phosphorus pentachloride, and discovered that a trichlorophosphazo compound (III) was formed initially, rather than an *N*-phosphoryliminochloride.[9]



(III)

The above process was called the "phosphazo reaction". The resulting phosphazo compounds (III) are very hygroscopic and readily converted to the corresponding phosphoryl dichlorides (IV) in the presence of hydroxylic reagents.[10–13]



(IV)

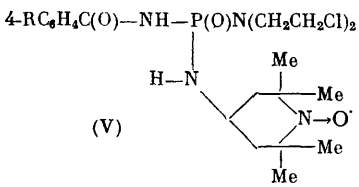
The acylaminophosphoryl dichlorides (IV) can be simply converted to the corresponding diesters on treatment with alkali metal alkoxides or alcohols.[14–20]

$$\underset{\text{(IV)}}{RC(O)NHP(O)Cl_2} \xrightarrow{2R^1OH \text{ or } 2R^1ONa} RC(O)NHP(O)(OR^1)_2.$$

In a similar way, the dichloride (IV) is readily converted into dithioesters,[14,19] bis(ethylenimides),[21] diamides[14,19] and hydrazides[22] of general formula (I).

$$RC(O)NHP(O)Cl_2 + 2HR^1 \rightarrow RC(O)NHP(O)R_2^1,$$
$$R^1 = SR^2,\ NHR^2,\ NHNHR^2,\ \overbrace{NCH_2CH_2}.$$

Sequential treatment of aroylaminophosphoryl dichlorides with bis(2-chloroethyl)amine in the presence of triethylamine, followed by 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl, affords the corresponding phosphoric acid triamides (V) which possess antitumour activity.[23] The intermediate monoamide need not be isolated.



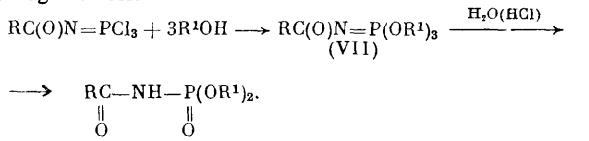
(V)

R = H, F, Me.

Diarylphosphinic acid *N*-arolyamides (VI) may be prepared from arylmagnesium bromides. These amides resist hydrolysis.[24]

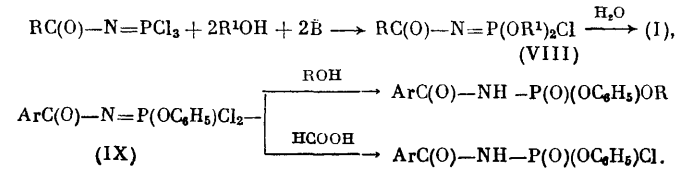
$$\underset{\text{(VI)}}{ArC(O)-NH-P(O)Ar_2}.$$

The ultimate stage in preparing *N*-acylphosphoromonoamidates need not involve the conventional displacement of halide. Thus, trialkoxy- or triaryloxy-*N*-acylphosphazenes (VII), obtained by treatment of the corresponding trichlorophosphazo compounds with alcohols and phenols, respectively, are converted to *N*-acylphosphoromonoamidates by action of water, aqueous ethanol, or dry hydrogen chloride.[14,17,20,25,26]



It should be pointed out that triaryloxy-*N*-acylphosphazenes (VII, R^1 = aryl) are very easily hydrolysed. In fact, very high yields of diaryl *N*-acylphosphoromonoamidates are obtained simply by exposing these phosphazenes to moist air, water or 96% ethanol.[26–28]

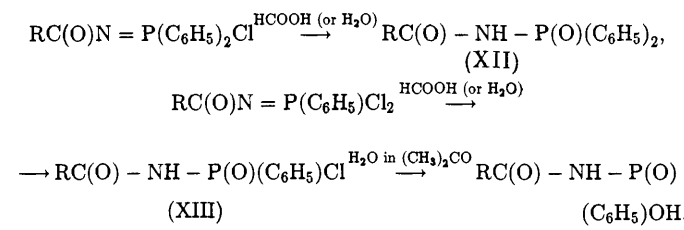
In another route, *N*-acylphosphoromonoamidates are obtained from trichlorophosphazenes via partial replacement of chlorine atoms, followed by hydrolysis, alcoholysis or acidolysis of the resulting monochloro- or dichlorophosphazenes, (VIII) and (IX).[14,17,26]



In a similar way, *N*-phosphorylated thioamides of general structure (XI) are prepared from the corresponding phosphazenes (X) (having alkyl, alkoxy, amino or other functionality on phosphorus together with one or two chlorine atoms) on treatment with hydrogen suphide in trifluoroacetic acid.[29,30]

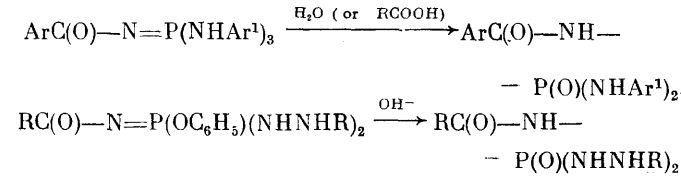
$$\underset{\text{(X)}}{RC(O)-N=PR_n^1Cl_{3-n}} + H_2S \rightarrow \underset{\text{(XI)}}{RC(O)-NH-P(S)R_n^1Cl_{2-n}}$$
$$R^1 = Alk,\ AlkO,\ NR_2,\ NHR;\ n = 1, 2.$$

P-Aryl-substituted *N*-phosphorylated amides, (XII) and (XIII), are obtained by hydrolysis or acidolysis of the corresponding aryl- or diaryl-chloro(*N*-acyl)phosphazenes.[25,31]



The monochlorinated amides (XIII) are readily converted to the corresponding *N*-acyl(phenyl)phosphonamidic acids by vigorous hydrolysis with aqueous acetone.[31]

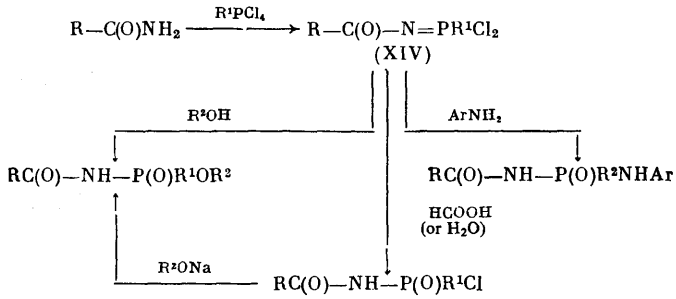
Acylaminophosphoryl diamides and dihydrazides have been conveniently prepared by hydrolysis or acidolysis of the corresponding triamino- or dihydroazido-phosphazenes, obtained from *N*-acyltrichlorophosphazenes.[22,32]



Structurally varied *N*-phosphorylated amides may be obtained by phosphorylation of carboxamides with halogenophosphoranes, e.g. phenyl-,[33] methyl-[34] and trichloromethyltetrachlorophosphorane,[35] in place of phosphorus pentachloride. Reactions

with these tetrachlorophosphoranes do not proceed as readily as reaction with PCl_5. The initially formed alkyl- or aryl-(dichloro)phosphazenes (XIV) may be easily converted to the corresponding *N*-phosphorylated amides by treatment with water, acid, alcohols or amines, as shown in Scheme 1.

Scheme 1



Methods of preparing *N*-phosphorylated amides via the phosphazo reaction are fairly straightforward and afford the desired product in high yield. However, such routes are not generally applicable. For example, the interaction of aliphatic carboxylic acid amides with PCl_5 proceeds to give both phosphazo compounds and chlorinated amides.[9] As a consequence, this method is not suitable for preparing simple *N*-phosphorylated *N*-acylamides unsubstituted in the acyl fragment, e.g. the pesticide acephate.

As an alternative to the phosphazo reaction the Staudinger reaction, based on trialkyl phosphites and acyl azides, can be applied to the preparation of *N*-acylphosphazenes. The resulting *N*-acyliminophosphates are converted to the desired *N*-phosphorylated amides on treatment with dry hydrogen chloride.[36,37]

$$(RO)_3P + R^1C(O)N_3 \longrightarrow (RO)_3P{=}NC(O)R^1 \xrightarrow[-RCl]{HCl} (I).$$

The synthesis of *N*-phosphorylated amides may also be achieved by another route: acylation of *N*-arylphosphazenes with acetyl chloride. Kabachnik and Gilyarov[39] showed that the trialkyl *N*-phenyliminophosphates formed by the Staudinger reaction are converted to *N*-acetyl-*N*-phenylphosphoromonoamidates on treatment with acetyl chloride. This is one of only a few methods reported in the literature for the preparation of *N*-phosphorylated amides having a tertiary nitrogen atom.

$$(RO)_3P + C_6H_5N_3 \xrightarrow[-N_2]{} (RO)_3P{=}N{-}C_6H_5 \xrightarrow{CH_3C(O)Cl} \longrightarrow (RO)_2P(O){-}N(C_6H_5){-}C(O){-}CH_3 + RCl.$$

A number of routes to *N*-phosphorylated amides are based on the functionalisation of phosphorus(V) acid derivatives in which the phosphorus atom is bonded to an unsaturated nitrogen-containing group. Thus, *N*-phosphorylated iminochlorides (XV, X = Cl), which are isomeric with *P*-chloro-*N*-acylphosphazenes, undergo hydrolysis and alcoholysis to give the corresponding *N*-phosphorylated amides. The latter are also obtained by hydrolysis of *N*-phosphorylated iminoesters (XVI).[16,17,28,39]

$$R{-}C(X){=}N{-}P(O)(OR^1)_2 \xrightarrow{H_2O\ (ROH)} (I),$$

(XV), (XVI)

X = Cl (XV), OR^2 (XVI).

There is also an unusual route to *N*-phosphorylated amides based on the interaction of aryl *N*-(diaryloxyphosphinyl)thioimidates with 25% H_2O_2 in acetic acid or with concentrated nitric acid.[40]

$$Ar{-}C(S{-}Ar^1){=}N{-}P(O)(OAr^2)_2 \xrightarrow{H_2O,\ [O]} Ar{-}C(O){-}NH{-}P(O)(OAr^2)_2.$$

The authors gave no details on this reaction.

A variety of *N*-phosphorylated amides with a functionalised acyl chain can be prepared by reaction of *N*-phosphorylisocyanates with compounds having a labile hydrogen atom. Thus *N*-phosphorylated amides are obtained in 36–61% yield by interaction of isocyanates (XVII) with acetic or propionic acid in the presence of a catalytic amount of sulphuric acid. Evidently, the reaction proceeds via an unstable anhydride (XVIII) which undergoes decarboxylation.[41]

$$(RO)_2P(O) - N = C = O + R^1COOH \xrightarrow{H_2SO_4\ (cat.)}$$

(XVIII)

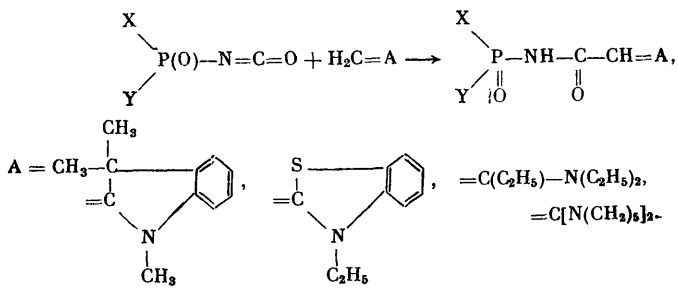
$$\longrightarrow [(RO)_2P(O){-}NH{-}C(O)OC(O)R^1] \xrightarrow[-CO_2]{} (RO)_2P(O){-}NH{-}C(O)R^1,$$

(XVIII)

R=CH_3, C_2H_5; R^1=C_2H_5.

Benzoic acid, however, does not participate in this reaction.

In another route based on phosphorylisocyanates, nitrogen-containing methylenic compounds add to the latter to give *N*-phosphorylated derivatives of α,β-unsaturated carboxylic acid amides.[42]



The above-described routes to *N*-phosphorylated and *N*-thiophosphorylated amides are essentially based on the intermediate formation and subsequent conversion of compounds with an unsaturated phosphorus atom, such as phosphazo compounds. Since there are limitations in the choice of the acyl group and the

Table 1. Synthesis of phosphorylated amides and thioamides by alkylation of amides and thioamides.

Anylamide	Acylating agent	Reaction conditions	Product	Yield %	Reference
		Acylation of phosphoramides			
$(RO)_2P(S)NHNa$	$ClC(O)C_6H_5$	Benzene, 20 °C	$(RO)_2P(S)NHC(O)C_6H_5$	50	[30]
$(RNH)_3P=S$	$ClC(O)CCl_3$	Benzene, 20 °C, Et_3N, 10 h	$RNHP(S)[NRC(O)CCl_3]_2$	Not given	[43]
$(RO)_2P(O)NH_2$	$ClC(O)R^1$	Without solvent, 30 °C, $PhNEt_2$, 3 h	$(RO)_2P(O)NHC(O)R^1$	64–72	[45]
$(EtO)_2P(O)NHR$	$[CF_3C(O)]_2O$	Pyridine, 20 °C	$(EtO)_2P(O)NRC(O)CF_3$	95	[50]
$(RY)(R^1S)P(O)NHR^2$	$ClC(O)R^3$	Benzene, Methylene chloride, chloroform, THF, 0–60 °C, 2–24 h	$(RY)(R^1S)P(O)NR^2C(O)R^3$	Not given	[47]
$R_2P(S)NHNa$	$ClC(O)R$	THF, 70 °C, 3–5 h	$R_2P(S)NHC(O)R$	8–87	[51]
$(iso\text{-}PrO)_2P(S)NH_2$	$ClC(O)C_6H_5$	Acetone, 20 °C, KOH, dibenzo-18-crown-6, 15 min	$(iso\text{-}Pro)_2P(S)NHC(O)C_6H_5$	36	[52]
$(R^1O)_2P(X)NH_2$	$ClC(O)R$	Acetone, 20 °C, KOH, crown ether	$(R^1O)_2P(X)NHC(O)R$	50–65	[53]
$R(ClCH_2CHFO)P(S)NH_2$	$[CH_3C(O)]_2O$	concd. H_2SO_4 (catalyst), 20–55 °C, 15 h	$R(ClCH_2CHFO)P(S)-NHC(O)CH_3$	Not given	[57]
$(RO)_2P(S)NH_2$	$[CH_3C(O)]_2O$	Methylene chloride, H_3PO_4, heat, 3 h	$(RO)_2P(S)NHC(O)CH_3$	98	[58]
$(RO)_2P(S)NH_2$	$R^1CH=C=O$	H_3PO_4 (catalyst) in MeCOOH, 20 °C, 3 h	$(RO)_2P(S)NHC(O)CH_2R^1$	86	[59]
$(RX)(R^1S)P(Y)NHR^2$	$CH_3C(O)OC(O)H$	THF, N_2, BuI	$(RX)(R^1S)P(Y)NR^2C(O)H$	88	[55]
$(RO)_2P(S)NH_2$	$ClC(O)C_6H_5$	Benzene, NaOH	$(RO)_2P(S)NHC(O)C_6H_5$	15	[30]
$(C_2H_5O)_2P(S)NH_2$	$ClC(O)C_6H_5$	Benzene, C_5H_5H	$(C_2H_5O)_2P(S)NHC(O)C_6H_5$	25	[30]
		Phosphorylation of acylamides			
$RC(X)NHNa$	$ClP(S)R_2^1$	THF, 70 °C, 3–5 h	$RC(X)NHP(S)R_2^1$	46–89	[51]
$C_6H_5C(O)NHNa$	$ClP(S)(OR)_2$	Benzene, heat, 3 h	$C_6H_5C(O)NHP(S)(OR)_2$	20–60	[30]
$CH_3C(S)NH_2$	$ClP(S)(OPr\text{-}iso)_2$	Acetonitrile, *t*-BuOK, 20 °C, 15 min	$CH_3C(S)NHP(S)(OPr\text{-}iso)_2$	15	[52]
$RC(O)NH_2$	$ClP(S)(OR)_2$	NaH in THF, heat, 16 h	$RC(O)NHP(S)(OR)_2$	19	[54]
$RC(O)NH_2$	$ClP(S)(OR)_2$	1 : 5 DMSO/Benzene, KOH, 5–25 °C	$RC(O)NHP(S)(OR)_2$	45	[54]
$CH_3C(O)NH_2$	1. $[(C_2H_5O)_2P]_2O$ 2. RI	1. 20 °C, 10 days 2. 20–80 °C, ⩽ 6 h	$CH_3C(O)NHP(O)(R)(OC_2H_5)$	Not given	[36]

substitution of the phosphoryl residue, the method has certain, and sometimes obvious, limitations. For this reason, there has been interest in the direct phosphorylation of amides and thioamides with phosphorus acid chlorides and in the acylation of phosphorus(V) acid amides with acyl or thioacyl halides:

$$\left.\begin{array}{l} RC(X)NH_2 + ClP(Y)R_2^1 \\ R_2^1P(Y)NH_2 + ClC(X)R \end{array}\right\} \xrightarrow[-HCl]{} R{-}\underset{\underset{X}{\|}}{C}{-}\underset{\underset{H}{|}}{N}{-}\underset{\underset{Y}{\|}}{PR_2^1}.$$

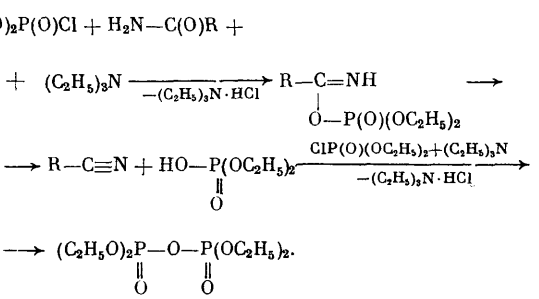
Most success has been achieved by applying the second of these routes. Thus, a whole range of methods is available for preparing (I) based on the interaction of phosphorus(V) and thiophosphorus(V) acid amides with acyl halides. Such reactions have been carried out both in the presence of base (to 'fix' hydrogen chloride)[43–45] and in the absence of base.[46–49] Tertiary *N*-phosphorylated amides have also been prepared by acylation of *N,N*-disubstituted phosphoramidates with acyl halides in the presence of pyridine.[50] These routes are quite suitable for the preparation of oxygen-containing *N*-phosphorylated amides and provide the desired products in an acceptable yield (Table 1).

Various methods involving acylamine metallation have been adapted for the effective preparation of *N*-thiophosphorylated amides. However, the yield of the latter is within a wide range (8 to 87%), depending on the structure of the starting materials.[30,51,52] Only a moderate yield (36%) of *N*-thiophosphorylated amides is obtained by acylation of thiophosphorus(V) acid amides with acyl halides in acetone in the presence of KOH and crown ether,[52] while, in superbasic media (DMSO/KOH), the yield of desired product is 24%. The authors note that under these conditions it is possible to prepare *N*-phosphorylated and *N*-thiophosphorylated amides which cannot be obtained by direct acylation of phosphorus(V) acid amides.[53,54]

Carboxylic acid anhydrides are also effective as the acylating agent. Thus, treatment of phosphorus(V) acid amides with butyllithium at −78 °C, followed by acetic formic anhydride, affords an entire range of *N*-phosphorylated amides and thioamides possessing pesticidal activity.[55] Acylation of thiophosphorus(V) acid amides can also be achieved with acetic anhydride in the absence of catalyst or in the presence of catalytic amounts of sulphuric or phosphoric acid.[56–59] Ketenes may also be used as the acylating agent in acetic acid containing sulphuric acid as catalyst.[59]

It is less convenient to prepare *N*-phosphorylated and *N*-thiophosphorylated amides by phosphorylation of carboxylic acid amides with phosphorus(V) acid halides. Thus, attempts to synthesise *N*-phosphorylated amides by treatment of carboxylic acid amides with dialkyl phosphorochloridates in the presence of triethylamine were unsuccessful. Under these conditions phosphorylation afforded the corresponding tetraalkyl pyrophosphates and nitriles, rather than the desired (I),[45] as shown in Scheme 2.

Scheme 2

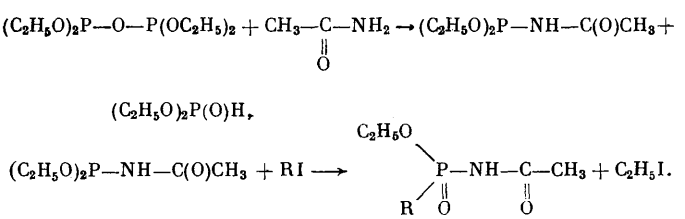


Tetraalkyl pyrophosphates and phenyl isocyanide were obtained by using formanilide.[45] Similar results were obtained on the interaction of amides with phosphono- and thiophosphono-chloridates.[60]

However, if the above phosphorylation is carried out on *N*-metallated acylamines rather than acylamines themselves, the desired displacement takes place in one step. Thus, *N*-sodio derivatives are phosphorylated with thiophosphorochloridates in 46–89% yield[51] (see Table 1). However, thiophosphorylation of amides in the presence of sodium hydride is not very effective (~18% yield), while in superbasic media (DMSO/KOH) the yield of *N*-phosphorylated amides can be increased to 45%.[54]

Phosphorus acid anhydrides are, evidently, also suitable for the phosphorylation of acylamines. Thus, *N*-phosphorylated acetamides may be prepared by using tetraethyl pyrophosphite as phosphorylating agent: the initially formed diethyl *N*-acetylphosphoromonoamidite then undergoes Arbuzov reaction with alkyl iodides to give the corresponding *N*-acetylphosphonamidates,[37] as shown in Scheme 3.

Scheme 3



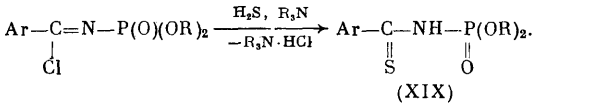
However, this route is more of theoretical than preparative interest, partly because the phosphorylating agent is not readily available and partly because it is difficult to separate the desired product for the diethyl phosphite formed as by-product.

2. Synthesis of *N*-phosphorylated thioamides

Although *N*-phosphorylated amides and thioamides are structurally similar, it is not always possible to adapt methods developed for the preparation of *N*-phosphorylated amides to the preparation of thioamide analogues. In recent years, a rather specific route has been developed for the synthesis of sulphur-containing *N*-phosphorylated acylamines. It is based on the addition of thio- and dithio-phosphorus acids to compounds containing a carbon-nitrogen multiple bond. The analogous addition of organophosphorus acids has not yet been reported. This highlights the necessity to distinguish the synthesis of *N*-phosphorylated and *N*-thiophosphorylated amides from that of *N*-phosphorylated and *N*-thiophosphorylated thioamides.

Attempts to adapt the phosphazo reaction to the preparation of thioamide derivatives, largely undertaken by Kirsanov, et al. in 1960,[61] met with failure. Thus, it was shown that the interaction of thiobenzamide with PCl_5 under the conditions of the phosphazo reaction leads to a complex mixture of products (HCl, PCl_3, $PSCl_3$, nitriles, thiadiazoles, and other unidentified compounds), rather than to the desired *N*-thioacylphosphazenes.[61]

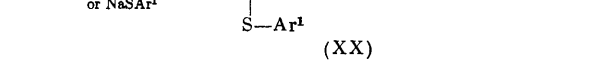
However, cleavage of *N*-dialkoxyphosphoryl- and *N*-diaryloxyphosphoryl-iminochlorides with H_2S proceeds quite readily to give the corresponding *N*-phosphorylated thioamides (XIX). This is analogous to the hydrolysis of iminochlorides (XV).



(XIX)

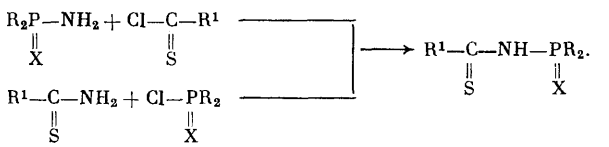
The above reaction can be achieved by using a tertiary amine as base, and leads to a high yield of desired product (70–98%).[61]

N-Phosphorylated thioamides (XIX) may also be obtained in 60–90% by treatment of (XV, R = aryl) either with thiophenols (in the presence of tertiary amine) or with sodium arylmercaptides, followed by hydrolysis of the resulting thioiminoesters (XX) in aqueous alcoholic media containing a base.[40]



(XX)

For the preparation of *N*-phosphorylated thioamides and *N*-thiophosphorylated thioamides from readily available starting materials, more attention has been focussed on acylation or phosphorylation routes with acid chlorides (see earlier and in Tables 1 and 2), according to the following scheme:



The first of these methods, however, has no preparative value since thiocarboxylic acid chlorides are not readily available and, in many instances, are extremely unstable. The second route, based on the reaction of thioamides with phosphorus(V) acid chlorides is more effective.

In 1967 the synthesis was reported of *N*-(diphenylthiophosphinyl)thioacetamide by interaction of diphenylthiophosphinyl chloride with thioacetamide, as well as by action of methyllithium on diphenylthiophosphinyl isothiocyanate.[62] However, in each instance, acetonitrile and a diphenyldithiophosphinate were formed instead of the anticipated *N*-thiophosphinylthioamide (I, R = Me, R^1 = Ph, X = Y = S). Similar results were obtained for the interaction of diphenylthiophosphinyl chloride with the sodio-derivative of thiobenzamide.[63] However, the latter reaction with dimethyl- and dibenzyl-thiophosphinyl chloride does afford the desired *N*-thiophosphinylthioamide (I, R = Ph, R^1 = Me, $PhCH_2$, R^2 = H, X = Y = S) in 60–67% yield[51,63] (see Table 2).

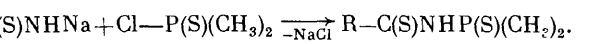


Table 2. Phosphorylation of thioamides.

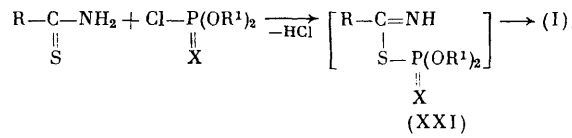
Thioamide	Phosphorylating agent	Reaction conditions	Product	Yield, %	Reference
$RC(S)NHNa$	$(CH_3)_2P(S)Cl$	THF, heat	$RC(S)NHP(S)(CH_3)_2$	60–67	[51, 63]
$CH_3C(S)NH_2$	$(iso\text{-}PrO)_2P(S)Cl$	*t*-BuOK in anhydrous MeCN	$CH_3C(S)NHP(S)(OPr\text{-}iso)_2$	15	[64]
$C_6H_5C(S)NH_2$	$(iso\text{-}PrO)_2P(S)Cl$	NaH, THF, heat, 15 h	$C_6H_5C(S)NHP(S)(OPr\text{-}iso)_2$	4	[65]
$RC(S)NH_2$	$(R^1O)_2P(S)Cl$	THF, $R_4N^+Cl^-$ (R = Et, Bu)	$RC(S)NHP(S)(OR^1)_2$	37–45	[53, 54, 66]
$RC(S)NH_2$	$(R^1O)_2P(S)Cl$	Dibenzo-18-crown-6, KOH, MeCN	$RC(S)NHP(S)(OR^1)_2$	51–66	[53, 54, 66, 67]
$RC(X)NH_2$	$(R^1O)_2P(Y)Cl$	DMSO, KOH	$RC(X)NHP(Y)(OR^1)_2$	65–80	[53, 54, 66]

The *N*-thiophosphorylthioamide (I, R = Me, R^1 = OPr-*i*, R^2 = H, X = Y = S) was obtained in 15% yield by treatment of diisopropyl dithiophosphorochloridate with the potassium salt of thioacetamide, prepared by treatment of the latter with potassium *tert*-butoxide.[64] The same reaction with thiobenzamide in the presence of sodium hydride gave only a small amount of desired product.[65] Phosphorylation of thioamides with phosphoryl chlorides does not take place in the absence of base or with weak organic bases.

Recently, *N*-phosphorylated thioamides and *N*-thiophosphorylated thioamides were prepared under phase transfer catalysis or in superbasic medium by treatment of thioamides with phosphoryl and thiophosphoryl chlorides (see Table 2). The yield of desired product is 37–45% in 50% KOH containing a quaternary ammonium salt as phase transfer catalyst.[53,54,66] The yield can be increased to 62–66% if solid KOH/crown ether is used in place of the above 2-phase procedure with a quaternary ammonium salt and aqueous base, under which conditions undesired hydrolysis of the phosphoryl chloride takes place to some extent.[53,54,66,67]

In spite of the undoubted advantages of phase transfer catalysis for the phosphorylation of thioamides, the method is not applicable to the reaction of thioacetamide with dialkyl phosphorochloridates or to the reaction of thiobenzamide with dimethyl phosphorochloridate.[64–66] However, these reactions are possible in superbasic media, e.g. solid KOH in dimethyl sulphoxide.[53,54,66] The method can be used for the preparation of all four types of compound (I) with any organic substituent at the (thio)carbonyl or (thio)phosphoryl centre (see Table 2).

By analogy with the reaction of secondary N-sodiothioamides with acyl chlorides, which involve initial formation of *S*-acylthioimidates,[68] it has been proposed that the above phosphorylations proceed with the initial formation of an *S*-phosphorylthioimidate (XXI), which subsequently isomerises to give (I) by 1,3-*S*→*N*-(thio)phosphoryl group migration:



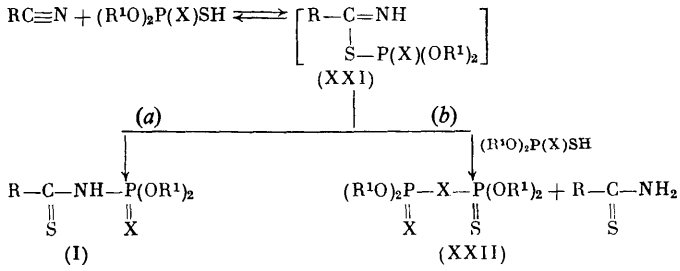
(XXI)

Apparently, the formation of intermediate (XXI) is dependent on a number of factors, which to a large extent compensate one for the other. Thus, in strongly basic media, deprotonation of acylamines is relatively facile, but, on the other hand, strong solvation of the phosphorus atom, bearing an effective positive charge, hinders the S_N2 displacement at phosphorus. It would also appear that the inductive effects of substituents at the carbon atom of the (thio)carbonyl group and at phosphorus on the rate of substitution are in the opposite sense: on the one hand the effect is to increase the acceptor properties of R, thereby facilitating *N*-deprotonation, and on the other hand to decrease the nucleophilic properties of the conjugate amide anion. Thus, structure-reactivity relationships involving phosphoryl chlorides are difficult to interpret. In this context, it is necessary to consider the effect of all the groups linked to phosphorus, both on the phosphorylation step and on the isomerisation of the intermediate (XXI) to give (I). The latter process also involves an S_N2 displacement at phosphorus, again subject to the juxtaposition of various intermolecular and intramolecular forces. Thus, the reaction in question is subject to a fine balance of various factors (electronic, steric, catalytic, medium effects), so that it is critical to select the appropriate method for each particular case.

N-Phosphorylated and *N*-thiophosphorylated thioamides may also be prepared by the reaction of monothio- and dithio-phosphorus(V) acids with nitriles.[69–74] This reaction proceeds via addition of the thiophosphorus(V) acid to the cyano group with the initial formation of the corresponding *S*-phosphorylthioimidate (XXI). The latter isomerizes to the corresponding *N*-(thio)phosphorylated thioamides (I, X = S, Y = O; see route (a) of Scheme 4) via 1,3-*S*→*N*-migration of the (thio)phosphoryl group. It should be

pointed out that the *S*-phosphorylthioimidates (XXI), being excellent phosphorylating agents in themselves, also undergo cleavage of the P–S bond by the starting thiophosphoric acid, with the result that carboxylic acid thioamides and (tri)thiopyrophosphates (XXII) are formed as by-products in a concurrent step of the reaction, i.e. path (b).

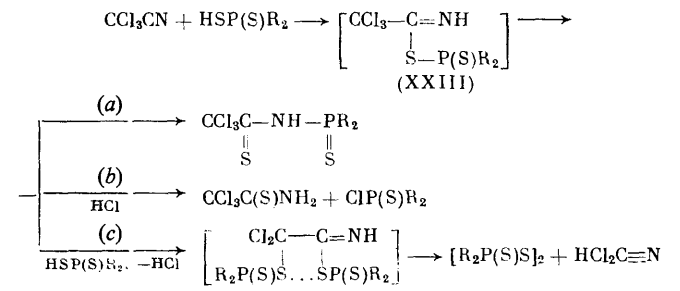
Scheme 4



The yield of phosphoramides (I) depends on the nature of the nitrile, the structure of the thiophosphoric acid, the proportion of the reactants, the reaction conditions, and the presence of impurities. The highest conversion of dithiophosphoric acids to thioamides (I) was achieved with aromatic nitriles.[71,75–78] Aliphatic nitriles either do not react at all or are converted to the corresponding *N*-thiophosphorylated thioamides only in small yield. In this instance, pathway (b) (Scheme 4) is the predominant step.[75] The method is not suitable for preparing *N*-diphenylthiophosphinyl-thioamides since diphenylthiophosphinic acid reacts with nitriles only by pathway (b).[72,79,80]

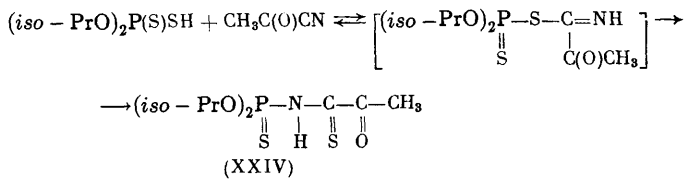
O,O-Dialkyl hydrogen thiophosphates are noticeably less reactive towards nitriles,[65,69,70,74] being converted to *N*-phosphorylated thioamides (I) only in 2.5–12% yield.[65] In no instance has it been possible to isolate the intermediate thioimidates (XXI) by reaction of (di)thiophosphoric acids with nitriles, although there is one publication in which the authors incorrectly assigned an *S*-dithio-phosphorylthioimidate structure to what, in fact, were *N*-thio-phosphorylated thioamides.[72] Only in the reaction with chloroacetonitrile has it been possible to detect the intermediate formation of *S*-dithiophosphorylthioimidates (XXIII) by ^{31}P NMR spectroscopy; in this instance, the intermediates undergo a number of transformations over the course of several hours.[81,82]

Scheme 5

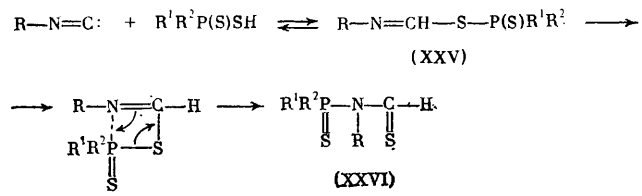


As shown in Scheme 5, only one of the ensuing reactions of (XIII), path (a), leads, via isomerisation, to *N*-thiophosphorylated thioamides, which were isolated in low yield. Decomposition with hydrogen chloride is also an energetically favourable reaction of (XIII), i.e. path (b) and in a third option, the intermediate may react with the starting dithiophosphorus(V) acid, i.e. path (c). This is a redox step which results in the formation of dichloroacetonitrile and a bis(dialkylthiophosphoryl) disulphide.

The reaction of dithiophosphorus(V) acids with benzoyl and acetyl cyanide is equally complex.[83,84] In the reaction with acetyl cyanide, it is only possible to isolate an *N*-thiophosphorylthioamide (XXIV) by treatment with *O,O*-diisopropyl hydrogen dithiophosphate. However, the yield of (XXIV) was only 12%.[71,84]



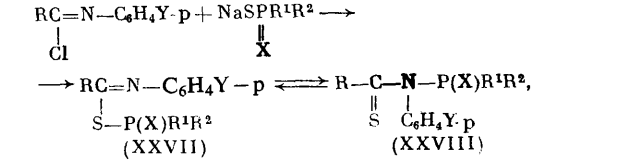
N-Thiophosphorylated thioformamides are readily formed by interaction of dithiophosphorus(V) acids with isonitriles, the method being similar to the reaction with nitriles. Thus, treatment of dithiophosphoric acids with 2,6-dimethyl- and 2,6-diethyl-phenyl isocyanide affords α-adducts (XXV),[84] which isomerise into the corresponding *N*-thiophosphorylthioformamide (XXVI).[71,86]



where R = C_6H_{11}, C_6H_5, 4-$CH_3C_6H_4$, 2,5-$(CH_3)_2C_6H_3$, 2,6-$(CH_3)_2C_6H_3$, 2,6-$(C_2H_5)_2$. C_6H_3; R^1,R^2 = AlkO

It has been established that the rearrangement of (XXV) to (XXVI) is a first-order reaction.[85] By substituting *O,O*-dimethyl dithiophosphate for *O,O*-diethyl dithiophosphate, the rate of the rearrangement is increased. Reaction is clearly slower with acidic dithiophosphonates (as opposed to dithiophosphates), and derivatives of diphenyldithiophosphinic acid do not rearrange at all.[85–87] Isomerisation is enhanced as the nucleophilicity of the nitrogen atom increases.[79,80] Formamides of type (XXVI) were not formed by reaction of isonitriles with dialkyl phosphoric[88] and monothiophosphoric acids or with monothiophosphonic acids.[89]

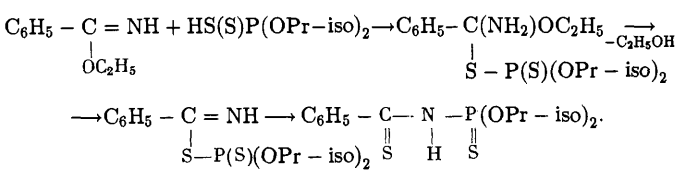
Tertiary *N*-phosphorylated thioamides and *N*-thiophosphorylated thioamides (XXVIII) may be prepared by reaction of iminochlorides with monothio- and dithiophosphorus(V) acids.[87,90] With acid derivatives having an O–P–S residue, reaction proceeds by attack of the sulphur atom.



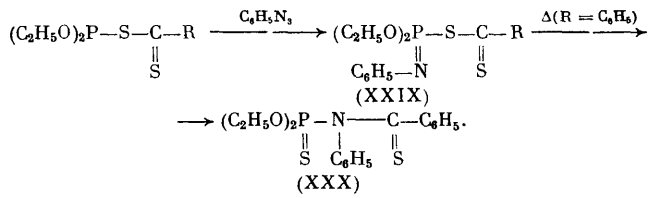
where R = C_6H_5, R^1 = R^2 = AlkO, X = O, S, Y = H, Br, CH_3, CH_3O, NO_2.

In certain instances, the thioamides (XXVIII) are formed as an equilibrated mixture with their thioimidate form (XXVII).

A low yield (3–5%) of *N*-thiophosphorylated thioamides has also been recorded by interaction of dithiophosphoric acids with iminoesters.[71,82,91,92]



Recently, tertiary *N*-thiophosphorylated thioamides, e.g. (XXX), have been obtained from *O,O*-dialkyl S-thioaroyl thiophosphorimidates (XXIX), which undergo imide-amide rearrangement by S→N-migration of the thiocarbonyl group within the S–P–N residue.[93] The rearrangement also takes place on distillation of the product obtained by Staudinger reaction of *O,O*-dialkyl S-thioacyl monothiophosphites with phenyl azide.



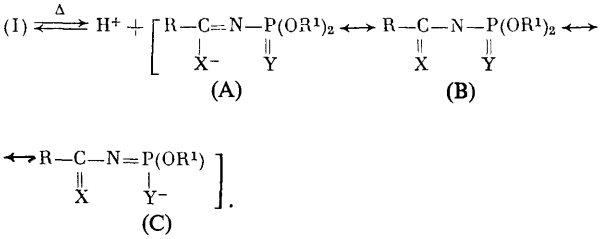
A similar rearrangement, involving migration of a trifluoroacetyl group within the O–P–N residue, has been observed with *O*-acylphosphazo compounds.[94]

III. The structure of *N*-phosphorylated amides and thioamides

Each of the four types of *N*-phosphorylated amide (I) contain three potentially reactive centres—a carbonyl (or thiocarbonyl) group, a phosphoryl (or thiophosphoryl group), and a secondary >N–H group with a labile hydrogen atom. Each of these groups migrates fairly easily, thereby facilitating proto-, acylo- and phosphoro-tropic processes.[36,51,87,95–97] The question of deprotonation and hydrogen migration to the basic centres X, Y and N in (I) has already been addressed quite thoroughly in the literature.[36,37,51,95–97]

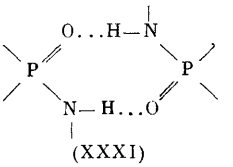
Amides (I) are moderately strong acids. From potentiometric data, it has been calculated that the acid dissociation constants, pK_a, in water[36,96] or aqueous alcoholic media[36,51,95–99] are in the range 4.16–10.7, depending on the nature of the substituent in the acyl and phosphoryl residue.

Numerous and diverse IR-spectroscopic studies on (I) have been carried out, primarily to analyse prototropic shifts and determine the character of hydrogen bonding in these compounds. It has been shown that under normal conditions in solution and in concentrated media, they exist exclusively in the amide form;[36,37,95,97–104] dissociation of the amide hydrogen may only take place at fairly high temperature in solution or on melting. The electronic structure of the resulting anion may be represented by three canonical forms:



On varying the conditions (in solution, in the melt, or on heating), the contribution of each structure may change. The corresponding shifts in the electron density of the anion can be detected in the IR spectrum of the compounds.[104] At the same time, ^1H and ^{31}P NMR spectroscopy indicates the extent of intramolecular hydrogen bonding of the type P=S(O)...H–N and C=O(S)...H–N.[105]

The structures of compounds (I) are dependent to a large extent on the nature of the hydrogen bonding in the various associated amide forms. In *N*-phosphorylated amides, hydrogen bonding of the type C=O...H–N[98,101] or P=O...H–N[36] may be evident. However, in *N*-phosphorylated thioamides, the thioacyl group does not participate in hydrogen bonding; in such compounds, the molecules are associated in the form of cyclic hydrogen-bonded dimers of type (XXXI).



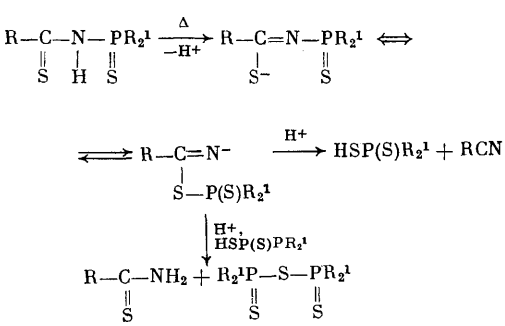
The IR spectra of *N*-thiophosphorylated thioamides indicate that the character of the hydrogen bonding depends on the nature of the acyl group. Derivatives of thioacetamide (I, R = Me, R^1 = OPr-*i*, R^2 = H, X = Y = S) are stabilised in the solid state by intermolecular hydrogen bonding of the type C=S...H–N, which is easily disrupted on dissolving the compounds in carbon tetrachloride. Thiobenzamide analogues (I, R = Ph, R^1 = OPr-*i*, R^2 = H, X = Y = S), however, are characterised by hydrogen bonding of the type P=S...H–N, which is also disrupted on dissolution.[104] Carbonyl analogues of these compounds are associated by intermolecular hydrogen bonding involving the carbonyl oxygen;[104] however, in the solid phase and in solution one cannot exclude the possibility of hydrogen bonding with the thiophosphoryl group. Hydrogen bonding in *N*-phosphorylated thioamides (I, X = S, Y = O) can be simply represented by the dimeric structure (XXXI), the thiocarbonyl group being unassociated. It has been shown[104] that the majority of compounds of type (I) exist in solution or in the melt as an equilibrated mixture of associates each having a distinct electronic structure.

IR- and ^1H or ^{31}P NMR-spectroscopic studies of *N*-(diisopropoxythiophosphoryl)thioacetamide at high temperature (80–170 °C).[104] have provided evidence on the chemical processes which take place under these conditions (Scheme 6).

Table 3. Bond lengths for compounds of general formula $R-\underset{\underset{X}{\|}}{C}-\underset{\underset{R^2}{|}}{N}-\underset{\underset{Y}{\|}}{PR_2^1}$

Compound	R	R^1	R^2	X	Y	Bond lengths, Å							Reference
						C=X	C–N	N–H	P=Y	N–P	N...Y	H...Y	
(I, *a*)	C_6H_5	CH_2CH_2N	H	O	O	1.211	1.376	0.71	1.475	1.671	2.84	2.14	[108]
(I, *b*)	m-IC_6H_4	CH_2CH_2N	H	O	O	1.226	1.364		1.428	1.661	2.78	1.81	[109]
(I, *c*)	p-FC_6H_4	CH_2CH_2N	H	O	O	1.219	1.375	0.79	1.473	1.664	2.84	2.06	[110]
(I, *d*)	p-$CH_3OC_6H_4$	CH_2CH_2N	H	O	O	1.215	1.385	0.98	1.482	1.664	2.89	1.91	[111]
(I, *e*)	$CH_2=CHCH_2OC_6H_4$	CH_2CH_2N	H	O	O	1.220	1.378		1.468	1.678	2.84	1.91	[112]
(I, *f*)	CH_3	OPr-iso	H	S	S	1.643	1.345	0.80	1.905	1.684	3.346	2.55	[64]
(I, *g*)	C_6H_5	OPr-iso	H	O	O	1.185	1.386	0.76	1.443	1.649	2.79	2.07	[113, 114]
(I, *h*)	C_6H_5	OPr-iso	H	O	S	1.218	1.356	0.97	1.903	1.688	2.913	2.21	[52, 116]
(I, *i*)	C_6H_5	OPr-iso	H	S	S	1.635	1.354	0.99	1.912	1.686	3.613	2.72	[115, 116]
(I, *j*)	C_6H_5	OPr-iso	K	S	S	1.703	1.312		1.940	1.620	–	–	[113]
(I, *k*)	C_6H_5	OPr-iso	Hg	S	S	1.733	1.286		1.980	1.610	–	–	[117, 118]
(I, *l*)	C_6H_5	OPr-iso	Pb	S	O	1.740	1.268		1.492	1.634	–	–	[117, 119]
(I, *m*)	C_6H_5	OPr-iso	H	S	O	1.646	1.360	0.92	1.457	1.672	–	–	[119]
(I, *n*)	C_6H_5	OC_2H_5	H	S	O	1.633	1.359	0.82	1.456	1.667	–	–	[116]

Scheme 6

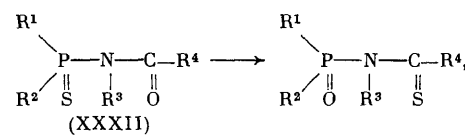


This has been supported by independent studies.[87,97]

The identification of nitriles, thioamides, dithiophosphates and trithiopyrophosphates among the products formed by thermolysis of *N*-thiophosphorylated thioamides provides unequivocal support for the above pathway (Scheme 6), which incorporates a protolytic dissociation and an amidothiophosphate-imidoyldithiophosphate rearrangement. These represent clear examples of 1,3-(N→S)-thiophosphoryl migration in secondary *N*-phosphorylated amides (see Ref. 87 and references cited therein).

Thiophosphoryl group migration in tertiary *N*-thiophosphorylated thioamides also takes place readily. In certain instances, such thioamides exist at room temperature as a tautomeric mixture, in which the proportion of the two forms may reach 1 : 1.[82,87,90] It has been shown that the position of the amide-imide equilibrium depends on several factors and to a large extent on the nature of the substituent on the tertiary nitrogen atom†.

Recently, it has been shown that tertiary *N*-thiophosphorylated amides readily undergo isomerisation wherein the oxygen atom of the carbonyl group and the sulphur atom of the thiophosphoryl group are transposed.[106,135]



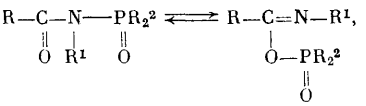
(XXXII)

R^1, R^2=CH_3O, C_6H_5; R^3=H, CH_3, C_6H_5; R^4=CH_3, C_6H_5, iso-BuO

For compounds (XXXII; R^3 = Me or Ph), the isomerisation proceeds even at 40 °C. However, (XXXII); R^3 = H) failed to isomerise. The rate of rearrangement decreases as follows: (XXXII; R^1 = R^2 = MeO) > (XXXII; R^1 = MeO, R^2 = Ph) > (XXXII; R^1 = R^2 = Ph). Benzoylamides (R^4 = Ph) rearrange significantly more readily than acetamide derivatives (R^4 = Me).

† The factors responsible for phosphorylotropic processes in compounds of type (I) have been analysed in more detail in earlier reviews.[82,87] Of necessity, the present review only touches on more recent data in this area.

With oxy-analogues (I, X = Y = O), N→O-phosphoryl migration has been detected under the conditions of electron impact mass spectrometry.[107]



$R = CH_3$, C_6H_5; $R^1 = H$, CH_3; $R^2 = CH_3O$, C_2H_5O, C_2H_5.

Data obtained from X-ray structural analyses of amides (I) and certain of their metallated derivatives (Table 3) confirm the amido(thio)phosphate structure for these compounds. There was no evidence to support any isomeric structure. From these structural analyses of compounds (I), it is quite clear that the *N*-benzoyl derivative (Ia), its analogues (Ib–e), and compounds (If–i) (studied by ourselves) are associated by intermolecular hydrogen bonding. Compounds (Ig) and (Im) are associated by hydrogen bonding of the type N–H...O=P; in compound (Im) the molecules are linked in the form of a centrosymmetrical dimer, while in the oxygen analogue (Ig) the dimer is associated with other molecules in the crystal lattice. In the *N*-thiophosphorylated thioamide (Ii), hydrogen bonding forces the molecules into uniformly extended spiral chains. The molecules of compound (Ih) also exist as a uniform chain linked by hydrogen bonding of the type N–H...O=C.

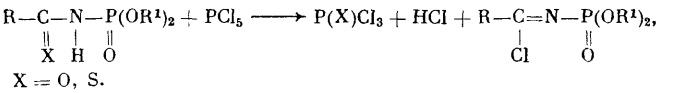
The P=S and P=O bond lengths in compounds (I) are as would be anticipated.[120] The nitrogen atom is planar tricoordinated, the P–N bond length being shorter than the norm (1.77 Å) indicative of partial double bond character. All the compounds in the Table contain the atomic grouping, PNHC(Y)C, the planarity of which provides evidence for π-delocalisation of the double bond, O=C=N, as is found in peptides. This is supported by the bond lengths for compounds (Ig) and (Ih).

In the thioamide anion (Ij), the P=S and C=S bond lengths are longer than in the neutral molecule (Ii), while the P–N and N–C bond length are shorter. This confirms that the negative charge is delocalised in the fragment XCNPY.[113] In the mercury and lead complexes (Ik, Il), the C=S and P=S(O) bond lengths are even greater, approximating to single bonds, while the P–N and N–C bonds are even shorter.[117–119]

IV. Chemical properties

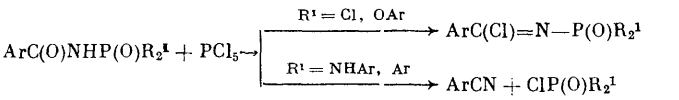
N-(Thio)phosphorylated amides and thioamides participate in a variety of chemical reactions by involvement of one or more of their potentially reactive centres: the labile hydrogen (in secondary amides), the nucleophilic atoms of oxygen or sulphur, and the electrophilic atoms of phosphorus and carbon of the P=X- and C=Y-groups. However, in their reactivity, compounds (I) are markedly different, depending on the nature of atoms X and Y and their bonding, and on the nature of the substituents at the (thio)carbonyl and (thio)phosphoryl centres.

N-Phosphorylated amides (I, X = Y = O) are relatively inert and only a limited number of their reactions have been studied. The replacement of chlorine atoms at the phosphorus centre has been discussed in section II.1. *N*-Acyl- and *N*-thioacyl-phosphoromonoamidates, obtained by alcoholysis of the corresponding dichlorides, react with PCl_5 to give the corresponding *N*-phosphorylated iminochlorides[39,61] which are valuable synthons for the preparation of other derivatives of I.[12,13,17,34,121]

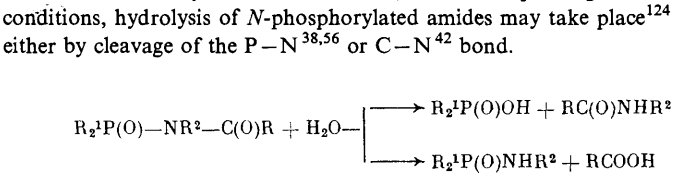


X = O, S.

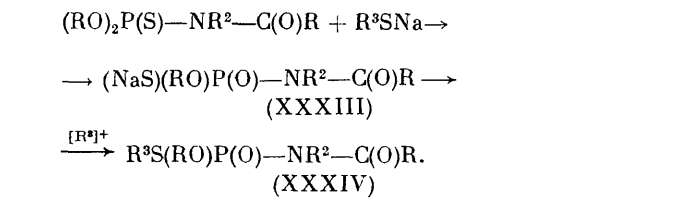
The reaction of PCl_5 with arylcarboxylic acid *N*-phosphinylamides depends on the nature of the substituents in the phosphinyl group: dichloro- and diaryloxy-phosphinyl derivatives are also converted into iminochlorides, whereas bis(arylamino)- and diaryl-phosphinyl derivatives are cleaved to give the corresponding phosphorus(V) acid chloride and aryl cyanide.[15,24]



As *N*-phosphorylated amides (I, X = Y = O) are weakly acidic, they are readily converted to the corresponding salts on treatment with alkali metal hydroxide or alkoxide;[20,122,123] depending on the conditions, hydrolysis of *N*-phosphorylated amides may take place[124] either by cleavage of the P–N[38,56] or C–N[42] bond.

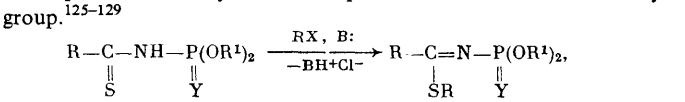


Treatment of tertiary *N*-thiophosphorylated amides with sodium alkylmercaptides effects isomerisation of the thiophosphoryl groups to give the corresponding sodium thiolophosphoramidates (XXXIII) which are readily converted to diesters (XXXIV) with alkyl halide. The products are analogues of acephate.[46]



Attempts to alkylate *N*-phosphorylated amides with alkyl halides in the presence of triethylamine were without success, even on prolonged heating of the reactants,[125] Evidently, the nucleophilicity of the OPNCO group is insufficient for nucleophilic substitution under these conditions.

Amides (I), where either or both of the oxygen atoms (X,Y) are replaced by sulphur, are considerably more reactive. The alkylation of *N*-phosphorylated thioamides (I, X = S, Y = O) and *N*-thiophosphorylated thioamides (I, X = Y = S) with alkyl halides takes place exclusively at the sulphur atom of the thiocarbonyl group.[125–129]



Y = O, S; R = Alk, CH_2COOH, $CH_2COOH \cdot N(C_2H_5)_3$, $CH_2C(O)OCH_3$, CH_2CN.

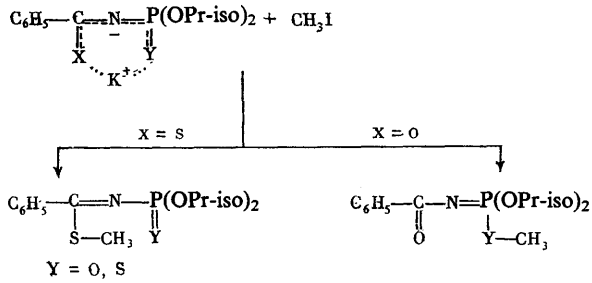
Complete regioselectivity was observed on alkylation with monochloroacetic acid, -acetic acid ester, -acetonitrile, and -acetic acid triethylammonium salt.[126]

On methylation of (I, X = O, Y = S) with diazomethane, S-methylation of the thiophosphoryl group was preferred over N-methylation by a factor of 9:1.[128] However, on alkylation of dimethylthiophosphinic N-thiobenzoylamide with diazomethane, the sulphur atom of the thiocarbonyl group is marginally more reactive than the sulphur atom of the thiophosphinyl group (by a factor of 6:5).[51]

$$C_6H_5C(S)NHP(S)(CH_3)_2 \xrightarrow{CH_2N_2} C_6H_5C(SCH_3)=N-P(S)(CH_3)_2 + C_6H_5C(S)-N=P(SCH_3)(CH_3)_2.$$

With the *N*-potassio derivatives of (I), the regioselectivity of alkylation is higher[124] (see Scheme 7). Thus. methylation of *N*-phosphorylated and *N*-thiophosphorylated *N*-potassiothioamides takes place exclusively at the thiocarbonyl group, irrespective of the nature of the Y atom (O or S); in contrast, with *N*-phosphorylated and *N*-thiophosphorylated amides, reaction takes place only at the phosphoryl (or thiophosphoryl) centre. The yield of alkylated product is always high (73–86%).[129]

Scheme 7



These studies verify that the regioselectivity of alkylation of (I) is dependent on the nature of the nucleophilic centres present and on the reaction conditions. The sulphur atom of the thiocarbonyl group possesses the highest nucleophilicity and polarisability. Suitably activated thiophosphoryl and phosphoryl groups may also be alkylated, but the carbonyl oxygen is effectively inert under these conditions. Alkylation of the XCNPY function can be promoted by increasing the basicity of the medium: by choosing a stronger base (or superbase), by the addition of crown ethers, or by conducting the reaction under phase transfer catalysis conditions. The nature of the alkylated product depends also on the type of amide: *N*-thiocarbonyl derivatives afford imino(thio)phosphates, whereas *N*-acyl derivatives yield phosphazo compounds (see Scheme 7). The nitrogen atom is relatively inert, presumably for steric reasons

The high nucleophilicity of the thiocarbonyl group in *N*-phosphorylated and *N*-thiophosphorylated thioamides is the salient factor determining their reactivity. In the absence of catalyst, these thioamides add to compounds with a carbon-nitrogen multiple bond. Thus, interaction with *N*-acetyltrichloroacetaldimine under mild conditions leads, exothermically, to adducts (XXXV) in >90% yield. The reaction takes place over several hours.[130]

$$(RO)_2P(X)-NH-C(S)-R^1 + CCl_3CH=N-C(O)-CH_3 \longrightarrow (RO)_2P(X)-N=C(R^1)-S-CH(CCl_3)-NH-C(O)-CH_3$$

X=O, S. (XXXV)

In a similar way, the thiocarbonyl sulphur of *N*-thiophosphorylated thioamides reacts with cyclohexyl isocyanide to give S-iminoformyl derivatives:[131]

$$XC_6H_4-C(S)-NH-P(S)(OR)_2 + \text{cyclo-}C_6H_{11}N=C: \rightarrow (RO)_2P(S)-N=C(C_6H_4X)-S-CH=N-C_6H_{11}\text{-cyclo}$$

Evidently, reactions of thioamides (I) may proceed via an initial isomerisation into an imidoyl thio- or dithiophosphate. Thus, *N*-thiophosphorylated thioformamides (XXVI) interact with aromatic amines by nucleophilic attack at the methine carbon of the intermediate anil (XXXVI) to give the corresponding formamidine salts of dithiophosphoric acid O,O-diesters (XXXVII).

$$H-C(S)-N(Ar)-P(S)(OR)_2 \rightleftharpoons Ar-N=CH-S-P(S)(OR)_2 \xrightarrow{ArNH_2} [Ar-N=CH-NHAr]\cdot[HSP(S)(OR)_2]$$

(XXVI) (XXXVI) (XXXVII)

The latter compounds were also prepared independently from a mixture of the appropriate dithiophosphoric acid and anil.[71,86] Acidic cleavage of tertiary *N*-thiophosphorylated thioamides by protic reagents such as water or monothiophosphoric, acetic, thioacetic, and trifluoroacetic acid is thought to proceed in a similar way.[132] It is proposed that this reaction, which takes place even at room temperature, involves an intermediate imidoyl dithiophosphate formed via amide-imidoyl tautomerism. The protic reagent then reacts to give the corresponding thioamide and anhydride (XXXVIII).[132]

$$R-C(S)-N(R^1)-P(X)(OR^2)_2 \rightleftharpoons R-C(S-P(X)(OR^2)_2)=N-R^1 \xrightarrow{HA} R-C(S)NHR^1 + A-P(X)(OR^2)_2$$

(XXXVIII)

A=OH, XP(S)(OR³)₂, OC(O)CH₃, XC(S)CH₃, OC(O)CF₃.

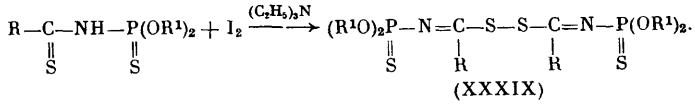
A number of redox reactions of *N*-thiophosphorylated amides and thioamides have also been studied. The outcome depends on the nature of the reagent. Thus, mercuric oxide effects replacement of the thioacyl sulphur atom by oxygen, thereby converting *N*-phosphorylated thioamides to the corresponding amide.[61]

$$ArC(S)NHP(O)(OR)_2 + HgO \rightarrow ArC(O)NHP(O)(OR)_2 + HgS.$$

Nitrogen oxides, iodine in ethanolic KOH, and hydrogen peroxide react with *N*-thiophosphorylated thioamides by sequential replacement of the two sulphur atoms by oxygen.[133] The phosphoryl sulphur is replaced initially, followed by the thiocarbonyl sulphur:

$$R-C(S)-NH-P(S)(OR^1)_2 \xrightarrow{[O]} R-C(S)-NH-P(O)(OR^1)_2 \xrightarrow{[O]} R-C(O)-NH-P(O)(OR^1)_2.$$

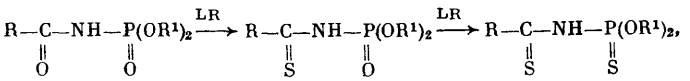
The oxidation of *N*-thiophosphorylated thioamides with iodine in carbon tetrachloride takes a completely different course in the presence of triethylamine:[133,134]



(XXXIX)

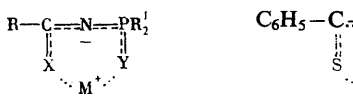
The disulphide (XXXIX) is also formed in small amounts by interaction of *N*-thiophosphorylated thioamides with lead oxide.[119]

There is also the possibility of sequential replacement of the oxygen atoms by sulphur, i.e. the conversion of *N*-phosphorylated amides to *N*-thiophosphorylated thioamides.[133] Lawesson's reagent (2,4-*bis*(*p*-methoxyphenyl)-1,2,3,4-dithiadiphosphetane 2,4-disulphide) is very effective for this purpose.[70]

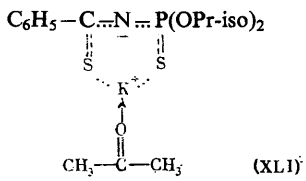


where LR = Lawesson's reagent.

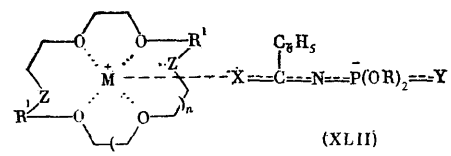
Recently, several publications have appeared (mainly from our own research) on the synthesis and properties of metallic salts of (I),[54,67,97,113,117–119,136,137] Alkali metal salts are formed from (I) by treatment of the amides and thioamides with alkali metal hydroxide or alkoxide. These salts can also be obtained by phosphorylation of amides and thioamides with (thio)phosphorochloridates under phase transfer catalysis conditions in the presence of base and a crown ether.[104,113] Salts of type (XL), their solvate complexes (XLI), and crown ether complexes (XLII) may all be prepared by these routes.



(XL)



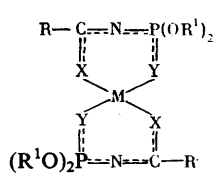
(XLI)



(XLII)

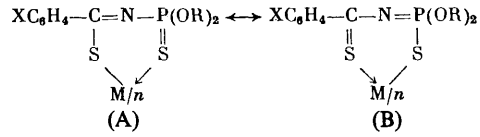
X, Y = O, S; Z = O, NH; n = 0, 1; M = Na, K; R = Alk; R^1 = $-(CH_2)_2-$ o-C_6H_4

Both Na^+ and K^+ complexes of type (XL) (X and Y = O or S) have been prepared.[113,117] Amides (I) also form 1:2 complexes (XLIII) with divalent metal cations.[51,66,97,118,119,136,137]



(XLIII)

These complexes are obtainable from both metal salts (M = Co^{2+}, Cu^{2+}, Ni^{2+}, Zn^{2+}, Pb^{2+}, Pd^{2+}, Hg^{2+}, etc.) and metal oxides (M = Hg, Pb). IR-, NMR-, and EPR-spectroscopic studies of [XLIII, M = Ni(II), Cu(II), Hg(II)] have shown that complexes exist as an equilibrated mixture of two isomeric forms, structure (A) predominating.[97,136]



(A) (B)

Spectrophotometric and potentiometric determinations of the stability of these complexes indicate that those with sulphur ligands are more stable. In complexes of the type ML_2, electron-accepting substituents (X) in the benzene ring of the thioacyl fragment tend to destabilise, and electron-donating substituents stabilise the structure. X-Ray analyses have also been performed on the mercury and lead complexes of *N*-phosphorylated thioamides (XLIII),[118,119] the bond lengths [for compounds (Ik) and (Il)] being given in Table 3.

V. Practical applications

As was mentioned earlier, of all the compounds of type (I), most attention has been given to O,S-dimethyl *N*-acetylthiophosphoromonoamidate which is a highly effective insecticide with low toxicity and a broad spectrum of activity. The compound is known under its commercial name, acephate, which is marketed by many companies throughout the world.[138] It is primarily a contact insecticide with limited systemic activity, being degraded in plants relatively quickly to give non-toxic products. In the soil, it is effective, on average, over 15 days, and it is completely deactivated within a year. According to the French company Chevron, which markets acephate under the name of Orthene, its protective action lasts from 7–10 days.[139]

The toxicity of the compound is relatively low: LD_{50} 945 mg/kg (orally in rats); 361 mg/kg (orally in mice); 2000 mg/kg (s.c. in rabbits).[49,139]

Two reviews on the chemistry and biological properties of acephate have been published[140,141] (the data therein being excluded from the present review). More recent information on the compound is given below. There have been dissertations on a whole range of problems associated with the use of acephate in the battle against pests and crop disease. The compound is very active against ticks and plant lice,[142–148] ants,[149,150] tobacco and maize infestations,[151,152] the larvae of ticks,[153] and termites.[154,155] There are also data on the use of acephate as an antiviral agent in plants,[156] and as a compound which affects the growth and quality of certain floral cultures.[157]

In a number of formulations containing acephate and a second active ingredient, synergism has been observed with a number of compounds: 2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate, metoxil or carbaryl; peremetrin, O,O-dimethyl S-[α-(ethoxycarbonyl)benzyl] dithiophosphate, S-(3-phenyl-2(1*H*)-pyrazinon-5-yl) O,O-diethyl thiophosphate (in 1:4 proportion), ethoprophos (in 1:3 to 5:1 proportion), basudin (in 1:4 to 4:1 proportion), and 0.2–4% epoxidised linseed oil.[157–179] These combinations have been used successfully to combat various plant infestations, house flies, mosquitoes, etc.

As acephate is used extensively in agriculture, much attention has focussed on methods of detecting traces of this compound and one of its more toxic metabolites, O,S-dimethyl thiophosphoro-

monoamidate (monitor), in the surrounding soil,[180–182] in various organisms,[183] in biological samples,[184] in pesticidal formulations and commercial products,[185] in water, in food products, and in various agricultural products.[186–191]

A vast amount of research has been devoted to preparing analogues of acephate and diversely functionalised derivatives. The following *N*-acylaminophosphoryl derivatives, $(R^1Y)(R^2S)P(O)-NR^3-C(O)R^4$, have been reported: compounds where R^1 and R^2 = C_1-C_6-alkyl, alkenyl, alkynyl, R^3 = H or C_1-C_{18}-alkyl, R^4 = H, C_1-C_{18}-alkyl, C_3-C_8-cycloalkyl, C_2-C_{18}-alkenyl, C_3-C_{18}-alkynyl, Y = O,S;[48,49,192] compounds of type $(R^1S)(R^2O)P(O)NR^3-C(O)R^4$, where R^1 = Me, Et, $CH_2=CHCH_2$, $HC\equiv CCH_2$, R^2 = Me, Et, R^3 = H, Me, R^4 = H, alkyl, halogenalkyl, alkoxy, alkylthio, alkoxyalkyl, alkylthioalkyl, alkenyl, $(CH_2)_nPh$ (*n* = 1,2), $CH=CMe_2$, $CH=CHPh$, CH_2YPh (Y = O,S);[49,193] compounds of type $(R^1O)_2P(S)-NH-C(O)R$, where R^1 = C_1-C_3-alkyl, R = aliphatic residue with 0–4 halogen atoms, C_6-C_{12}-aryl with 0–2 halogen atoms;[58] compounds of type $(R^1O)_2P(S)-NH-C(O)CH_2R^2$, where R^1 = C_1-C_3-alkyl, R^2 = H, aliphatic residue.[59]

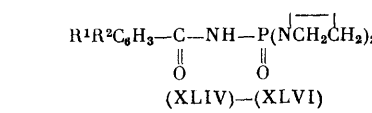
It has been shown that *N*-phosphorylated and *N*-thiophosphorylated halogenocarboxamides possess high herbicidal,[194] fungicidal,[194–197] and antimicrobial[198] activity; furthermore, acetylphosphates and -thionophosphates with halogenalkoxy groups on phosphorus also display the same pesticidal properties as amides (I).[56,57]

Patents have been deposited on pesticidal acephate salts and analogues thereof: $M^{2+}[(R^1O)(R^2S)P(O)-N=C(O^-)R]_2$, where M = Ca, Ba; R^1, R^2 = C_1-C_6-alkyl, R = C_1-C_{18}-alkyl;[122] $MS(R^1O)P(O)-NR_2-C(O)R$, where M = Na, K, NH_4, R^1 = C_1-C_6-alkyl, alkenyl or alkynyl, R^2 = H, C_1-C_6-alkyl, R = H, alkyl, phenyl, aralkyl or alkylaryl which may contain fluorine, chlorine, bromine, or a C_1-C_4-alkylthio group.[199]

It is reported that S-sodio derivatives may be used as starting materials for the preparation of acephate analogues, obtained by alkylation with alkyl halides or alkyl sulphonates[123] (see also Section IV and Ref. 46).

Numerous structure-activity studies have been carried out on acephate derivatives with pesticidal activity (see Ref. 49 and references cited therein). It has been found that it is the environment immediately surrounding the phosphorus atom which largely determines the biological activity of *N*-phosphorylated amides and thioamides. Thus, alkoxy and alkylthio groups on phosphorus impart pesticidal activity to amides (I). However, compounds with ethylenimino groups on phosphorus have another important practical use: as effective antiviral agents.[108–112] Bis(ethylenimino)-phosphoryl derivatives of substituted benzamides are the most active in this respect.[200]

In pharmacological studies of amides (I), most research has been devoted to evaluating the activity of *N*-bis(ethylenimino)phosphoryl-benzamide derivatives, notably benzoTEF (XLIV), fluorobenzoTEF (XLV), and diiodobenzoTEF (XLVI).[108–112]



(XLIV)–(XLVI)

(XLIV): $R^1=R^2=H$; (XLV): $R^1=H$, $R^2=4$-F;

(XLVI): $R^1=R^2=2,5$-I.

Clinically, benzoTEF has proved to be highly effective in the treatment of ovarian and lung cancer, and has also proved to be beneficial in the treatment of breast and stomach cancer, and other malignant diseases.[201] Fluorobenzoyl analogues of this drug have an even broader spectrum of therapeutic activity, having, for example, antiblastic properties.[202] Other analogues of benzoTEF have been synthesised and their toxicity (on s.c. and i.v. administration) measured. These data have shown that *n*-[bis(ethylenimino)-phosphoryl]-arylamines and-acylamines[21,203–209] generally possess lower toxicity than tris(ethylenimino)phosphate (TEF), which, having a relatively high LD_{100} value (30 mg/kg),[200] is widely used medicinally.

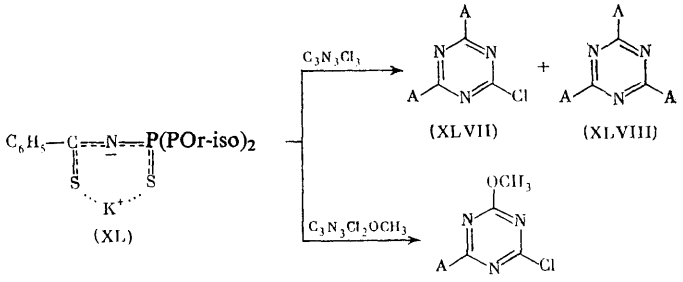
In view of the broad application of these compounds medicinally, there have been several reports in the literature on methods of identifying and assaying the drugs quantitatively in pharmacological preparations and in organisms.[210–214]

In recent years, other pharmacological uses of phosphorylated amides (I) have been studied. Their antiviral activity, for example, has been a topic of our researches.[67,215] Notably, it has been shown that acephate, *N*-thiophosphorylated thioamides (I, R = Me, R^1 = OPr-*i*, R^2 = H, X = Y = S), and the thiobenzamide analogue protect animals (white mice) exposed to influenzal pneumonia. The oxygen analogues (I, R = Ph, R^1 = OMe, R^2 = H, X = Y = O) do not possess antiviral properties, but the water-soluble N-sodio derivatives in certain instances do display an effective antiviral action.[67] A comparison of the antiviral activity of thioacetamide with that of the *N*-phosphorylated analogue has shown that there is little pharmacological difference between the two, but the phosphoryl derivative is less toxic.

Metallo-derivatives (XL) and (XLIII),[216] as well as crown ether complexes (XLII),[215] also possess antiviral activity. It has been found that the antiviral properties of these salts depends little on the nature of the organic substituents; it is the metal itself which largely determines their activity. A comparison of the antiviral properties of crown ethers and derivatives of type (XLII)[215] has shown that, whereas activity in the crown ethers is completely absent, the amide complexes (XLII), on the other hand, possess high activity. Effectively, it is the phosphorus-containing residue which is responsible for the biological activity, while the crown ether serves as lipophilic handle thereby facilitating penetration of the active agent across the cell membrane, i.e. enhances the rate of assimilation of the virucide in cells.[215]

In the search for new types of biologically active compound, a variety of functionalised *N*-phosphorylated amides and thioamides have been synthesised and tested. *N*-Substituted amides, obtained by alkylation with chloroacetic acid (see Section II[126,216,217]), are noticeably inferior to *N*-unsubstituted derivatives in their insecticidal and acaricidal properties. Triazine derivatives have also been prepared by treatment of *N*-potassio-*N*-thiophosphorylated thioamides with cyanuric chloride and its methoxy derivative. The former reacts by replacement of two or three chlorine atoms to give, for example, (XLVII) and (XLVIII), while the methoxy-analogue reacts by displacement of only one chlorine to give (XLIX). Compounds (XLVII) and (XLVIII) possess high fungicidal,

herbicidal and insecticidal activities, the former being 2.5 times as active as carbophos against sugar-beet lice.[218]



Among the metallo derivatives (XLIII), complexes with Cu(II), Ni(II), Co(II), Zn(II), Hg(II), Pb(II) and Ag(I) have also been found to possess insecticidal, fungicidal and antiviral properties.[54,216,218]

The synthesis of *N*-metallo derivatives of (I) broadens the potential value of these compounds. Thus, *N*-thiophosphorylated thioamides may be used as highly effective extractants, notably for the separation of copper from iron, zinc, lead, nickel, cobalt and other elements.[54,97,136,137] *N*-(Diisopropoxythiophosphoryl)benzamide, on the other hand, has been used in a liquid ion-exchange electrode for the determination of mercury in the presence of a variety of metal ions: Cu(II), Ni(II), Co(II), Zn(II), Cd(II), Pb(II), Mn(II), Fe(III), Cr(III), Be(III), Al(III), and Ag(I).[219]

In collaboration with others, we have also found new uses for amides (I) and their metallo derivatives (XL). Thus, amides (I) have been found to inhibit the corrosion of steel in concentrated solutions of mineral and carboxylic acids. In this respect, compounds with a P=S or C=S group are more effective than analogues with a P=O or C=O bond. These compounds offer 70–99.5% protection of steel in acids at varying concentration, and can also be used in galvanic systems.[220]

Potassium and sodium salts (XL) possess excellent sorption properties. In this instance, replacement of an oxygen atom in *N*-phosphorylated amides by an atom of sulphur leads (other things being equal) to an increase in chromatographic polarity constants relative to all standard sorbates; the potassium salts are more effective than sodium salts in this respect. The energy of activation of the absorbed molecules was found to be dependent on the nature of the organic substituents in the sorbent which determines their selectivity.[221]

Finally, it should be noted that macrocyclic complexes of structure (XLII) possess liquid crystal properties. On melting, compounds (XLII) are transformed into homogeneous smectic droplets (spherolites). On cooling with exposure to a narrow beam of light from a microscope, the droplets are seen to develop thread-like off-shoots. Smectic phases with structured layers are formed in these complexes. Compounds (XLII) are clearly of interest because they are mesomorphogenic in nature, and form an electrically conducting meso-phase. By contrast with crown ether complexes (XLII), alkali metal salt complexes (XL) do not display liquid crystal properties.[113,222,223]

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From the data presented in this review, it is clear to us that studies on the chemistry of phosphorylated amides have proved valuable and should continue to be so. In particular, the practical applications of *N*-phosphorylated amides and thioamides may even be extended to other fields. Even though polyfunctionalised amidophosphates are relatively accessible and display a broad spectrum of reactivity, they have been rarely employed as intermediates in organic synthesis. There are few reactions involving functionalisation of the XCNPY system, especially where the (thio)phosphoryl centre participates. The participation of the nitrogen atom of secondary amides in chemical reactions is an intriguing question. We await quantitative structure-reactivity data on the reactions of (I) which involve functionalisation and tautomerism. Evidently, many new developments will emerge from further studies on the complexation of (I), their extracting properties, and their use as analytical reagents for the determination and separation of heavy metal ion in biological samples, in sewage, and in industrial effluent. It is difficult to foresee what other important and interesting questions will be raised in connection with the chemistry and use of (I) and derivatives thereof.

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Translated from *Uspekhi Khimii* **60** 2220–2249 (1991) U.D.C. 541.64

Ageing and stabilisation of polymers

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ABSTRACT. The most recent information on the kinetic mechanisms of the degradation of polymers and methods of stabilising different classes of polymer materials is presented. Progress in the field of thermal, thermooxidative, ozone, photo-oxidative, radiation, mechanically initiated, hydrolytic, and biological degradation of polymers is reviewed. The problems in predicting the stability of polymers, their blends, and certain composite materials during storage and use are discussed. New methods of studying degradation processes are described. The effect of the specific nature of the solid state on reactions in a polymer matrix is examined.

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I. Introduction

Problems concerning the ageing and stabilisation of polymers still constitute a vital question for research chemists and practical personnel working in the field of macromolecular compounds. Prolongation of the lifetime of polymer products during use and storage is equivalent to increasing the manufacture of these products and improving their quality. A sufficiently accurate prediction of the lifetime of reliable operation enables polymer products to be used to a greater extent without risk of failure.

Problems relating to protection of the environment from polymer waste products have assumed prominence at the present time. The scientific principles of the degradation of used polymers to monomers followed by their polymerisation or the pyrolysis of polymers to low-molecular-weight compounds with recovery of the products obtained have been developed for this purpose. Since up to the present time a significant proportion (in many countries the main part) of polymer waste products has been burnt in special furnaces or on dumps, questions relating to environmental protection have proved to be closely linked to problems in the pyrolysis and burning of polymers. The secondary processing of used polymers to new polymer products is also of considerable importance.

The use of degradation processes for the modification of polymer products in order to improve their performance (principally to change their surface properties) and also the production of polymers with a controlled "lifetime" have once again assumed vital importance.

The question of preventing the degradation of polymers was first raised in our country in the second half of the 1940s.[1–3] It was developed further in studies by M B Neuman, et al.[4–6] Subsequently a strictly quantitative approach was applied to it.[7,8] From 1966 to 1984 studies on this problem were directed in our country by Academician Emanuel',[9,10] who extended the scope of research and established international cooperation.[11,12]

II. Effect of intermolecular interactions on the kinetics of degradation processes in a solid polymer

It was demonstrated in the studies of N M Emanual', et al.[9,10] that a solid polymer has a number of properties that are mainly dependent on the mobility of the polymer chain. The concept of "polychromatic kinetics" of the reactions in the polymer matrix was put forward, where, in addition to the molecular-weight distribution, the dependence of the rate constants of the fundamental chemical reactions on the diffusion properties of the system, the accessibility of the reacting bonds, the optimum nature of the structure of the activated complex, etc., should be taken into account. "Polychromaticity" of the reaction kinetics is mainly caused by energetic factors (quite a wide scatter of values of the energy of activation for a given fundamental reaction).

In recent years a new model has been put forward,[12–15] according to which the polychromaticity of the kinetics of reactions in a polymer matrix is due to a change in the entropy term that forms part of the expression for the rate constant. The number and distribution of the various types of intermolecular bonds (donor-acceptor, electrostatic, Van der Waals, etc.) in a sample of polymer

determine the distribution of unassociated and associated monomer units along the blocks.

Starting from the theory of an activated complex, an expression was obtained for the rate constant of scission of a polymer chain

$$k=k_0 \exp\left[(\alpha_1-\alpha)n\right], \quad (1)$$

where k_0 is the rate constant of reaction without taking into account the change in flexibility of the chain, α and α_1 are coefficients representing the loss in flexibility of the unassociated section of the chain with a length of n monomer units in the initial and transition states respectively. The term $\exp(\alpha_1-\alpha)$ mainly depends on the entropy of the system since α and α_1 characterise the loss in flexibility of the chain.

The constant k_0 usually has a similar value to the rate constant of a reaction involving low-molecular-weight products. It follows from Eqn. (1) that the energy of activation does not depend on the length of the block—the pre-exponential term of the rate constant varies with a change in length of the block. In the initial state the entropy of the system is distributed according to the absence of free rotation of the chain units.

Since in practice there is a distribution of unassociated monomer units with respect to block length, the reaction kinetics can be polychromatic. They depend on the past history of the sample, since block distribution is determined by the conditions of synthesis, processing, and operation of the sample in a stationary but not equilibrium state. With an increase in temperature both the rate constants of the reactions taking place and the ratios of blocks of different lengths change. With these concepts it is possible to interpret in a new way the dependence, which has been recorded by many research workers, of the rate of the process and the apparent energy of activation on temperature.

When a block of unassociated monomer units reaches a given length in the system, there is a thermodynamic possibility of chain scission in the middle of the block. From this a different interpretation can be given to the change in the degradation process from scission at the chain ends (low temperatures) to "random" scission (high temperatures), which occurs in a number of cases, and to reactions in cross-linked polymers only starting from a given temperature.

III. Effect of the supermolecular structure of a polymer on thermooxidative processes

The question concerning the nature and role of the supermolecular structure of amorphous polymers is related to the physicochemical behavioural characteristics of polymer products. In recent years quite a large amount of information on the role of supermolecular structures in polymer reactions has been published.

A number of scientists[16–23] have advanced the theory of the role of structural microheterogeneity in chemical reactions that occur in a polymer matrix. A model of heterophase processes in the solid state has been developed. It has been proposed that a polymer consists of a large number of small entities and the reactions in a polymer occur on their surface.

The role of structural microheterogeneity in chemical reactions was examined in studies of a model polymer chain reaction involving benzoyl peroxide. It was demonstrated in the case of vitreous polycarbonate,[16] cellulose triacetate,[17] polypropylene,[18] and molten polyethylene[19] that conversion of the macromolecules may involve successively induced heterogeneous reactions that occur in two structural zones of globular aggregates—in a relatively dense shell and in a looser three-dimensional microphase (the "roe" model).

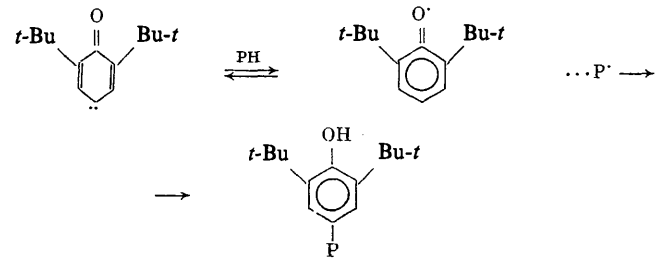
Studies on the oxidation of poly(ethylene oxide) showed that microheterogeneity predetermines the heterophase conditions for oxidation.[20,21] From the proposed structural kinetic model of reaction it was possible to find a kinetic equation that represents the change in concentration of hydroperoxide [ROOH]

$$d[ROOH]/dt = W_{max}^{ROOH}[ROOH]^{1/2}(C+[ROOH])^{-1/2} - aW_i k_{[ROOH][A]}[ROOH]\,t \quad (2)$$

and the corresponding integral expression for [ROOH]t, which is in agreement with the experimental data. In Eqn. (2) W_{max}^{ROOH} is the maximum rate of formation of [ROOH] attained at the moment of complete loss of the function as branching agent by hydroperoxide; C is a composite constant; W_i is the rate of initiation (initiation occurs by a heterogeneous mechanism at the interface of structural zones); $aW_i t$ is the concentration of aldehyde formed in the melt that reacts with ROOH and ensures that $[ROOH]_{max}$ is reached; $k_{[ROOH][A]}$ is the rate constant of the reaction between aldehyde and ROOH. This result is important in that it stimulates the interest of research workers in the elucidation of the role of supermolecular structures in the autooxidation of polymers. The theories relating to the role of microheterogeneity in the heterophase oxidation of polymers have so far not been recognised by the majority of specialists working in the field of thermooxidative degradation of macromolecules. However, there is clear evidence in favour of this hypothesis. If it is shown in future that the process in a polymer does occur precisely in this manner, it will be necessary to revise the considerable amount of quantitative data obtained previously. For example, many rate constants of processes in a polymer matrix may prove to be only apparent overall constants rather than true constants of the fundamental stage.

IV. A new method for studying features of the physical structure of polymer matrices

Davydov, et al.[24,25] have proposed a new method for studying the structure of polymer matrices using the reactions of triplet carbenes. These reactions occur in a polymer via the formation of intermediate radical pairs as a result of the transfer of a hydrogen atom from the C–H bond of macromolecules to a carbene followed by their recombination



where PH is a macromolecule of the polymer matrix.

The kinetics of the conversion of triplet carbenes reflect the features of the physical structure of a matrix at the level of the effective distances in radical pairs (of the order of 3–5 Å). The effect of an external magnetic field on the rate of this process at low temperatures has recently been detected.[24,25] In the case of poly(methyl methacrylate), for example, at a temperature of 77 K the maximum rate occurs at zero field and at a field of 5000 Oe (Fig. 1).[24] The magnetic effect may be attributed to structural features of PMMA,[24,25] if it is assumed that in this radical process two types of intermediate radical pairs differing in their geometric configuration are formed.

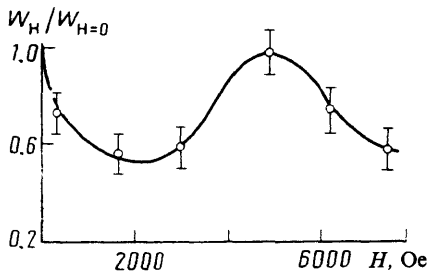


Figure 1. Dependence of the initial rate of conversion of carbenes in PMMA on the strength of the magnetic field.[24] $W_{H=0}$ is the initial rate when $H = 0$.

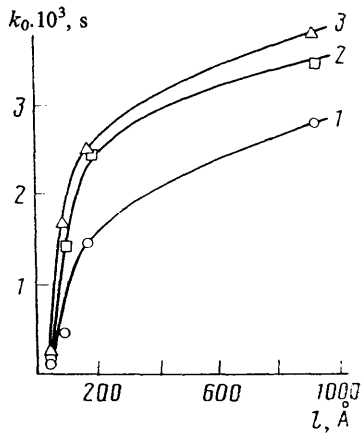


Figure 2. Dependence of the average rate constant for conversion of carbenes on the distance between Aerosil particles in filled PMMA at: *1*, 100; *2*, 113; *3*, 125 K.[25]

Modification of the physical structure of a matrix can be recorded from the change in kinetic parameters of the reaction of carbenes. For example, as the content of an inert filler (Aerosil) increases in PMMA to 65 wt.%, the rate constant of the thermal conversion of carbenes decreases by a factor of 10. The introduction of a filler modifies the physical structure of the polymer in the boundary layer. From kinetic analysis of this lattice reaction it is possible to determine the width of the boundary layer in filled polymers. It is clear from Fig. 2 that with a distance of less than 200 Å between the Aerosil particles, which corresponds to the apparent width of the boundary layer, there is a sharp fall in the rate of reaction.[25]

The method described here can be used to determine the structural features of composite materials (in this particular case—the width of the boundary layer). This has established its future potential.

V. Problems in the stabilisation of polymers during processing. Stabilisation at high temperatures

In recent years there has been increasing interest from research workers in questions relating to the stabilisation of polymer materials during processing, when the main factor causing degradation is mixing (in other words, a rapid shear deformation) of the melt.[11] Two types of stabiliser are recommended for use—amines of the class of sterically hindered piperidines and organic phosphites.[9]

These stabilisers reduce the degree of mechanical degradation processes in the polymers during their processing in an extruder and they considerably reduce the consumption of the principal stabiliser—the antioxidant that is introduced to prevent oxidative degradation of a polymer product during use and storage.

Currently the processing of polymers is being attempted in an inert atmosphere, which considerably reduces the problems related to mechanical oxidative destruction. Because of the high cost of the stabilisers the question has arisen concerning the reduction of their nonrational consumption in evaporation, washing out, bleeding, etc. As a result of this, researchers have shown greater interest in the problems of the solubility of stabilisers in a polymer and the diffusion of additives introduced into a polymer material.[7,26–30]

It was recently shown[27] that the solubility of antioxidants varies in accordance with temperature in a very complex manner and sometimes it even decreases as the tempeature increases. Phase transitions in the polymer constitute the reason for this; on passing through the melting point of the chemical added to the polymer, the heat of solution of the polymer changes and relaxation phenomena occur, leading to an irreversible change in polymer structure at high temperatures (above the glass-transition temperature T_g).

In recent years a property of the solution processes of additives (including stabilisers) such as the dependence of the solubility on the content of polar groups in aliphatic polyamides has been identified. On changing from polyethylene to polyamides-6 and -66 the solubility of the antioxidants usually passes through a maximum. With a small content of amide groups, increasing them leads to an increase in solubility, while when there is a high content, there is a decrease in solubility when they are increased. This is caused by the competition between the increase in solubility due to sorption of the antioxidant (phenol or amine) on the polar groups of the polyamide and its reduction because of the increase in the total compactness of the polymer that is cross-linked by amide–amide hydrogen bonds.[28]

Studies on the high-temperature stabilisation of polymers at $T >$ 200 °C are of considerable interest. Under these conditions conventional stabilisers (phenols, amines) are converted to initiators by thermal and thermooxidative degradation[8,9,11] because of the weakness of the PhO–H or Am–H bonds. Previously it was proposed to use salts of organic acids and metals of variable valence[31] as high-temperature stabilisers. These compounds, being

introduced into the polymer in advance, would decompose at high temperatures to metals or metal oxides in a lower oxidation state. Oxygen reacts with these thermolysis products much more rapidly than with the polymer. Thus, dispersed metals and their oxides protect the polymer from oxidation until they themselves reach a higher oxidation state. However, this method of stabilisation is not always effective, since the transition metal oxides can themselves be catalysts of thermooxidative processes.[8–11]

There may be greater future potential in certain stabilisers of a novel type[30]—polymeric or oligomeric compounds that degrade during oxidation to form free radicals that are free valence carriers. One of these stabilisers is poly(phenylenephenylstibine).[26]

Macroradicals that occur on the polymer chain are virtually immobile. That is why chain termination through recombination of macroradicals occurs extremely slowly even at elevated temperatures.[29,30] The introduction of low-molecular-weight radicals that are capable of migrating in the polymer matrix by diffusion leads to an increase in the rate of quadratic chain termination, i.e. a reduction in the rate of thermooxidative degradation. It is evident from Fig. 3 that small additions of the stibine $-[-C_6H_4Sb(C_6H_5)-]_n-$ reduce the rate of oxidation, whereas at high concentrations of the stibine this rate increases. If the rate of generation of the light radicals that mainly participate in chain termination is less than the rate of formation of the active macroradicals in the oxidation of the polymer, these light radicals will inhibit the reaction. However, an excess of light radicals assists oxidation as a result of their participation in chain propagation reactions. Antioxidants of this type only begin to be effective above a certain temperature—the so-called decomposition temperature.[26]

The proposed method for the stabilisation of polymers at high temperatures[30] is suitable not only during processing but also when heat-resistant polymers are being used.

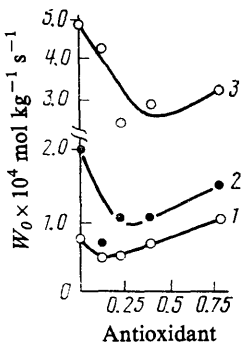


Figure 3. Variation in the rate of oxidation of poly(diphenylphenylene oxide) as a function of the concentration by weight of poly(phenylenephenylstibine) at: *1*, 653; *2*, 673; *3*, 693 K.[26]

Not only the chemical aspect of the reactions leading to inhibition of oxidation processes but also the physical factors related to the distribution characteristics of low-molecular-weight additives in the polymer matrix and the effect of these additives on the structure of the polymer melt have started to be taken into account recently. It is these effects that in a number of cases cause the acceleration of oxidation of a polymer when large concentrations of a reducing agent are introduced. Thus, the dependence of the induction period for the oxidation of polypropylene in the presence of gossypol (a sterically hindered phenol) on the concentration of dilauryl thiodipropionate (a polymer stabiliser) is shown in Fig. 4. The hydrocarbon heptadecane which simulates the hydrocarbon part of the dilauryl thiodipropionate molecule, behaves in a similar way to dilauryl thiodipropionate.[29] The physical aspect of this phenomenon is as follows. When the gossypol dissolves in the polymer its molecules are located in the so-called "potential holes". The number of these holes is limited by the solubility. Therefore, when another additive—dilauryl thiodipropionate (or heptadecane)—is introduced, some of the gossypol molecules are "knocked out" of the potential holes by these additives and are oxidised, resulting in an acceleration of the overall oxidation process.

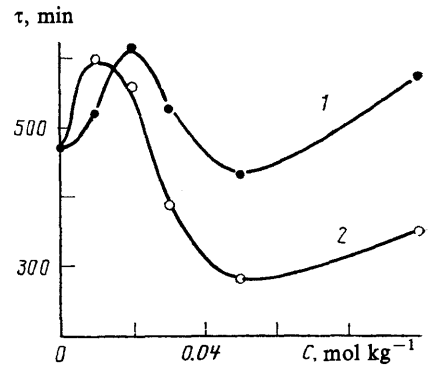


Figure 4. Dependence of the induction period for oxidation of polypropylene in the presence of 0.1 mol kg^{-1} of the natural stabiliser gossypol on the concentration of dilauryl thiodipropionate (*1*) and heptadecane (*2*) (T = 473 K, P_{O_2} = 300 mm Hg).[29]

An elucidation of the mechanism of the high-temperature inhibition of oxidation is one of the most important developments in studies of the chemistry of polymer degradation.[8] Although this process is very inconvenient to study as a considerable number of reactions are taking place simultaneously (several dozen reactions of this type have been identified up to the present time, including oxidation of the stabiliser itself),[32–36] practical requirements demand that increasing attention be given to high-temperature oxidation, since high temperatures are needed not only in polymer processing that is unavoidably accompanied by degradation but also in rapid methods of testing polymers for thermal and thermooxidative stability.

At the present time methods have been developed for the quantitative representation of the high-temperature inhibition of polymer oxidation.[32–36] For this purpose, the absorption of oxygen, accumulation of hydroperoxide (ROOH), and consumption of inhibitor (InH) are recorded and analysed throughout the whole induction period. By using a simple kinetic scheme[34,35] which includes kinetic chain transfer by the inhibitor radical (In$^{\cdot}$), it is

possible to represent the change in concentration of the three key reaction products—oxygen, hydroperoxide, and inhibitor.

Thus, a question that is important for the mechanism of inhibited oxidation of polymers—what happens (how complex do the kinetic mechanisms become) on changing from low temperatures, where the mechanism is quite simple and has already been established quantitatively,[37–42] to high temperatures[32–36]—has been resolved.

Scheme 1

$$R^{\cdot} + O_2 \xrightarrow{k_1} RO_2^{\cdot},$$

$$RO_2^{\cdot} + RH \xrightarrow{k_2} ROOH + R^{\cdot},$$

$$ROOH \xrightarrow{k_3} RO^{\cdot} + {}^{\cdot}OH \xrightarrow[O_2]{RH} 2RO_2^{\cdot}$$

$$RO_2^{\cdot} + RO_2^{\cdot} \xrightarrow{k_4} \text{molecular products} + O_2,$$

$$RO_2^{\cdot} + InH \xrightarrow{k_6} \text{inactive products},$$

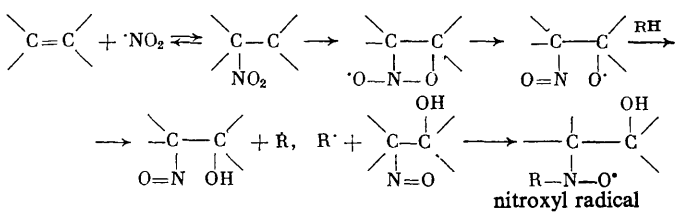
$$In^{\cdot} + RH \xrightarrow{k_7} InH\ (\text{molecular products}) + RO_2^{\cdot}.$$

VI. Reaction between polymers and atmospheric contaminants

In recent years quantitative studies on the effect of components that contaminate the environment on the degradation of polymers have started to appear in the literature. Particular attention has been given to a study of the reaction between nitrogen and sulphur oxides and polymers.[43–46] The kinetics and mechanism of reactions involving nitrogen oxides have been studied in the greatest detail. It has been shown, in particular,[44–46] that the reaction of nitrogen dioxide with the double bonds of macromolecules (including rubbers and vulcanised materials) may be one of the most important ways of initiating the free-radical reactions of polymer ageing in an atmosphere contaminated by industrial waste gases.[44–46]

The reaction between NO_2 and macromolecules containing  bonds has been studied by many methods—EPR, UV and IR spectroscopy, and others. It has been found that nitroxyl radicals are amongst the main reaction products. Usually the two-stage scheme adopted for reactions in solution (the formation of a nitroxyl radical, its conversion to an α-nitro-β-nitroso compound, and acceptance of a second nitroxyl radical by the latter) cannot explain the formation of $(R)_2-NO^{\cdot}$ radicals in the solid state.[44]

A mechanism has now been proposed in which the occurrence of successive "pseudolattice" reactions that have a minimum steric migration of the free valence and which form $(R)_2-NO^{\cdot}$ radicals is assumed.[45]



An $R^{\cdot}$ radical is formed in the immediate vicinity of the nitroso group $(R)_2-N-O^{\cdot}$ and a dialkylnitroxyl macroradical can be a product of the lattice reaction. The formation of $(R'-C=O)-(NO^{\cdot})-R$ radicals in poly(methyl methacrylate) in the presence of NO_2 indicates the decomposition of alkyl macroradicals that is accompanied by cleavage of ester groups with elimination of $(C=O)-OCH_3$.

The reaction of NO_2 with macromolecules containing double bonds is formally given by the kinetic equation[46]

$$\frac{[NO_2]_0}{[NO_2]_t} - 1 = k_{app}t\,, \qquad (3)$$

which reflects the properties of solid-state reactions. The reaction of rubbers with NO_2 is accompanied by a decrease in concentration of C–H groups and the formation of nitro $(R-NO_2)$ and nitrate $(R-O-NO_2)$ groups.

Thus, it has been demonstrated[43–46] that the formation of $(R)_2-NO^{\cdot}$ radicals in reactions between NO_2 and polymers containing double bonds is a free-radical lattice process in which an alkoxyl radical is formed as an unstable intermediate, being highly active in transfer and decomposition reactions with scission of the polymer chain. This leads to ageing of the polymer material.

VII. Ozone ageing of rubbers and vulcanised materials

At the present time considerable progress has been recorded in a kinetic representation of processes involving the ozone cracking of elastomers.[47–50] By improving experimental methods it has been possible to identify the reason for the divergence in experimental results recorded earlier and to elucidate the kinetic mechanisms of the growth of cracks and stress relaxation in samples.[47]

The curves of the dependence of the specific surface area of growing cracks (S_τ) on time τ at difference concentrations of ozone have a similar shape to the well-established characteristics of the rate of autooxidation of hydrocarbons[8] and elastomers.[9] However, in contrast to oxidation by oxygen the ozone ageing of rubbers and vulcanised materials is known to have the characteristics of a nonchain reaction[50] and it does not require an induction period. The chemical reactions that are responsible for its occurrence have molecular mechanisms. The apparent induction period of the dependence of S_τ on τ results from the phenomenon of surface restoration, as first detected by Rzumovskii, et al.[48] In this case the chains ruptured by ozone "escape" towards the interior of the product while the elastomer polymer chains that have not been degraded by ozone appear on the surface. The kinetics of the growth of cracks are satisfactorily represented by the equation for a straight line that is displaced from the origin. From an analysis of kinetic data it was possible to determine the analytical relationship between the surface of the cracks and the experimental parameters at any given moment of time.[49]

$$S_\tau = a + d\,[O_3]^m \left\{\tau - \frac{\gamma\left[\diagup C{=}C \diagdown\right]}{V_r([O_3]_0 - [O_3]_e)}\right\}, \qquad (4)$$

where S_τ is the specific surface of the cracks; a, d, and m are empirical constants; γ is the coefficient of surface restoration; V_r is the rate of introduction of the gaseous mixture into the reaction

volume; $[O_3]_0$ and $[O_3]_e$ are the concentrations of ozone at the entry and exit of the experimental chamber respectively.

A study of the kinetics of the decrease in strength in a sample on ozonisation of different types of rubbers showed[48] that the growth of cracks and stress relaxation essentially constitute two nonconcurrent processes. Induction periods are absent from the curves of the decrease in strength and the rates of decrease in strength are highest at the start of the process, whereas the rates of growth of cracks, on the other hand, increase with time.

It is now generally assumed[47] that the decrease in strength of a sample is a process involving two components—volumetric and surface. The first is dependent on the decrease in cross-sectional area of the sample from the growing cracks. This process is appreciable at the advanced stages of ageing. The second component is related to cleavage of the C=C bonds in the macromolecules of the surface layer. This process predominates at the early stages of reaction.[49]

The quantitative data obtained on ozone ageing of elastomers can be used to improve the accuracy of predicting the lifetime of reliable operation of rubbers and vulcanised materials in an atmosphere of ozone.[11]

VIII. Photodegradation and light stabilisation of a number of polymers

In the field of photodegradation and light stabilisation new data have been obtained on the mechanism of the photoconversion of polyamides,[51–56] and the mechanisms of the principal reactions for photoconversion of polymers such as poly(vinyl chloride) (PVC)[57] and cellulose and its derivatives[58,59] have been established. The effects of physico-structural factors and the acid-base properties of the medium on the light stability of polymers have been analysed in the case of the photooxidation of cellulose.[58]

Recent experimental data have made it possible to amplify and generalise the previously proposed mechanism of the photooxidation of aliphatic polyamides (PA). The general mechanism, as depicted below in Scheme 2, is based on the following arguments. The photooxidation of PA is a chain process whose development is governed by a specific succession of reactions involving peroxide macroradicals $PO_2^{\cdot}$ and low-molecular-weight radicals $X^{\cdot}$ (these would appear to be $HO_2^{\cdot}$ or $^{\cdot}O_2^{-}$).[51] An important route in the conversions of $PO_2^{\cdot}$ radicals is the elimination from them of light $X^{\cdot}$ radicals.[52] In this case an unstable intermediate A (or B) is formed, which is readily oxidised by atmospheric oxygen and converted to a ketoimide (K) and its kinetic analogue (K′) which are kinetic chain carriers and can act as photoinitiators of oxidation.[53]

Scheme 2

1) $PO_2^{\cdot} \xrightarrow{PA,\ O_2} PO_2^{\cdot}$

2) $PO_2^{\cdot} \longrightarrow A + X^{\cdot}$

2′) $PO_2^{\cdot} \longrightarrow B + X^{\cdot}$

3) $X^{\cdot} \xrightarrow{PA,\ O_2} PO_2^{\cdot}$

4) $A \xrightarrow{2O_2} K$

4′) $B \xrightarrow{2O_2} K'$

5) $K + X^{\cdot} \xrightarrow{PA,\ O_2} PO_2^{\cdot}$

5′) $K' + X^{\cdot} \xrightarrow{PA,\ O_2} PO_2^{\cdot}$

} macromolecular scission

6) $PO_2^{\cdot} + X^{\cdot} \longrightarrow$ chain termination

7) $K \xrightarrow{h\nu,\ 2O_2} 2PO_2^{\cdot}$

7′) $K' \xrightarrow{h\nu,\ 2O_2} 2PO_2^{\cdot}$

8) $PA \xrightarrow{h\nu,\ 2O_2} -2PO_2^{\cdot}$

K, K′ — sensitisers

$\sim C(=O)-NH\sim$.

A maximum optical absorption at 360 nm is characteristic of a ketoimide. The nature of its kinetic analogue, which absorbs light in the region of 313 nm, is still unclear. Products K and K′ readily react with $X^{\cdot}$ radicals, which results in macromolecular scission and propagation of the kinetic chain.[54] Chain termination occurs when $PO_2^{\cdot}$ and $X^{\cdot}$ radicals recombine.[55] Chain initiation is achieved by photolytic reactions of products K and K′, the inherent amide groups of the polymer, and the sensitiser introduced into it, the contribution of which varies according to the wavelength of light.[56]

With this proposed mechanism it is possible to represent quantitatively the photooxidation of PA on exposure to UV and longer wavelength radiation. The correlation between the calculated and experimental values of the rate of photooxidation of PA (W_{O_2}) is shown in Fig. 5.

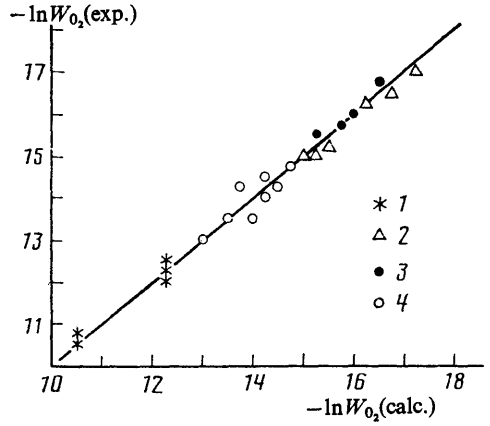


Figure 5. Correlation between experimental and calculated values of $-\ln W_{O_2}$ in the photooxidation of polyimide exposed to light radiation with wavelength: *1*, 254; *2*, 365; *3*, 313 nm; and *4*, in photosensitisation of the process with benzophenone.[51]

Equations have been obtained by Vichutinskaya, et al.[56] which can be used to determine the concentrations of $PO_2^{\cdot}$, K and K′ (the suffices of the rate constants correspond to the numbers of the reactions, W_0 is the rate of chain initiation):

$$[PO_2^{\cdot}] = \sqrt{\frac{k_3}{k_{2'}k_6} k_7 [K] W_0}, \quad (5)$$

$$[K] = \frac{k_2 k_3}{k_{2'} k_5} \frac{k_4}{(k_4 + k_{4'})}, \quad (6)$$

$$[K'] = \frac{k_2 k_3}{k_{2'} k_{5'}} \frac{k_{4'}}{(k_4 + k_{4'})}. \quad (7)$$

Directed research into new light stabilisers is being conducted on the basis of this mechanism. This task continues to be quite urgent as even the best of the known light stabilisers cannot reduce the rate of photooxidation by more than a factor of 5.

Currently it is not completely clear why the overall process according to the scheme given above can be represented in terms of the kinetics of conventional homogeneous reactions. So far no

characteristics of the system related to its solid state nature have been detected, although they evidently must exist.[8] Only in recent studies on chemiluminescence[51,52] were certain charcteristics suggesting the heterogeneous nature of photooxidation identified.

The role of such factors as the structure, molecular mobility, and pH of the medium in the ageing of polymers were revealed in studies on the photoageing of cellulose.[58,59] It was first shown that the rate of photoageing of cellulose is proportional to the content of the accessible amorphous phase. This means that photooxidation does not occur throughout the whole amorphous phase but only in that part which is accessible for low-molecular-weight compounds. On reducing the content of the accessible amorphous phase from 30 to 0%, the rate of photoageing decreases by a factor of 14.[59]

Another important factor in ageing is the molecular mobility. It can vary, for example, by plasticising cellulose with water. An increase in the content of water from 0 to 50% leads to a decrease in the rate of ageing by a factor of 6. This effect, according to Margolin, et al.,[58,59] is due to a sharp increase in the rate of radical recombination (i.e. termination of the oxidation chains) on increasing the molecular mobility of the macromolecules. Another possible explanation[9] is the decrease in reactivity of the peroxide radicals in chain propagation rections when they are hydrated with water molecules ($PO_2^{\cdot}\cdots H_2O$).

The third factor in the photoageing of cellulose—the pH of the medium—is of very considerable significance. It was found[58] that the rate of photodegradation of cellulose can vary by a factor of 10^2-10^3 according to the pH of the medium, and the minimum rate occurs in the region of pH 5. This is due to the catalytic nature of the reactions of radicals and products at the chain propagation stage of the oxidation process.

By varying the structure, molecular mobility, and pH of the medium, it is possible to achieve an increase in the light stability of cellulose by a factor of 100 – 1000. This indicates what practical significance there is in the application of these factors.

Despite the large number of studies on the degradation and stabilisation of PVC,[60] a solution to the question of its photodegradation and light stabilisation still remains very remote. In recent years the basic principles of the photodehydrochlorination and photooxidation of PVC—the main processes that occur during photoageing of this polymer—have been established.[57]

According to a mechanism put forward recently, photodehydrochlorination of PVC is a photochain process with a kinetic chain length of several tens of units, in which chain propagation occurs by photochemical conversion of alkyl and polyene radicals (Scheme 3).

Scheme 3

$$X \xrightarrow{W_0} P^{\cdot} \text{ – chain initiation}$$

$$P^{\cdot} \xrightarrow{k_1} P_1^{\cdot} \text{ – chain propagation}$$

$$\begin{cases} P_1^{\cdot} \xrightarrow{\alpha_2 k_{app}} P_2^{\cdot} + HCl \\ \cdots\cdots\cdots\cdots \\ P_1^{\cdot} \xrightarrow{k_{app}} P_n^{\cdot} + (n-1)HCl \end{cases}$$

$$\begin{cases} P_1^{\bullet} \xrightarrow{k_{1,1}} P_1 + P^{\bullet} \\ \cdots\cdots\cdots \\ P_n^{\bullet} \xrightarrow{k_{n,n}} P_n + P^{\bullet} \end{cases}$$

$$P_1^{\cdot} \xrightarrow{k_r} \text{inactive products}$$

$$P_1^{\cdot} \xrightarrow{k_{r,1}} \text{inactive products}$$

where W_0 is the rate of initiation, α_i is the probability of new radicals being formed, k_{app} is the apparent rate constant of reaction:

$$k_{app} = \varphi\varepsilon I. \tag{8}$$

Here φ is the quantum yield of radical conversion, ε is the extinction coefficient of radical absorption, I is the intensity of light.

From this kinetic scheme for the photodehydrochlorination of PVC, an expression can be readily obtained[57] from which the rate of dehydrochlorination can be calculated from known kinetic parameters.

$$W_j = \gamma\eta\alpha_j W_0, \tag{9}$$

where

$$\eta = \frac{k_1 k_{app}}{k_r + (k_1 + k_r)k_{r,1}k_{app}^{-1}}, \tag{10}$$

$$\gamma = \sum_{j=1}^{n}[R_j^{\cdot}]_{pl} \Big/ \sum_{j=1}^{n}[R_j^{\cdot}]_{rig}. \tag{11}$$

In this case the subscripts "pl" and "rig" refer to plasticised and rigid PVC respectively.

According to the proposed mechanism, the key parameters are the values of the extinction coefficient ε, the quantum yield φ of radical conversion, and also the intensity of light I. Moreover, with a knowledge of the proportion of the rigid regions in plasticised PVC, where radicals R_j are stable, the dependence of the rate of dehydrochlorination on the content of plasticiser can be given.

The photooxidation of PVC occurs as a process with a very short chain length and formally linear termination.[57] The possibility of migration of the free valence for considerable distances in solid PVC has been demonstrated by means of low-molecular-weight radicals. The results suggest the possibility of using light-stable antioxidants and also quenchers of excited states for the light stabilisation of PVC, which opens up new ways of increasing light stability.

In recent years a considerable number of studies have been published on the photoradical ageing of polymers,[61–67] namely, on the change in functional composition and structure of high-molecular-weight compounds as a result of the chemical reactions of electronically excited radicals and radical ions.

A considerable amount of data has been obtained on the quantum efficiency of photochemical reactions of macroradicals in various carbon-chain and heterochain polymers and on the effect of photon energy on the quantum efficiency of these reactions.[68–77] The efficiency of photodissociation processes of macroradicals can be represented satisfactorily in terms of a free-volume model. The mechanism and kinetics of the photoradical ageing of polycaproamide and poly(acrylic acid) at 77 K have been studied in detail. It has been established that the principal route of the reactions of electronically excited radical anions in these polymers is the ejection of an electron, the quantum yield of which increases with an increase in photon energy. Neutral macroradicals (median and terminal) are active sites of the photoradical ageing of poly(acrylic acid) and polycaproamide. In this case excited median macroradicals only undergo dissociation. Photoradical chain reactions involving median macroradicals have been identified in the degradation of a large number of different polymers, including poly(acrylic acid) and polycaproamide. In the case of poly(acrylic acid), for example, photodecomposition of median radicals can occur by two routes—with scission or without scission of the main polymer chain.

The second of these two reactions, which is the photochemical stage of chain propagation, is also accompanied by efficient rupture of the functional groups and the formation of a product (a ketene) whose subsequent reactions cause cross-linking of the polymer chains.

$$\sim CH_2\dot{C}(COX)CH_2\sim \xrightarrow{h\nu} \begin{cases} \longrightarrow \sim CH_2C(=C=O)CH_2\sim + X^{\cdot} & (I) \\ \longrightarrow \sim CH_2\dot{C}(COX)\dot{C}H_2 + \dot{C}H_2(COX)CH_2\sim & (II) \end{cases}$$

$$X^{\cdot} + \sim CH_2CH(COX)CH_2\sim \longrightarrow \sim CH_2\dot{C}(COX)CH_2\sim + HX, \quad (III)$$

$$\sim CH_2C(=C=O)CH_2\sim \longrightarrow \sim CH_2\ddot{C}CH_2\sim + CO. \quad (IV)$$

The quantum yields of these reactions have been determined.

By using the above results together with the experimentally determined apparent rate constants for macroradical recombination, it was possible to represent with considerable accuracy the kinetics of the change in concentration of the initial, intermediate, and final products of the photoradical ageing of poly(acrylic acid).[61–67]

An important fact which is consistent with the scheme given above has been established experimentally: by changing the dose of absorbed light radiation it is possible to produce a directed change in the molecular weight distribution of the polymer in which median macromolecules occur. With small doses the molecular weight distribution is determined by reaction (II), while with large doses it is determined by reaction (IV) and the subsequent formation of cross-links as a result of reactions involving the ketene.

In addition to the already well-established phenomenon of kinetic nonequivalence which was observed previously[57] during photoradical processes in different polymers, the levelling effect of the photon energy on the kinetic nonequivalence of sulphonyl macroradicals has recently been detected.[52,53]

A study of the photochemistry of macroradicals involved in forbidden transitions (the possibility exists for considerably extending the region of spectroscopic sensitivity) and an investigation of photoradical chain reactions, in particular the steric distribution of their products, should evidently be considered the most interesting developments of future research into the photoradical ageing of polymers.

IX. Kinetics and mechanism of oxidative reactions of stressed polymers

Studies of the effect of mechanical stresses on the structure, dynamics, and reactivity of polymers led to a number of unexpected new results.[78–83]

Structural stresses of an energetic nature increase or reduce the rate of a chemical reaction depending on the change in linear dimensions of the reaction site during reaction.[79]

$$\ln \frac{k_\sigma}{k_0} = \frac{\gamma\sigma}{RT}, \quad (12)$$

where k_σ and k_0 are the rate constants of the chemical reaction of the polymer in stressed and unstressed states respectively: σ is the stress; γ is the coefficient of sensitivity of the reaction to stress, equal to the product of a constant γ_a, which is inherent to each specific reaction, and a coefficient β, which takes into account the nonuniform distribution of stress on the bond ($\beta \geqslant 1$).

By establishing a quantitative relationship between the rate constant of reaction and the stress it was possible to classify different chemical reactions according to their sensitivity to the application of stress and also to study the supermolecular structure of the polymers.[78,79,81,82]

All chemical reactions can be divided into three groups in accordance with their sensitivity to deformational stresses.

1. Processes that are insensitive to applied stress; for these $\gamma_a = 0$.

2. Chemical reactions that are highly sensitive to stress; these have $\gamma_a \geqslant (0.5-1.0) \times 10^{-29}$ m^3. These include processes that are accompanied by scission of the main macrochains, for example, the hydrolysis of polyamides. Treatment of the results of Popov[79] using Eqn. (12) gives an estimated value of $\gamma_a \approx 2 \times 10^{-29}$ m^3.

3. Reactions having low sensitivity to stresses; for these $0 < \gamma_a < 0.5 \times 10^{-29}$ m^3. These include reactions of ozone with saturated polyolefins ($\gamma_a = 0.33 \times 10^{-29}$ m^3) and polyaminoimides ($\gamma_a = 0.05 \times 10^{-29}$ m^3).

By studying the supermolecular structure of polymers using Eqn. (12), it was possible to determine quantitatively the nonuniform distribution of stress on the bonds in oriented polyolefins—low- and high-density polyethylene and polypropylene ($\beta = 2-6$).

The supermolecular structure of isotropic polyamidoimides containing a fluorene ring (PAI-1), a nitrile group (PAI-2), and a *para*-phenylene group (PAI-3) were studied in particular detail with this method. In this case the coefficient β varies from 40 to 120 according to the chemical structure of the polyamidoimide. PAI-1 has the most ordered structure, and it is characterised by the lowest value of β and the lowest density, which provides the greatest opportunity for the formation of intermolecular hydrogen bonds.

Irreversible rearrangement of the supermolecular structure of polymers affects the dependence of the rate of their ozone oxidation on stress.[81] A particularly marked effect of this type of rearrangement occurs in the ozone oxidation of oriented polyolefins subjected to tension under conditions of stress relaxation. The additional orientation leads to an improvement in the fibrillar structure and a decrease in the rate of ozone oxidation.[82]

The physical and performance properties of polymers and the rate and mechanism of the chemical reactions occurring in them are determined to a considerable extent by the relaxation properties of the macromolecules and the mobility of low-molecular-weight additives,[78] since polymer products are generally used under conditions of mechanical stress and by the effects of temperature and oxidation. In order to resolve many scientific and practical problems, it is important to elucidate the effect of these factors on the molecular mobility of oriented polymers.

At the initial stage of stretching previously oriented samples (ε is about 6% for polyethylene and about 10% for polypropylene), the molecular mobility of the chains in the amorphous regions increases, with the magnitude of these changes depending on the molecular weight distribution, degree of orientation stretching, and degree of oxidation.[79] Deformation of samples with an average molecular weight and narrow molecular weight distribution at high degrees of stretching is accompanied by a decrease in molecular mobility.

Ozone oxidation produces a considerable increase in the rigidity of the amorphous regions,[81] which leads (at low degrees of oxidation) to an improvement in the mechanical properties of the polymer material.

A study of the effect of the orientation temperature (T_{or}) on the structure and strength of films of mixtures of polypropylene and high-density polyethylene (HDPE) showed that when T_{or} is higher than the melting point of the crystallites of HDPE, considerable changes occur in the polymer matrix. A new crystalline modification of PE is formed, the tensile strength decreases sharply, and the

melting point of the crystallites of PE and its degree of crystallinity are reduced. The combined experimental data suggest that the T_{or} of polyolefins should be close to the melting point of the more readily melting component of the mixture but should not exceed it.[78]

Ozone-oxygen oxidation of polymers substantially alters such characteristics of the physical structure of a polymer matrix as the melting point of crystallites of components of the polymer mixture, the polydispersion, and degree of crystallinity of the components.[82,83] As a result of oxidation there is a small decrease in the melting point and an increase in polydispersion of polyethylene and also a substantial decrease in melting point and polydispersion of polypropylene. When a mixture of polypropylene and polyethylene is treated with ozone, only the crystalline structure of the former is rendered amorphous to the extent of complete loss of crystallinity.[79]

Recently, unexpected effects relating to the action of mechanical stresses on the kinetics of oxidation of polyolefins have been revealed.[60] The oxidation of oriented polyethylenes, and particularly oriented and stressed polyethylenes, occurs in separate spatial zones of the reaction. The number of the latter and the characteristics of their distribution in space provide a basis for the assumption that they are formed around particles of contaminants that initiate the oxidation of the polymer.[82] Products of the conversion of polymerisation catalysts present in trace amounts in the polymer and also metal ions that have penetrated the polymer as a result of corrosion of the equipment (the polymerisation reactor, for example) can act as these particles. This in particular governs the variable thermooxidative stability of the same polymer synthesised using different catalytic systems.[8,9]

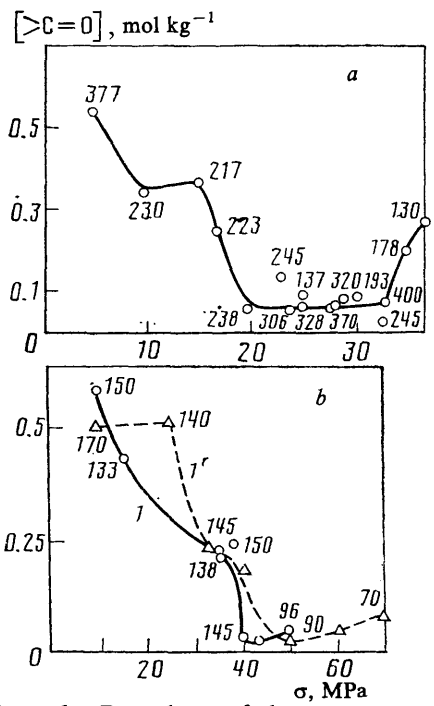


Figure 6. Dependence of the average concentration of carbonyl groups formed up to the moment of sample fracture on stress in the oxidation of oriented polypropylene: *a*, degree of stretching λ = 7.5, temperature of oxidation 120 °C; *b*, λ = 8.5, temperature of oxidation 130 °C.[78]

Mechanical stresses during oxidation primarily alter the permeability of the matrix. With low stresses the rate of translational diffusion of the low-molecular-weight radicals that are carriers of free valence from initiation "points" through the matrix falls (Fig. 6).[78] This leads to a marked decrease in the overall rate of oxidation under load. However, on increasing the stress above a given limit, mechanical radical initiation that is distributed throughout the polymer much more uniformly than initiation on contaminants starts to predominate.[82] At the same time the rate of oxidation of the polymer starts to increase again. With an increase in mechanical stress, not only the rate but also the oxidation conditions are altered. There is a change from a branched-chain process to a nonchain oxidation of the terminal macroradicals. These effects have the result that the criterion of rupture as a fixed average concentration of scissions or terminal oxygen-containing groups is not applicable to stressed polyolefins undergoing oxidation.[78]

Models for the rupture of stressed polyolefins undergoing oxidation which can be used in a number of cases to predict the longevity of various grades of polymers under various operating conditions have been proposed.[78–84] Analytical expressions that relate the longevity of a polymer to the number of initiation sites in samples and their growth rate have been obtained. The number of sites depends on the conditions of polymerisation, purity, and formation and their growth rate depends on the polymer structure and the oxidation conditions. All this makes it possible to develop new principles for increasing the stability of polymers without the use of traditional stabilisers. Careful removal of contaminants, increasing the degree of initial stretching, etc., are required for this purpose.

X. Radiation ageing of polymers

Bykov, et al.[85–87] have studied in detail the phenomena of shrinkage and cracking in polyolefins, in particular polyethylene, during radiative oxidation.

A well-defined sandwich structure consisting of an external oxidised layer and an internal unoxidised layer will be formed in thick films (plates, cable insulation) as a result of the diffusion-controlled flow of oxygen. The oxygen-containing compounds formed in the oxidised layer alter the conformation of the initial molecules. In this case mechanical stresses develop, leading to cracking of the polymer to the depth of the oxidised layer. The thickness of the oxidised layer and hence the depth of the cracks depends on the strength of ionising radiation.

In thin films that are oxidised to a uniform depth (oxygen permeates a sample quite rapidly) cracking does not occur, but shrinkage that is related to the accumulation of polar groups during oxidation is observed. The shrinkage of thin films and the cracking of thick films are governed by the same structural reorganisation processes—cracking starts at the moment when shrinkage reaches a given critical magnitude.[85–87]

A post-effect that is not related to post-radiative oxidation is characteristic of both the phenomena studied—shrinkage and cracking. The structural reorganisation processes that give rise to shrinkage and cracking are delayed relative to oxidation. The characteristic time lag is ~1 month.[88]

A kinetic model was developed, making it possible on the basis of common arguments to represent the phenomena of shrinkage and cracking as the result of radiation oxidation.[85–88] Using this model a

method was developed for determining the guaranteed operating lifetimes of cable insulation made of polyethylene. At the present time this method is being tested in the cable industry.

XI. Hydrolytic degradation of heterochain polymers

All heterochain polymers undergo degradation by reacting with water.[89–91] The hydrolysis reactions are catalysed by acids and bases. In dilute solutions of acids and bases (the so-called pH region) the rate of these reactions increases in proportion to the concentration of solvated H^+ and OH^- ions.[89] In more concentrated acid and base solutions the dependence of the rate of hydrolysis on the composition of the medium is more complex. Thus, for example, the rate of hydrolysis of amides increases with an increase in concentration of $H_5O_2^+$ ions and reaches a maximum value for aliphatic amides when the concentration of H_2SO_4 is 15% (for aromatic amides this occurs at about 50% H_2SO_4) and then decreases. The decrease in the rate of degradation at higher concentrations of sulphuric acid is related to the formation of an unreactive protonated form of the amide bond.[91] Because of this, the view was expressed[89] that solutions of polyamides in concentrated sulphuric acid should be stable.

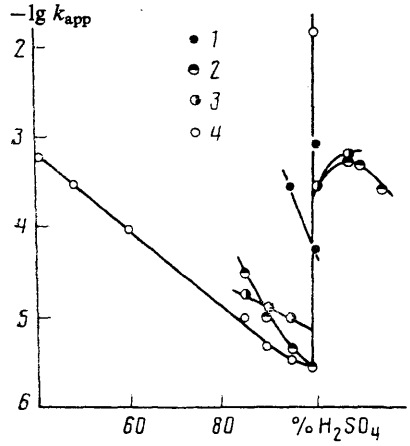


Figure 7. Dependence of the rate constants for degradation of polyamide on the concentration of H_2SO_4 at 80 °C:[89] *1*, polybenzamide; *2*, poly(*p*-phenylene terephthalamide); *3*, poly(*m*-phenylene terephthalamide); *4*, polycaproamide.

However, it was recently shown[90,91] (Fig. 7) that the rate constants for degradation of aliphatic and aromatic polyamides decrease as the content of H_2SO_4 increases up to 99.5%, while when it rises further to 100% they increase sharply. This change in reactivity has no analogies in the chemistry of low-molecular-weight amides. This is believed[91] to occur because the polymer state of the material assists the development of high local concentrations of protonated amide bonds in solution, with the result that the properties of the medium are changed in the immediate vicinity of the polycation.

The results obtained are important for the chemistry of aromatic fibre-forming polyamides since concentrated sulphuric acid is the only readily available solvent for these polymers.

It was recently demonstrated at a quantitative level that mineral acids act as catalysts of the polycyclodehydration of poly(*o*-hydroxy-amides) in solution. When mineral acids (hydrochloric, sulphuric, phosphoric) are introduced into a mixture containing poly(*o*-hydroxyamides) in dry *N*-methyl-2-pyrrolidone, two reactions—hydrolysis and cyclodehydration—occur simultaneously.[91] By changing the conditions of the reaction it is possible to direct it along a given route. With these data it is possible to predict the stability of poly(*o*-hydroxyamides) in aggressive media. They are of potential benefit in terms of the synthesis of these polymers, since they can be used to alter the reaction conditions (reduce the temperature, for example) so as to direct it on the cyclodehydration route.

Similar results have been obtained for a large number of polyamides, polyimides, polybenzoxazoles, and other polymers.[90,91]

XII. Interaction of polymers with biological media

Recently a complex analysis of the structure properties, and stability of poly(ether–urethanes) for medical use was carried out.[92–95] The use of block copolymers for the manufacture of artificial organs (cardiac chambers, cardiac valves, etc.) and a number of medical products (for example, catheters) makes it necessary to develop a scientifically based system of requirements to be imposed on these materials. A comprehensive approach has been developed for studying materials and products used as membranes, diaphragms, and certain other elements of an artificial heart, involving the application of a number of spectroscopic and diffusion methods.[92]

In virtually all of the materials of this type there is an intermedite (mixed phase) that consists of polyether and polyurethane residues, and this is responsible to a considerable extent for a whole set of physicochemical and mechanical properties of the material (and products made from it).[93] A correlation has been established between the degree of structural heterogeneity and the adsorption properties of the surface of poly(ether–urethanes) relative to blood plasma proteins (formation of blood clots on the polymers),[94] which is extremely important in relation to the specific conditions of using the products.

A comprehensive approach has been suggested[95] for studying the kinetics of adsorption of blood plasma proteins on the surface of the block copolymers, including the development of a kinetic diffusion model for the process, a method of determining the physicochemical parameters of the system polymer–protein, and a prognosis of the composition and structure of the adsorbed layer as a factor that is of definite significance in determining the thrombosis-resistant properties of segmented poly(ether–urethanes).[92–95]

A diffusion method and an H–D isotope exchange method specially developed for this class of polymers were used to determine their essential properties (water adsorption capacity, coefficients of diffusion and permeability) which it was necessary to take into account during use and storage of the materials.[94]

In recent years a new problem concerning the production of substitute materials for various biological tissues and systems has arisen on the borderline between mechanics, biology, and medicine. Polymer materials are increasingly being used for this purpose.[96–101]

For a polymer implant, not only the biological compatability but also the rheological compatibility is of considerable importance. Rheological incompatibilty, i.e. a lack of correspondence between the biochemical properties of the transplant material and the redesigned organ or tissue, results in very severe stresses developing at the points where they are connected. Therefore, in developing synthetic materials for medical application, the question of predicting their deformations and strength and structural characteristics is a vital one as is a determination of these properties after prolonged exposure of the material to an aggressive medium under conditions of continuous cyclic stress.

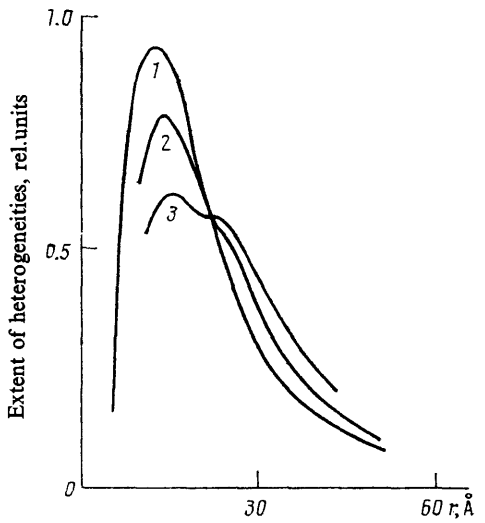


Figure 8. Distribution by size of microheterogeneities in PET fibres at different periods of implantation:[96] *1*, initial material; *2*, 3 months; *3*, 8 years.

In this connection studies were made on poly(ethylene terephthalate) (PET) that was subjected to biomechanical stresses in the transplantation of ligaments and tendons.[96–99] Braided tissue bands made of PET fibres were used with perpendicular interweaving of filaments. The residence of such fibres in an organism leads to irreversible changes in the structural characteristics of the material (Fig. 8), for example, a redistribution of microheterogeneities (the proportion of small pores decreases).[96] The number of small pores on the surface can decrease through an increase in their size as a result of the hydrolysis of PET[89] and also through penetration of the pores by collagen tissues of the organism.[97]

The change in structure of the fibres has an effect on their creep, which increases as the residence time of the PET material in the organism increases (Fig. 9).[97] The increase in deformation mainly occurs because of sorption of tissue liquid by the material.[97] As a result of the sorption of liquid under a continuous load (for example, the operation of a ligament in a living organism, an orientation strengthening of PET fibre occurs.[98]

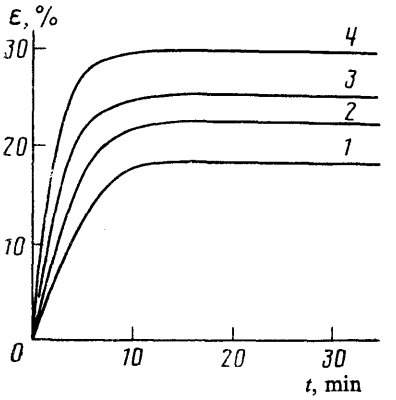


Figure 9. Creep of PET fibres at different periods of implantation:[97] *1*, initial material; *2*, 3 months; *3*, 1 year; *4*, 8 years.

A general prediction of the possible changes that occur in Lavsan (PET) substitute materials for ligaments and tendons can be made (Fig. 10).[89,96–98]

$$P = P_0(1 - k_{app} t d d_0^{-1} \rho^{-1})^2, \quad (13)$$

where P_0 and P are the initial and continuing tensile strengths respectively; k_{app} is the apparent rate constant for degradation; t is the residence time in the organism; d_0 and d are the initial and continuing average diameters of a simple filament of PET; ρ is the density of the PET fibre. This equation can be used to determine the average time taken for the ligaments and tendons to lose 50% of their strength. This time is estimated to be 30 ± 2 years.[96]

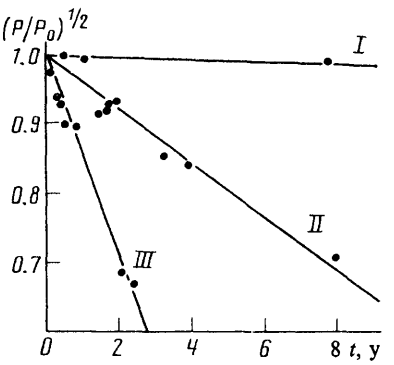


Figure 10. Dependence of the relative tensile strength of materials made of PET on the residence time of an implant in the human organism (*I*, PET ligaments and tendons, *II*, PET gauze) and rabbit (*III*) PET gauze.[98]

There is considerable interest in recent studies[99,100] related to the use of polymers subject to biodegradation in equipment for the controlled release of drugs. Drugs are released in proportion to the

surface erosion of these polymers. This usually occurs with zero-order kinetics, which corresponds to the therapeutical requirements of the supply of drugs to the organism.

The kinetic principles for representing the process of drug release from polymers undergoing bioerosion have recently been developed.[99,100] The molecular weight distribution of the initial polymer affects the kinetic parameters of drug release. The case where residues of a drug are connected to a polymer chain has been examined in terms of the kinetics. From the integral kinetic equations obtained it is possible to determine all of the required kinetic parameters. There is also the possibility of the nonuniform release of drugs due to the formation of soluble biodegradation products throughout the whole polymer.[100]

In general the following processs can occur in biodegraded polymer products:[89]

– adsorption of substances present in tissues of a living organism or of microorganisms on the surface of the material;

– destruction of the material either as a result of the specific action of living organisms that can use the polymer material as a nutritional source or by the action of an aggressive medium, including the action of metabolic products from microorganisms.[101–106]

When the first process occurs, the chemical structure does not change as a rule; the material acts as a support on which the adhesion and growth of colonies of microrganisms occur or collagen-like capsules are formed (when the material is used as an implant).

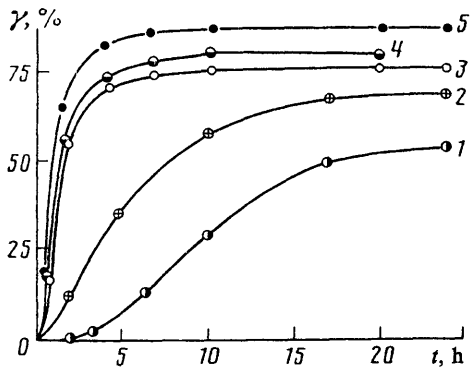


Figure 11. Kinetic curves for adhesion of colonies of spores of *Aspergillus niger* to the surface of different polymers: *1*, polyethylene; *2*, epoxy resin; *3*, poly(methyl methacrylate); *4*, cellophane; *5*, acetylcellulose (25 °C, 90% relative humidity).[105]

The second process leads directly to ageing of the polymer material through the action of chemically active agents. In this case the "bulk" operating properties are changed.

The kinetics curves of adhesion are satisfactorily given by the equation[105]

$$\ln(\gamma/\gamma_0) = -kt, \qquad (14)$$

where γ and γ_0 are respectively the proportion of particles remaining on the polymer surface after adhesion over a period t and the proportion of particles irreversibly adhering under these conditions; k is the rate constant for formation of adhesive bonds between the spores of microorganisms and the surface of the material.

The kinetic curves for the growth of biomass are satisfactorily given by the exponential function[106]

$$m/m_\infty = 1 - \exp(-kt), \qquad (15)$$

where m and m_∞ are respectively the continuing and final quantities of biomass on the surface of the polmer. In this case m_∞ is greater, the higher the solubility of water in the polymer. To illustrate this, the kinetic curves for adhesion and growth of biomass on different polymers that have been plotted according to Eqns. (14) and (15) are shown in Figs. 11 and 12.

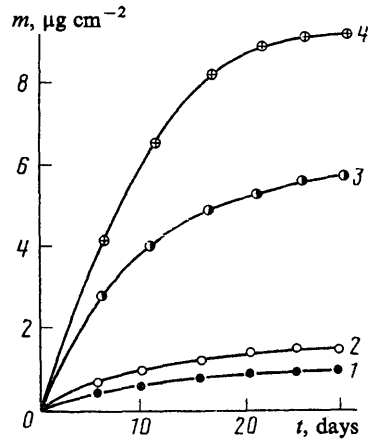


Figure 12. Dependence of the accumulation of biomass consisting of spores of *Aspergillus niger* on residence time on the surface of different polymer films (25 °C, relative humidity 90%): *1*, polyethylene; *2*, fluoropolymer; *3*, poly(ethylene terephthalate); *4*, cellulose.[106]

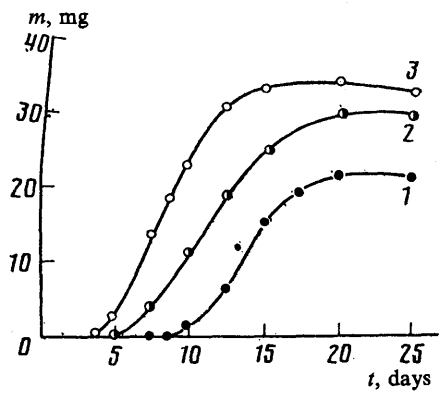


Figure 13. Kinetic curves for growth of *Aspergillus niger* biomass on canvas subjected to thermal humid ageing.[106] Ageing time, h: *1*, zero (initial material); *2*, 400; *3*, 1000 (25 °C, relative humidity 90%).

Under real conditions, degradation and biodegradation of the polymer material can occur simultaneously. The kinetic curves for the accumulation of biomass on canvas consisting of flax and cotton that has undergone thermohumid ageing followed by the growth of fungal spores are given in Fig. 13. It is clear that an increase in the time of ageing leads to an increase in the growth of biomass.[106]

Thus, the biological stability of a polymer material is governed by a combination of complex physicochemical processes involving adhesion, biological growth, and biodegradation which occur under certain external conditions.

XIII. Protection of materials with polymer coatings

One of the methods of protecting materials from the effect of aggressive media is to deposit protective polymer coatings on their surface. However, since the polymer coating itself is also degraded on contact with aggressive media, its service life is finite if it is a question of protecting a metal, and the aggressive medium, on reaching the metal surface, causes it to corrode.[9,11,89,91,94] Therefore, there is still considerable interest in studying ways of reducing the rate of penetration of aggressive media through protective polymer coatings.

A method of protection that is related to the introduction of additives which absorb oxygen and thus inhibit its participation in the thermooxidative degradation of polymers[107] is effective if the concentration of the aggressive medium (ozone, oxygen) is of the order of thousandths of a percent.[11] When the pressures of the aggressive medium are close to atmospheric, this method of protection is ineffective.

An experimental study of the efficiency of binding fillers such as oxides of beryllium, cadmium, magnesium, calcium, and alkaline earth metals and alkali metal hydroxides in the inhibition of diffusion of solutions of hydrochloric, hydrofluoric, and nitric acids in foamed plastics, polyarylate, polypropylene, and other polymers showed that the inhibitory effect depends in a complex manner on the nature of the polymer and the acid as well as on the concentration of the aggressive medium.[108]

The simplest model of the inhibitory effect of protective additives involves two possible mechanisms.[108] A diffusing molecule A binds with additive B in the polymer either reversibly as in

$$A + B \overset{K_e}{\rightleftharpoons} (AB),$$

where K_e is the equilibrium constant, or irreversibly as in

$$A + B \xrightarrow{k_1} (AB),$$

where k_1 is the rate constant of reaction. In both cases the diffusion coefficient (D_0) of molecules A in the initial polymer decreases after introduction of the additive as a result of these reactions, which immobilise a proportion of the diffusing molecules. Specially introduced low-molecular-weight compounds as well as certain functional groups of macromolecules, such as amide and amine groups in a polyamide, can act as additives in relation to diffusing HCl and H_2O molecules.[109]

The calculated curves for distribution of the diffusing component A throughout the coating at the same moment in time with reversible and irreversible binding and in the absence of binding are shown in Fig. 14, while the kinetics of formation of the "free" diffusing component A at the polymer–metal interface are displayed in Fig. 15. In this case the inhibitory effect with irreversible binding is equal to 30, while with reversible binding it is equal to 5.

The calculations demonstrate that under certain conditions the introduction of absorbents into the polymer can slow down the progress of the front of an aggressive medium towards a metal surface by a factor of several tens.

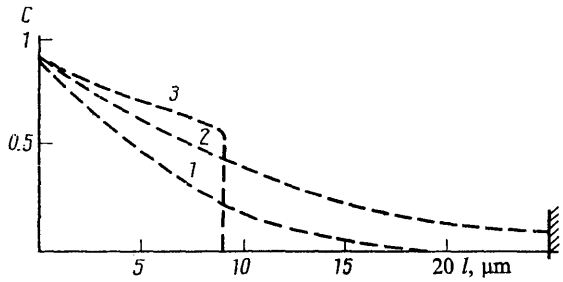


Figure 14. Calculated curves for distribution of the diffusing species throughout the coating 2 min after diffusion has started when $D_0 = 7 \times 10^{-13}$ m^2 s^{-1}:[109] *1*, reversible binding; *2*, absence of binding (no additives); *3*, irreversible binding.

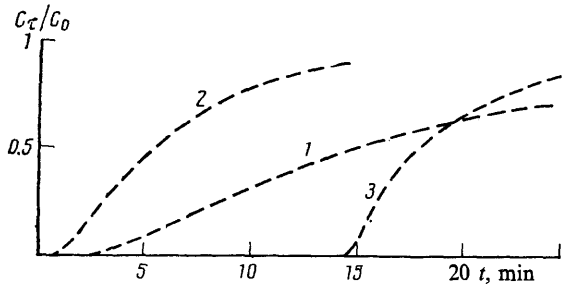


Figure 15. Accumulation of "free" diffusing species at the polymer–metal interface[109] (C_0 is concentration of diffusing species at the interface between coating and medium, C_τ is the continuing concentration of diffusing species at the metal interface: *1*, reversible binding; *2*, absence of binding (no additives); *3*, irreversible binding.

XIV. Predicting the properties of polymer products

The problems of polymer ageing are inseparably linked to a prediction of the change in their properties under real operating conditions.[9–11,89,91] It has been demonstrated in practice that predictions based on exiting rapid test methods frequently give erroneous results, since the mechanisms that are typical of real operating conditons are not reproduced during rapid testing. In order to determine to what extent the effects are equivalent, it is first of all necessary to make a detailed study of ageing mechanisms under natural climatic and artificial conditions.[110–122]

In order to conduct systematic studies on polymer materials for ageing under natural conditions in a warm humid climate, an experimental unit was developed and produced for determination of

molecular mobility, relaxation and phase transitions, viscoelastic properties, and the structure of polymers based on the use of current high-sensitivity methods.[110–122]

The information already collected at this stage can be used to classify the mechanisms of physicochemical reactions of different classes of polymers during atmospheric ageing in a moist subtropical zone. Data are currently being collected on the link between the physicochemical reactions and the change in macroscopic properties of the polymers and on the role of individual climatic factors in the ageing of polymer materials. An interactive information system that is designed for processing the results of kinetic tests and predictions has been developed.[123–126] In order to represent data, the user can select a suitable function from a suggested library of standard models. Unknown parameters are determined by maximum probability based on prior information. Statistical treatment of the results with determination of the accuracy of the parameter estimates and a check of the statistical hypotheses are carried out. Provision is made for planning the experiment, transforming the results using different anamorphisms, and presenting the results in the form of graphs, tables, and storing them. This program forms the basis of the first machine-readable standard in the country.

A method for predicting the photochemical response to a given polychromatic effect on a polymer with an unknown spectroscopic sensitivity has recently been developed.[123,124] The necessary and sufficient conditions for correctness have been determined and an original regularisation method has been developed. The results are presented in the form of a corridor of admissible response values.

The proposed method has already found practical application in solving problems in applied photochemistry, and it can be used to determine much more effectively the photosensitivity of polymer materials being used under real conditions. A package of computer programs has already been developed for putting this method into effect. An investigation of the mechanism of action of classical inhibitors such as phenols and amines is in progress, in order to provide a prediction of their efficiency as stabilisers for polymers.[127,128]

carbonised polyimides (Fig. 16) with a maximum coking value is achieved with a quasi-isothermal heat regime, a statistical inert atmosphere, a relatively high content of nitrogen atoms in the main polyimide chain, and by orientation of the sample.[130]

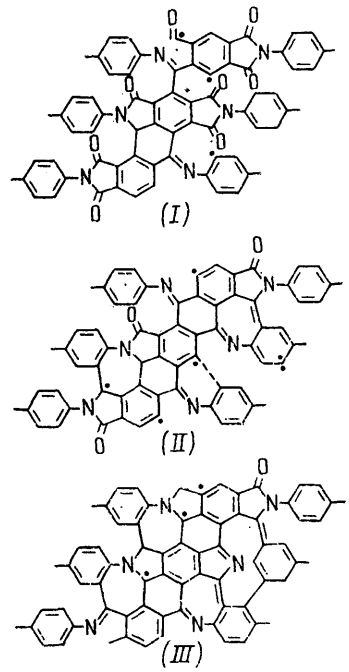


Figure 16. Structural scheme for carbonisation of polypyromellitimide at: *I*, 525; *II*, 575; *III*, 625 °C.[129]

XV. Ageing and stabilisation of heat-resistant polymers

The ageing and stabilisation of heat-resistant polymers can be suitably studied at temperatures above 300 °C, and in a number of cases above 400 °C.[127–139] Polyimides constitute the best known examples of this class of polymers. Two approaches to the stabilisation of heat-resistant polymers have already been examined above in Section V.[26,30,31]

Recently there has been a considerable growth of interest in studying thermochemical reactions that occur at temperatures of 500 °C and above. This is related not only to the problems of thermal and thermooxidative stability of polymers but also to research into their combustion processes, the primary stage of which is pyrolysis of the polymer to gaseous products.[140] At these temperatures thermal degradation is characterised by substantial rearrangement of the whole macromolecular structure (of the polyimide in this case) with the formation of carbonised products that are more or less ordered and mainly consisting of condensed aromatic and heterolytic species.[127,128] One of the aims of these studies is to establish the optimum conditions for obtaining polyimide materials that have a maximum "cooking value" and at the same time acceptable mechanical properties. The preparation of

An effective way of stabilising heat-resistant polymers, in particular polyimides, is to refine their methods of synthesis[131] with the aim of substantially reducing the cyclisation temperature of the prepolymers. This trend, which is not related to classical stabilisation methods,[132] can be used in a number of cases to perfect the structure of the polyimides and improve their thermal stability and other important properties.[133]

The use of polyimides for the heat stabilisation of other so-called large-tonnage polymers should be regarded as having future potential.[134] The use of a polyimide in combination with poly(vinylpyrrolidone), furfuryl alcohol, and epoxy resins results in the formation of composite materials in which the polyimide structure acts as a unique heat-resistant framework, substantially increasing the heat stability of polymer fillers.[135–139] According to thermal analysis data,[134–139] the heat resistance increases by 100–150 °C in the case of poly(vinylpyrrolidone) and by approximately 200 °C for furan and epoxy resins. The second component in turn imparts a number of valuable properties to the polyimide such as thermohydrolytic stability and high-temperature adhesion to metals and graphite materials.

At the present time this is the most promising development in research into ageing processes and in seeking ways to stabilise heat-resistant polymers.

XVI. Conclusion

The ageing of polymers and the stabilisation of polymer materials remains, as before, a vital problem. At the present time the accent of research has shifted from individual polymers to polymer blends and composites.[121] The transition to multicomponent systems complicates the task, since in this case additivity does not usually occur. It was demonstrated back in the 1960s that even in the co-oxidation of two hydrocarbons,[142] each of which is separately oxidised under given conditions, cases are possible where only one compound (R_1H) is oxidised in the mixture, and the other (R_2H) is not oxidised. In essence this occurs because hydrocarbon R_2H is regenerated by R_1H according to Scheme 4.

Scheme 4

$$R_1H + O_2 \longrightarrow R_1^{\cdot} + HO_2^{\cdot}$$
$$R_1^{\cdot} + O_2 \longrightarrow R_1O_2^{\cdot}$$
$$R_1O_2^{\cdot} + R_1H \longrightarrow R_1OOH + R_1^{\cdot}$$

$$R_2H + O_2 \longrightarrow R_2^{\cdot} + HO_2^{\cdot}$$
$$R_2^{\cdot} + R_1H \longrightarrow R_2H + R_1^{\cdot}$$
$$R_2^{\cdot} + O_2 - \times \longrightarrow$$

Investigations are continuing into the specific nature of the polymer state with regard to the reactivity of interacting species in the polymer matrix[143,144] and the mobility of molecular chains and low-molecular-weight compounds in polymers under different conditions. Particular attention is being given to the effect of structural relaxation of vitreous polymers on the kinetics of chemical reactions. A model that has been proposed[143,144] can be used to represent qualitatively the majority of known kinetic effects of structural relaxation of vitreous polymers.

There is no doubt that studies to establish cases of synergism and antagonism in the stabilisation of polymers in the presence of several stabilisers and other chemical additives will be continued. Multifunctional stabilisers that contain a number of functional groups in the same molecule, acting by different mechanisms and thus creating a synergistic effect, are of increasing interest. The application of polymeric stabilisers for the stabilisation of polymers operating at high temperatures is expanding. At high temperatures they are quite mobile (and therefore effective), while at the same time they are not washed out and do not bleed like low-molecular-weight stabilisers. The development of new, more sensitive methods has been proposed[145] for studying polymer degradation processes that would allow the conditions of testing to approximate to real operating conditions and hence markedly increase the accuracy of predicting the lifetime of reliable operation and preservation of polymer products.

Degradation processes are starting to be used more extensively for the modification of polymer products in order to improve their properties.

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Translated from *Usepkhi Khimii* **60** 2250–2280 (1991) U.D.C. 577.152:547.466

Enzymic methods of resolving racemates of amino acids and their derivatives

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ABSTRACT. The review is devoted to modern methods of resolving racemates of amino acids and their derivtives by the action of enzymes. Processes of enantioselective enzymic hydrolysis are considered for both *C*- (esters, amides, amino acid nitriles) and *N*-derivatives (acyl- and alkoxycarbonylamino acids) and also for their cyclic derivatives. Examples are given of the catalytic preparation of optically active derivatives from racemic amino acids.

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I. Introduction

Optically active amino acids are used widely in various branches of the national economy, including agriculture (food additives, herbicides), the food industry (sweeteners, aroma-producing agents, products for dietary foods), and medicine (infusion solutions, therapeutic agents). The precipitate growth of the industrial manufacture of optically active amino acids is linked primarily with the discovery of new opportunities for their use. For example, the introduction into manufacture of the artificial sweetening agent aspartame has caused a multiple increase in the volume of manufacture of L-phenylalanine and L-aspartic acid in the last five years (Table 1).[1]

Table 1. Manufacture of L-phenylalanine and L-aspartic acid.[1]

Year	Amino acid	Main area of use	Total cost (millions of dollars)
1979	*L*-Phe	Infusion solutions	7.4
1984	*L*-Phe	Aspartame	~100.0
1979	*L*-Asp	Therapy, aroma-producing agents	1.2
1984	*L*-Asp	Aspartame	~15.0

The improvement of methods of obtaining amino acids using new achievements in biotechnology has enabled a significant reduction in the cost of optically active amino acids which, in its turn, has opened up possibilities for using them in new areas and has significantly extended market salts. The manufacture of lysine is a graphic example of the effect of such technology on the price and volume of manufacture of this amino acid (Table 2).[1]

Table 2. Manufacture of L-lysine.

Year	Manufacturing efficiency (arbitrary units)	Mean cost (dollars pound^{-1})	World production (millions of pounds)	Total cost (millions of dollars)
1956	1	23.7	0.2	5
1969	4	4.45	7.0	31
1980	8	2.10	90.0	189

As a rule chemical synthesis of amino acids leads to a racemic product, the preparation of enantiomers requires an optical resolution step. Existing methods of resolving racemates of amino acids may be divided into three main groups, 1) physicochemical methods, 2) chemical and 3) biotechnological (with the participation of enzymes or cells of microorganisms). Physicochemical methods include mechanical separation, selective crystallisation and chromatographic separation. Chemical separation of a racemic amino acid or a derivative is effected with a chiral compound and one of the diastereomers is removed by crystallisation, chromatography, etc.

The first two methods are suitable for solving analytical problems and for the large scale separation of a limited number of amino acids (for example L-glutamic acid using selective crystallisation), but they are not suitable for the industrial preparation of a large selection of optically active amino acids.

The most widespread methods of obtaining enantiomeric amino acids at the present time are those using enzymes or microbial cells. Work published before 1982 is not considered in the present review, this was included in the review by Shvyadas and Galaev.[2] A high reaction rate and stereospecificity are the features of enzymic reactions. The significant acceleration of the reaction when using enzymes may be demonstrated by the following example. The rate

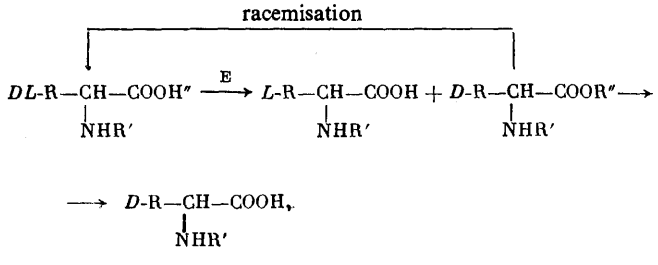
constant for the non-enzymic hydrolysis of urea is 4.15×10^{-5} sec^{-1} at 100 °C while the rate constant for the reaction catalysed by urease is 3×10^{4} sec^{-1} at 20 °C. Another no less important feature of enzymes is their specificity in reaction and in substrate. The specificity may be absolute or almost absolute since some enzymes act on molecules of only one substrate while others act on molecules with marked differences in structure, such as on a whole class of compounds. As a rule enzymes display high reaction specificity but some of them are capable of catalysing 'foreign' reactions. For example the majority of hydrolases catalyse reactions typical of transferases. In addition some groups of enzymes catalyse different types of reaction, i.e. they display a multicatalytic function. In the majority of cases enzymes 'correctly' demonstrate absolute stereospecificity in catalysis when they act on part of a molecule linked with a chiral centre in the substrate or form chiral products from achiral substrates. Racemases and isomerases are exceptions in this respect. Even enzymes possessing wide specificity in relation to substrate structure may display absolute stereospecificity. For example D-amino acid oxidases (EC 1.4.3.3.) catalyse the oxidation of a wide range of primary and secondary D-amino acids while not affecting L-amino acids. L-Amino acid oxidases (EC 1.4.3.2.) act in a similar manner. Stereospecificity is not an obligatory property of enzymes acting on groups distant from a chiral centre in a substrate. Carboxyesterase (EC 3.1.1.1.) catalyses the hydrolysis of the ethyl esters of L- and D-tyrosine at the same rate. On the whole stereospecificity, which is natural for enzymes, is difficult to achieve by chemical means in spite of the fact that asymmetric synthesis has developed significantly in recent years.

By virtue of these factors the enzymic methods of obtaining optically active amino acids have been at the centre of attention of investigators for several decades. They may be divided into two groups, 1) enantioselective enzymic hydrolysis of amino acid derivatives and 2) the enantioselective enzymic derivatisation of amino acids and their derivatives.

II. Enantioselective enzymic hydrolysis of amino acid derivatives

1. Esters of amino acids

The enantioselective enzymic fission of esters as a method of obtaining optically active amino acids was already known at the beginning of the century.[3]



E – enzyme.

The reaction products are the L-amino acid and the ester of the D-isomer which is subjected to non-enzymic hydrolysis of racemisation for subsequent reintroduction into the process for resolving the racemate. Many enzymes of animal and microbial origin are known which possess esterase activity. The best studied of them is α-chymotrypsin, distinguished by high activity and enantioselectivity of action primarily in relation to specific substrate, viz. esters of aromatic *N*-acylamino acids. Its high cost and non-availability in large quantities hinders the application of this enzyme for the separation of racemates in practice. Immobilisation of the enzyme enables the cost of the biocatalyst to be reduced. At the present time the investigation of the chymotryptic hydrolysis of specific substrates is directed mainly towards the development of continuous processes for obtaining optically active amino acids.[4,5] *N*-Acetyl-L-phenylalanine is obtained from its racemic methyl esters in a membrane-reactor (capacity 1.3 $kg\ m^{-2}\ d^{-1}$).[4]

Another way to reduce the cost of biocatalyst is to use cheaper enzymes such as proteases of microbial origin or whole cells. Glaenzer and collaborators[6,7] studied the use of bakers' yeast *Saccharomyces cervisiae* for the enantioselective hydrolysis of raemic *N*-acetylaminoacid esters. It was known previously[4] that the cells of *S. cerevisiae* possess oxido-reductase activity. They catalyse the enantiospecific reduction of ketones, but there are very few data on their hydrolytic activity. It turned out that they are capable of hydrolysing esters of *N*-acetylamino acids with an unbranched chain with a high degree of enantioselectivity (Table 3).

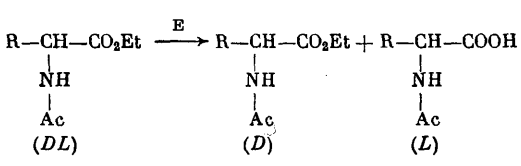


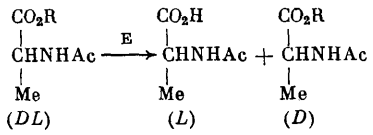
Table 3. Enantioselective anaerobic hydrolysis of *n*-acetylamino acid esters [DL-AcNHCH(R)COOEt] by cells of *Saccharomyces cerevisiae*.

Substrate No.	R	Yield of D-AA ester, %	Enantiomeric excess, %	Substrate No.	R	Yield of D-AA ester, %	Enantiomeric excess, %
1	Me	47	100	4	CH_2CHMe_2	48	92
2	Et	48	96	5	CH_2Ph	38	97
3	iso-Pr	75	13	6	CH_2CO_2Et	49	86
3	iso-Pr	38	80 *	7	$CH_2CH_2CO_2Et$	46	89

* Aerobic hydrolysis.

Substituents in the β-position inhibit the reaction (Table 3, substrate 3), γ-substituents do not show this negative effect (Table 3, substrate 4). Hydrolysis does not occur in the case of substrates with an *N*-acetylamino group in the β-position. When two chemically different ester groups are present (Table 3, substrates 6 and 7) reaction occurs only at the α-ester group, not affecting the ω-group of esters of *N*-acetyl-L-aspartic and -glutamic acids. The hydrolytic action of α-chymotrypsin has similar characteristics.

Changes in the ester component do not as a rule display a significant effect on the course of the hydrolysis of *N*-acetylalanine ester.



R is methyl, ethyl n-propyl, iso-propyl, n-butyl, n-octyl, benzyl, cyclohexyl, t-butyl.

The t-butyl ester is not hydrolysed, the methyl ester is hydrolysed somewhat more slowly than the remaining esters of primary and secondary alcohols, the rates of fission of which are approximately the same and the enantiomeric excess is at least 96%.

Since the esterase actions of *S. cerevisiae* cells and of α-chymotrypsin have much in common it has been suggested that proteinases are the main active principle. To confirm this the hydrolysis of substrate 1 was catalysed by mutant strain ABYS1 of the yeast, which is characterised by a lack of non-specific proteases and carboxypeptidases, and also by the wild strain X-2180-Ia (Table 4).

Table 4. Enzymic hydrolysis of *N*-acetyl-DL-alanine ethyl ester.

Reaction time, h	*S. cerevisiae*		Wild strain X-2180-1 A		Mutant strain ABYS1	
	Enantiomeric excess, %	Yield of D-ester, %	Enantiomeric excess,%	Yield of D-ester, %	Enantiomeric excess, %	Yield of D-ester,%
24	92	not determined	89	52	1	95
48	100	47	100	43	2	81

In many cases the use of enzymes and microbial cells for the fission of racemic esters is limited by the low water solubility of the substrates. The use of two-phase systems of 'water–immiscible organic solvent' is not always possible. For example, on adding chloroform or ethyl acetate to the aqueous system containing the enzyme and substrate, the hydrolysis of esters of *N*-acetylamino acids (alanine, phenylalanine, phenylglycine) is not observed.[8] This is evidently linked with a shift in the direction of ester synthesis in the 'hydrolysis–synthesis' equilibrium of the given system. To solve this problem Fadnavis and collaborators[8] have proposed carrying out the enzymic hydrolysis of esters in reverse micelles. The authors considered that cells of microorganisms, possessing enzymic activity, may in principle be considered as a system containing an enzyme immobilised by inclusion in or addition to the cell wall. To confirm this hypothesis the hydrolysis of esters of *N*-acetylamino acids has been carried out with cells of *S. cerevisiae* crosslinked with glutaraldehyde in an aqueous medium and in reverse micelles [organic phase was chloroform–isooctane (1 : 9 by volume), the detergent being bis(2-ethylhexyl)sulphosuccinate, sodium salt] (Table 5).

Table 5. Hydrolysis of *N*-acetyl-DL-amino acid methyl esters of bakers' yeast in aqueous medium and in reverse micelles.

No	Substrate*	Product**	Reaction time, h		Yield, %		Enantiomeric excess, %	
			water	reverse micelles	water	reverse micelles	water	reverse micelles
1	Phg	1*a*	72	48	64	60	96	98
		1b	72	48	60	46	>99	>99
2	Phe	2*a*	48	24	57	53	98	98
		2b	48	24	56	48	99	99
3	Ala	3*a*	60	32	72	65	97	96
		3b	60	32	52	40	>99	>99

* *N*-Ac-DL-AA methyl ester.
** a, *N*-Ac-L-AA, b, *N*-Ac-D-AA.

Table 6. Hydrolysis of *N*-Z-amino acid esters [Z-NH-CH(R)CO_2R'] by lipase.

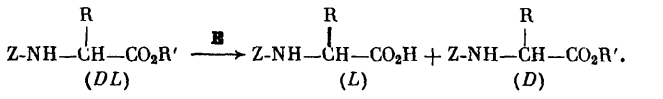
No.	R	R′=CH_2CH_2Cl						R′=CH_2CF_3	
		A. niger		*P. fluorescens*		*C. cylindracea*		PP	
		A	B	A	B	A	B	A	B
1	Methyl	36	89	46	16	38	7	39	21
2	Ethyl	40	96	49	52	36	7	40	97
3	n-Propyl	27	86	43	58	–	–	39	98
4	n-Butyl	32	85	52	60	42	30	38	92
5	n-Pentyl	44	95	25	80	47	66	40	87
6	n-Hexyl	31	94	47	87	–	–	33	61
7	iso-Propyl	14	92	8	53	–	–	Not a substrate	
8	$Ch_2=CHCH_2$	34	86	40	52	31	27	38	93
9	Benzyl	32	94	12	57	35	63	40	>99
10		37	94	40	70	35	43	44	89

Note. A is the extent of conversion, %; B the excess of L-enantiomer, %.

No enzymic hydrolysis of the D-enantiomer was observed, spontaneous hydrolysis in the reverse micelles was less than 1.5% in 72 h (less than in aqueous medium). The advantages of using reverse micelles are evident in the case of substrates with low solubility, such as in the hydrolysis of 5 g substrate 1 (Table 5) in 200 ml in 72 h. The enantiomeric excess of unreacted D ester was 30% in aqueous medium and 75% in the reverse micelle medium.

The search for enzymes capable of hydrolysing esters of racemic amino acids led to the discovery of the esterase activity of lipases.[9,10] It is known from the literature that lipases are capable of the fission

of esters of racemic alcohols and carboxylic acids, they are also readily available, inexpensive and stable. Investigation of the hydrolysis of the substrate *N*-Z-α-amino-DL-heptanoic acid ester with lipase from six microorganisms showed that the best results were obtained with the lipase from *Aspergillus niger* and satisfactory results with the lipase from *P. fluorescens* and *C. cylindracea*. Using these three enzymes and a porcine pancreas lipase (PPL) the ester hydrolysis has been effected for a series of natural and synthetic acids (Table 6).



In the general case the enantioselectivity of lipase action decreases in the series PPL ≈ *A. niger* lipase > *P. fluorescencs* lipase > *C. cylindracea* lipase. Three types of unnatural amino acids: 1) with unbranched hydrocarbon chain (Table 6, substrates 2–6), 2) with an unsaturated bond (Table 6, No. 8) and 3) with a heteroaromatic ring (Table 6, No. 10) in the side chain R were separated with high values of the enantiomeric excess (85–95%) by lipases from *A. niger* and from pancreas (except for substrate 6) although the reactions were not optimised. The good result was particularly important in the case of substrate 10 (Table 6) since other enzymic processes (such as the use of acylase I) do not lead to resolution of the racemate of this heteroaromatic amino acid.

It is known that transferring from esters of amino acids with an *N*-acylamino group to esters of amino acids with a free amino group leads to a reduction in the enantioselectivity of enzymic hydrolysis.[11] However in many cases the selectivity is sufficiently large and it is possible to separate enantiomeric amino acids with a free amino group by enzymic enantioselective hydrolysis of their esters. One of the most widely used biocatalysts for this purpose is α-chymotrypsin. Investigations of recent years in this direction may be separated into two main groups. The first group contains work on the development of efficient continuous processes using immobilised α-chymotrypsin.[12,13] The cost of the process may be reduced by racemising the D-isomer and subsequently reintroducing it into the separation process.[14] Such processes may be effected in two-phase 'water–immiscible organic solvent' systems.[15,16]

The second group comprises work devoted to the chymotryptic fission of racemic amino acids containing substituents in the side chain R[17] or at the α-carbon atom.[18] The methyl (or ethyl) esters of *ortho*-(*meta*-, *para*-)fluoro-DL-phenylalanine may be separated into enantiomers in high yield and enantiomeric purity.[17]

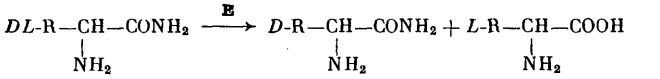
It is known that the introduction of an α-substituent significantly reduces the rate of enzymic hydrolysis. For example, on introducing an α-methyl group into the *N*-acetyltyrosinamide molecule the hydrolysis rate is reduced 10^5 times which is seemingly linked with the incorrect orientation of the bond being hydrolysed.[19] The effect is less significant for amino acid esters. However there is a need for optically active α-aminoacids. They are used in investigations of the link between structure and activity in peptide hormones, conseqently the enzymic separation of their racemic derivatives is of significant interest. The resolution of the methyl esters of α-methyl-DL-amino acids (tryptophan, phenylalanine and *para*-fluorophenylalanine) has been effected (37 °C, pH 5.0, time 30–40 h).[18]

The high enantioselectivity of enzyme action enables the preparation of L-isomers in good yield (33–36%) and optical purity (96% for α-methyl-L-tryptophan). Contamination by the isomer was attributed to spontaneous non-enzymic hydrolysis since no hydrolysis of D-esters by chymotrypsin was observed.

The use of enzymes (or enzyme complexes) from microorganisms or whole cells is an alternative to the use of expensive enzymes of animal origin for esters of amino acids with a free amino group as for esters of *N*-acylamino acids. The fission of the methyl esters of DL-phenylalanine and DL-tyrosine and the benzyl ester of DL-alanine has been effected on a preparative scale (25 g).[20] The scope for ester hydrolysis by the alkaline protease from *Bacillus licheniformis*, the main component of which is subtilisin A (Carlsberg subtilisin), was investigated. The enzyme is stable and active at room and higher temperatures (the half-live for inactivation at 60 °C is about 5 h) and over a wide pH range (6–12). The enantioselective hydrolysis of a racemate leads to the preparation of the product in high yield (L-phenylalanine 48%, D-phenylalanine methyl ester 42.5%) and enantiomeric purity (L-enantiomer 90%, D-enantiomer 100%). Subtilisin 8350, obtained by replacing six amino acids in the protein chain of subtilisin BPN′ from *Bacillus amiloliquefaciens*, has been used for the separation of the esters of several amino acids with a free amino group and also of *N*-acylamino acids.[21] The modified enzyme proved to be 50 times more stable than the initial enzyme in water and 100 times more stable in anhydrous dimethylformamide. Practically 50% conversion was achieved in the resolution of racemic esters. The yields of product and unreacted substrate were more than 40% and the enantiomeric excess was more than 91% (the initial enzyme possessed low selctivity).

2. Amino acid amides

In the general case the enantioselective enzymic hydrolysis of amino acid amides proceeds by the scheme.



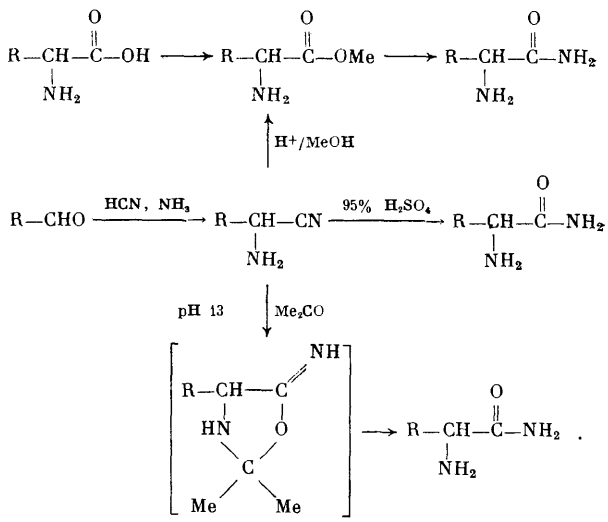
Enzymes possessing amidase activity are encountered in many microorganisms. Both purified enzymes and their complexes[22] and whole cells[23–25] may be used for the resolution of racemates. The possibility of using the proteolytic complex pronase from *Streptomyces griseus*, containing serine proteases and aminopeptidases, for the separation into enantiomers of the racemic amides of leucine, phenylalanine and tryptophan has been studied.[22] The hydrolysis of amino acid amides catalysed by pronase is characterised by high values of the rate, enantioselectivity and degree of conversion of the L substrate. DL-Leucine amide may also be separated into antipodes in 50% yield by whole cells of *Enterobacter cloacae*, *Pseudomonoas sp.* etc.[23] The L-aminopeptidase from *Pseudomonas putida* enabled separation of Met and Phg amides into optical antipodes.[24] Enzymes are encountered possessing an enantioselective action in relation to a D substrate.[26–28] DL-Valine amide may be separated into antipodes using either cells of *Pseudomonas rasea*, which hydrolyse L-amino acid amides (yield of L-valine was 50%, 40 °C, time 5 h),[25] or cells of *Rhodococcus erythropolis*, which hydrolyse D-amino acid amides (yield of D-valine 38–47%, 40 °C, time 2 h).[27] The D-amidase from a strain of *Ochrobactrum anthropi*, isolated from soil, has been partially purified and characterised.[28] Data on substrate specificity are given in Table 7. In addition the rates of hydrolysis for L-substrates (with the exception of norvaline and norleucine) have been determined and were less than 0.1% of the hydrolysis rate of the D-enantiomer.

Among the few studies devoted to the enzymic separation of amino acid amides some[29–33] occupy a special place. Regarding the industrial enzymic separation of amino acids to be promising and fully competitive with asymmetric synthesis and chemical separation, the authors have carefuly developed all the stages of obtaining optically active amino acids from racemic amides, beginning with the preparation of the starting materials. It is known that amides may be obtained from amino acids through the corresponding esters. It is probably more expedient to use as starting materials the α-aminonitriles which are intermediates in the synthesis of amino acids from aldehydes by the Strecker reaction. The conversion of α-aminonitriles into the corresponding amides may be effected by various routes. A promising method[29] has been proposed which is a one-stage conversion of an aminonitrile into the amide through an intermediate oxazolidine in alkaline medium in the presence of catalytic quantities of acetone (yield of product was over 90%).

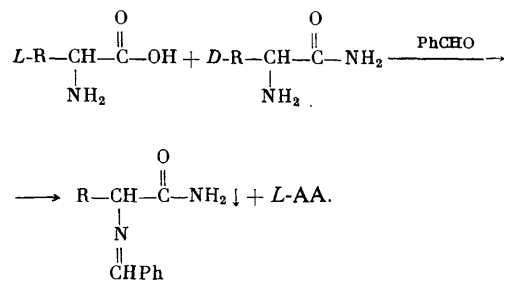
Table 7. Amidase activity of the enzyme from *Ochrobactrum anthropi.*

Substrate D-AA amide	V_{rel}*, %	Substrate D-AA amide	V_{rel}*, %	Substrate D-AA amide	V_{rel}*, %
Phe	100	Norleu	40	Phg	15
Tyr	97	Ala	33	Pro	9.7
Trp	96	Met	28	Lys	2.5
Leu	46	Norval	15	His	1,5

* V_{rel} is hydrolysis rate.



Many microorganisms are known which produce aminopeptidases (such as *Aspergillus* etc.). However, their use for separating amino acid amides, in the authors' opinion, is limited by low activity, narrow substrate specificity and undesirable side effects. A search carried out showed that the enzyme preparation of aminopeptides from *Pseudomonas putida* possessed the best characteristics. The high (almost 100%) enantioselectivity was combined with a very broad substrate specificity. The relative activity varied from 20% (L-phenylalanine amide) to 100% (D-phenylglycine amide), substrate concentration may be as high as 20% without affecting the activity of the enzyme. A considerable virtue is that the reaction may be conducted over a wide pH range. Traditional methods such as ion exchange chromatography or extraction are used for the separation of the L-amino acid and the D-amino acid amide. In those cases when the D-amino acid is required the authors suggest using one of the other methods developed by them. The first consists of the use of biocatalysts possessing no enantioselective action. Such a biocatalyst was found which was an enzyme with amidase activity towards L and D substrates from cell preparations of *Rhodococcus erythropolis.* The yields of the D-amino acids obtained by this method were very high in comparison with the usual chemical hydrolysis. Another method is based on the formation of a Schiff's base, from benzaldehyde and the D-amino acid amide, which is practically insoluble in water (and therefore readily isolable).



Acid hydrolysis at temperatures below 100 °C of the compound obtained give the D-amino acid without racemisation. The D- and L-amino acids obtained in this way possess high optical purity (99% and more).

In those cases when the D-enantiomer is not widely used it is expedient to subject the D-substrate to racemisation for subsequent reintroduction into the separation process. For this purpose a racemisation process was developed for the Schiff's base, i.e. for an *N*-(or un)substituted benzilidene-amino acid amide, in aqueous organic medium in the presence of base.[31] The racemate of the Schiff's base obtained was hydrolysed to the DL-amino acid amide which was subjected to enantioselective hydrolysis by an enzyme from *Pseudomonas putida.* The method[29–32] developed has enabled separation of racemates of phenylglycine, *p*-hydroxyphenylglycine, valine, phenylalanine, tryptophan, methionine, lysine, thienylglycine and their derivatives. The structural elements for the amino acids required for the development of the enzymic activity from *Pseudomonas putida* are an unsubstituted amino group and an α-hydrogen atom. Since α-alkylated amino acids are of significant scientific and commercial interest a new biocatalyst has been developed from *Mucobacterium neoarum* which possesses amidase activity towards α-alkylated amino acids.[33] The enantiomers of α-methylvaline, -leucine, -phenylalanine, -4-methoxyphenylalanine and α-ethylphenylalanine have been separated in high yield and enantiomeric purity (for example, the yield of α-methyl-L-leucine was 49.5% and of α-methyl-D-leucine amide 48.7%).

3. Amino acid nitriles

It is known that many strains of microorganisms such as *Corynebacterium sp., Nocardia rhodochrous, Pseudomonoas sp., Pencillium sp., Escherichia coli* and several others are capable of catalysing the hydrolysis of nitriles to the corresponding amides or acids and because of the variety of microorganisms the substrate spectrum is extremely broad. This comprises aliphatic and aromatic nitriles, α-hydroxy and α-aminonitriles.[34,35]

Many strains have been investigated[36] and among them was *Brevibacterium sp.* R312 which hydrolyses practically every water soluble nitrile to the corresponding acid but the reaction does not occur enantioselectively. The selection of strain R312 was effected in a medium containing fluoroacetamide, which is toxic for it, since hydrolysis to fluoroacetic acid occurs by the action of the non-specific amidase. Screening enabled selection of several mutants not carrying out this reaction and one of them A_4 was chosen for subsequent investigations. The spectrum of nitrilase activity of A_4 and R312 proved to be absolutely identical which confirmed the hypothesis that the enzyme system causing the hydrolysis of nitriles comprises two enzymes, a nitrilase and an amidase. Investigation of the amidase activity of whole cells and cell extracts showed that R312 hydrolyses practically all amides investigated with the exception of acrylamide, methacrylamide, L- and D-asparagine and D-glutamine, though the latter is hydrolysed by cell extracts. The amidase activity of A_4 is appreciably less. It hydrolyses only formamide, urea, nicotinamide, L-glutamine and amides of α-amino acids, although on hydrolysis of amides of DL-amino acids the yield did not exceed 50% and the hydrolysis product was the L-amino acid.

Additional investigations confirmed the enantioselectivity of the action of the enzyme. D-Aminopropionamide is not a substrate but the D-enantiomer is converted quantitatively into L-alanine. The use of strain A_4 enabled separation of the racemate of α-amino-γ-methylthiobutyronitrile quantitatively in 2–3 h. The hydrolysis products are L-methionine and D-methionine amide, the latter may be subjected to racemisation or hydrolysis to the D-amino acid by strain R312. Similar processes enabled the preparation of L-alanine, L-α-aminobutyric acid, L-phenylalanine, L-valine and L-leucine.

In the process of separating racemic aminonitriles with a strain of *Pseudomonas MY-1*[37] it was evident that two enzymes were participating, a DL-aminonitrilase and an enantioselective amidase. Separation of the enantiomers of DL-phenylglycine nitrile to the L-amino acid and the D-amino acid amide occurs quantitatively in 0.5 h at 15 °C. Optically active L-Phe may be obtained from the whole mass of racemic derivative as a result of a combined process in which hydrolysis of the DL-aminonitrile occurs to the DL-amino acid amide under the action of cells of *Acinetobacter calcoaceticus* with subsequent hydrolysis of the amino acid amide and racemisation of the D-phenylalanine amide by cells of *Arthrobacter* ATCC 31652.[38]

There are however data indicating that the participation of enantioselective amidases in the hydrolysis process is not the sole route for the resolution of racemic nitriles. It has been shown[39] that optically active amino acids and their amides (such as L-leucine amide) may be obtained from racemic nitriles by the enantioselective action of a nitrilase (strain 311).

4. Acylamino acids

The enantioselective hydrolysis of *N*-acylamino acids by acylase is the most widespread method for the large scale separation of enantiomers of amino acids.

$$\underset{\substack{|\\ \text{NHCOR}'\\ (DL)}}{\text{R—CH—COOH}} \xrightarrow{\text{E}} \underset{\substack{|\\ \text{NH}_2\\ (L)}}{\text{R—CH—COOH}} + \underset{\substack{|\\ \text{NHCOR}'\\ (D)}}{\text{R—CH—COOH}}.$$

The industrial development of this method, including the process of racemising the D-enantiomer for subsequent reintroduction into the separation process, was effected in the fifties and sixties by Tanabe Seijaku Co. Ltd.

At the end of the sixties a fermentor was built containing acylase immobilised by ionic binding to DEAE-Sephadex for the continuous production of amino acids. This was the first industrial application of immobilised enzymes. Since 1969 several types of fermentors have been developed for obtaining L-methionine, L-valine, L-phenylalanine and other amino acids from their racemic *N*-acyl derivatives.[40,41]

Enzymes possessing acylase activity are isolated from animal, plant and microbial sources. The most studied acylase of animal origin is the enzyme from porcine kidney, viz. acylase I, which is specific for aliphatic amino acids.

Acylases from animals belonging to four classes have been investigated.[42] These are fish (silver carp), amphibians (frog), birds (pigeon) and mammals (mouse, rat, cat, dog, cow, pig) in addition to human acylase. Freshly prepared kidney homogenates served as the enzyme source. Substrates used are the *N*-acetyl derivatives of DL-amino acids (norvaline, norleucine, valine, leucine, glutamic acid, phenylalanine and tryptophan) and *N*-chloroacetyl-DL-phenylalanine and *N*-formyl-DL-methionine. The character of the substrate specificity proved to be similar for the majority of animals. The maximum rate was displayed in the hydrolysis of *N*-formyl-methionine. The specific activity of the enzymes varied more than 16 times (from 4.2 for frog to 65.5 μmole min^{-1} mg $protein^{-1}$ for cow) so assessment of substrate specificity was carried out in relative units (for *N*-formylmethionine V_{max} = 100%). The rate of hydrolysis for the unnatural amino acid *N*-acetylnorleucine was 30–49%. Comparison of the hydrolysis rates of amino acids with branched and unbranched side chains (leucine, valine and norleucine, norvaline) showed that the latter were more suitable substrates (the difference in rate was 1.2–4.0 times). The *N*-acetyl derivatives of aromatic and dicarboxylic amino acids were poor substrates ($0.5\% \leqslant V_{rel} \leqslant 10\%$). As might have been expected replacement of the acetyl group by chloroacetyl leads to a 2–3-fold increase in rate. The substrate specificities of porcine acylase (PA) and human acylase (HA) differed somewhat. The maximum hydrolysis rate was observed for *N*-acetylnorleucine (V_{rel} = 208% for PA, 124% for HA), *N*-acetylnorvaline was in the second place (181% for PA, 110% for HA) and *N*-formylmethionine in third place (100%). The remaining substrates behaved in a similar manner with the other acylases. The data obtained are in good agreement with the previously proposed structure for the active centre as a narrow hydrophobic cleft of length five methylene units,[43] and suggest that the original and main role of the enzyme is the hydrolysis of *N*-formylmethionine.

Enzymes possessing acylase activity are encountered in many microorganisms.[2] They are inexpensive, available in large quantities and are used widely for the resolution of racemates of acylamino acids.[44–53] Up to the present time development has been conducted

on the application of free enzymes and microbial cells,[44–47] however the advantage of using immobilised enzymes was demonstrated indisputably even in the late sixties (the efficiency of using an immobilised enzyme for three months was more than 10 times greater than for the free enzyme).[54] The various methods of immobilising aminoacylases have been discussed.[55] The substrate specificity of microbial acylases is appreciably broader than that of acylase I. Substrates were not only the aliphatic amino acids but also derivatives of aromatic and dicarboxylic acids.[2] An investigation has been carried out of specificity in relation to the acyl group of phenylalanine for fungal acylase (for which aromatic amino acids are good substrates) and for acylase I.[56] The relative rate was studied at the pH optimum determined for each acyl group for fungal acylase (pH 6–7.5) and at pH 7 for acylase I. The hydrolysis rate fell in the series formyl > chloroacetyl > acetyl > propanoyl > butanoyl > pentanoyl > hexanoyl > ethyloxycarbonyl ⩾ benzyloxycarbonyl (Z) [t-butyloxycarbonyl (Boc) ≈ 0] on catalysis with fungal acylase and in the series butanoyl > chloroacetyl > propanoyl > pentanoyl > acetyl > hexanoyl > formyl > ethoxycarbonyl ⩾ benzyloxycarbonyl (t-butyloxycarbonyl ≈ 0) on catalysis with acylase I. Derivatives of the urethane type were significantly less reactive than the usual acyl derivatives, neither t-butyloxy nor benzyloxycarbonyl derivatives were subject to hydrolysis in practice. The correlation between the chain length of the hydrocarbon fragment of the acyl group [$H-(CH_2)_n-C(O)$, n = 0 to 5] and the relative rate of hydrolysis is shown in Fig. 1. The hydrolysis of N^{α}-formyl-N^{ε}-t-butyloxycarbonyl-DL-ornithine was effected by acylase (yield of L-amino acid was 48.5%, of D-amino acid derivative 44%) which confirms the suitability of the formyl group for practical separations.

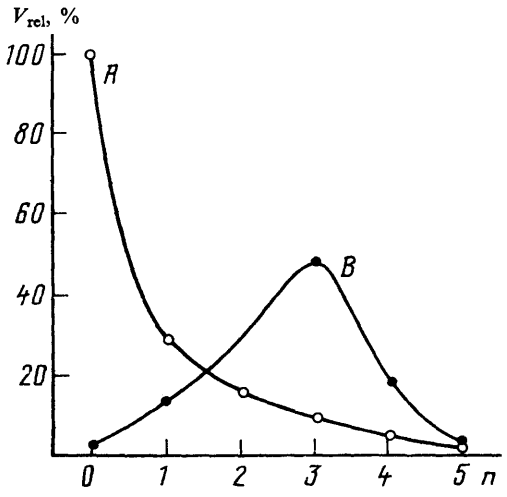


Figure 1. Dependence of the relative hydrolysis rate of *N*-acylphenylalanine by *A*, fungal acylase and *B*, acylase I on the number of methylene units (*n*) in the acyl group.

The kinetics of the enantioselective hydrolysis of *N*-acetyl-DL-amino acids (methionine, leucine, alanine, valine, serine, tryptophan, phenylalanine and phenylglycine) by acylase from *Aspergillus oryzae*, free and immobilised on DEAE-Filtradex R50, have been investigated.[57,58]

With the aim of broadening the application of acylase for obtaining optically active amino acids a search for new enzymes possessing acylase activity has been carried out[59,60] as has a clarification of such activity for enzymes of other classes.[61,62] The acylase from *Comamonas testosteroni* specific for acyl-L-proline was discovered in this way.[59] The high enantioselectivity enables resolution of *N*-acetyl-DL-proline into enantiomers. Replacement of the acetyl group by chloroacetyl accelerates the rate of hydrolysis of the *N*-derivatives of L-proline 3.6-fold. No reaction took place in the case of the benzoyloxycarbonyl and t-butyloxycarbonyl derivatives, the activity in relation to the derivative of other amino acids was one to two orders of magnitude less than for *N*-acetyl-L-proline. An acylase from *Bacillus thermoglucosidius* has been investigated.[60] The enzyme is specific for aliphatic amino acids (V_{rel} = 100% for *N*-acetyl-L-methionine), the hydrolysis rate for aromatic amino acids was approximately one order of magnitude less.

The majority of *N*-acetyl derivatives of acidic and basic L-amino acid and the *N*-acetyl-D-amino acids investigated (methionine, leucine, valine) were inert to the action of this enzyme (V_{rel} < 1%). Replacement of the acetyl group by chloroacetyl leads to an increase in rate V_{rel} of approximately 10-fold. The benzoyloxycarbonyl and t-butyloxycarbonyl derivatives were inert. The enzyme investigated has much in common with acylase I and with the acylase from *Asp. oryzae*. They all contain Zn^{2+}, are activated by Co^{2+} ions, have pH optima 8.0–8.5 and have similar amino acid compositions. However the activity of the acylase from *Bacillus thermoglucosidius* was approximately two orders of magnitude greater with the *N*-chloroacetyl derivative of DL-alanine and DL-norleucine. In addition the enzyme is distinguished by a high stability under extreme conditions. On heating to 70 °C for 10 min its activity was fully preserved, to 80 °C 90% was retained. It was stable to organic solvents (ethanol up to 50%, isopropanol up to 30%). The activity (80%) was retained in the presence of 5% sodium dodecyl sulphate and 85% in 8 M urea at 37 °C for 30 min. These special features of the acylase from *B. thermoglucosidius* suggest it may have promise in the preparation of optically active amino acids.

The same authors detected acylase activity towards acylamino acids in the purified dipeptidase from *B. stearothermophilus* which was 3–30% of its activity in the hydrolysis of dipeptides.[61] However this enzyme displayed higher specificity towards aromatic amino acids (V_{rel} = 100% for *N*-acetyl-L-methionine, 110% for *N*-acetyl-L-tyrosine and 160% for *N*-acetyl-L-phenylalanine). As in the previous case replacement of the acetyl group by chloroacetyl leads to an increase in V_{rel} of at least 10-fold. The ability of polymixin acylase to hydrolyse *N*-acyl derivatives of amino acids, although with low enantioselectivity has been shown.[62] Of all the acyl groups investigated containing from 2 to 16 carbon atoms the decanoyl (C_{10}) derivatives were most readily subject to hydrolysis. It must also be mentioned that when preparing the enzyme under specific conditions it is able to remove a Z protecting group (although with a low rate).

D-Amino acids are being used more widely in recent years. Communications on the presence of D-acylase activity in certain microorganisms is of special interest in this respect. D-Aminoacylases from microorganisms of *Pseudomonas*[63,64] and *Streptomyces*[65,66] species were known previously. Low enantioselectivity was a disadvantage of these enzymes which limited their use for the manufacture of D-amino acids. An investigation has been carried out[67] of 800 strains of microorganisms isolated from soil and

one strain *Alcaligenes dentrificans* DA 181 was found to be a source of D-aminoacylase, possessing high activity and enantioselectivity towards *N*-acyl-D-amino acids. The enzyme, expressed under optimum conditions, possesses an activity of 250 μmol h^{-1} ml^{-1} (D-acylase from *Pseudomonas Sp.* has 10 μmol h^{-1} ml^{-1},[64] and from *Streptomyces olivaceus* 84 μmol h^{-1} ml^{-1} [65]). The maximum specific activity, 108 600 μmol h^{-1} ml^{-1}, was displayed in the hydrolysis of *N*-acetyl-D-methionine (*Pseudomonas sp.* 6.8 μmol h^{-1} ml^{-1} and *Str. olivaceus* 571 μmol h^{-1} ml^{-1}). The enzyme catalyses the hydrolysis of L substrates to an insignificant extent (Table 8).

Table 8. Relative hydrolysis rate of D- and L-substrates by the aminoacylase from *A. dentrificans*.

Substrate	V_{rel}, %		Substrate	V_{rel}, %	
	D-enantiomer	L-enantiomer		D-enantiomer	L-enantiomer
N-Ac-Met	100	0.1	N-Ac-Trp	33	0.6
N-Ac-Phe	81	0.3	N-Ac-Asp	17	0.0
N-ClAc-Val	66	0.0	N-Ac-aloIleu	12	*
N-Ac-Leu	60	0.4	N-Ac-Val	6	0.0
N-Ac-Ala	25	0.8	N-Ac-Phg	5	*

* Not determined.

Table 9. Separation of amino acid racemates by aminoacylase.

R	Acyl group	Enzyme*	Co^{2+}	Yield, %		Enantiomeric purity, %	
				L	D	L	D
Et	Ac	AI	–	40	32	>99.5	>99.5
Et	ClAc	AI	–	40	41	>99.5	>99.5
Pr	Ac	AA	+	33	32	>99.5	>99.5
CH_2=$CHCH_2$–	ClAc	AI	–	41	33	>99.5	>99.5
trans-Me–CH=CH–CH_2	Ac	AA	+	33	38	99	93
cis-Me–CH=CH–CH_2	Ac	AI	–	44	47	>99.5	>99.5
	ClAc	AI	+	37	42	99	84
	Ac	AA	+	50	50	95	98
	Ac	AA	+	45	41	99	**
	ClAc	AI	+	51	31	93	**
	ClAc	AI	+	43	46	91	80
	ClAc	AI	+	30	63	97	48

*AI is acylase I, AA is acylase from *Aspergillus sp.*

** The free amino acid was not isolated.

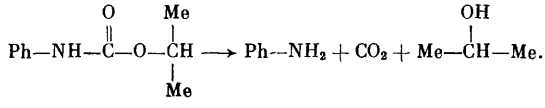
*** *N*-Acyl derivatives of α-methyl-AA.

The use of aminoacylases for the separation of enantiomers enables rarely encountered and unnatural optically active amino acids to be obtained. The racemic acyl derivatives of such amino acids and also of α-methylamino acids are separated into enantiomers by acylase I and by the acylase from *Aspergillus sp.* in preparative quantities (Table 9).[68]

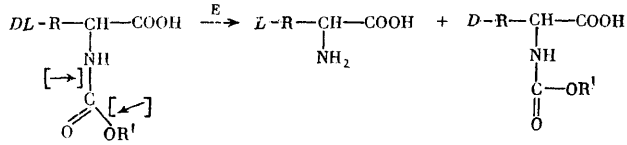
The values for the enantiomeric purity given in Table 9 characterise the significant enantiospecificity of the action of the enzyme (the amino acids isolated were not recrystallised). In the case of *N*-acyl-α-methyl-AA, the activity in relation to which was low (V_{rel} < 1%, for *N*-acetylmethionine V_{rel} = 100%), hydrolysis was effected with acylase I enclosed in a membrane which made it possible to use large quantities of protein many times in small reaction volumes. It was not expedient to use the acylase from *Asp. oryzae* since its specific activity was two orders of magnitude lower than that of acylase I.

5. Carbamates of amino acids

Many pesticides contain carbamate groups, such as NH(CO)OMe. It was shown previously that breakdown of *N*-phenylcarbamates occurs in soil under the action of microorganisms.[69]



With the development of an efficient method for the chemical synthesis of carbamates of amino acids[70] the possibility arose of obtaining optically active amino acids by enzymic breakdown of these derivatives. With this aim Kula and collaborators attempted to effect the hydrolysis of carbamates of several amino acids with an esterase from porcine liver, a hydantoinase from *Pseudomonas fluorescens* DSM 84, the urease from black beans, an acylase from porcine kidney and an acetylcholinesterase from porcine and human erythrocytes.[71,72] Enantioselective enzymic hydrolysis of the carbamates of amino acids occurs according to the following scheme.



Enantioselective removal of the *N*-alkoxycarbonyl group was observed only in the case of acylase and acetylcholinesterase. Of the three *N*-substituted DL-amino acids investigated, the alkoxycarbonyl derivatives of alanine, valine and *N*,*N*′-α,ε-disubstituted DL-lysine, acylase hydrolysed the carbamates of alanine and valine with both methoxy- and with ethoxycarbonyl (EOC) substituents. In the case of the alkoxycarbonyl derivative of lysine complete hydrolysis occurred but only with a methoxy carbonyl (MOC) group. Acetylcholinesterase effected the decomposition of the *N*-MOC derivatives of all three amino acids but in the case of lysine hydrolysis occurred regioselectivetly at the α substituent. The *N*-EOC derivatives were not hydrolysed. The pH optimum for the action of acetylcholinesterase was 7.5–8 and for acylase 7.5. The Michaelis constant (K_M) for the hydrolysis of *N*-MOC-DD-alanine was 68 mM for acetylcholinesterase and 8.2 mM for acylase. The activity of each of the enzymes in the hydrolysis of valine and lysine

derivatives was approxitimately the same but was one order of magnitude less in the hydrolysis of α,ε-bis(MOC)-DL-Lys. The activity of acetylcholinesterase was 15–20 times less than the activity of acylase but the size of the latter in the hydrolysis of *N*-MOC-DL-Val(Ala) was less than 1% activity of acylase in the hydrolysis of *N*-acetylmethionine (values of K_M are of the same order) (Table 10).

Table 10. Hydrolysis of amino acid carbamates by acylase from porcine kidney (temperature 37 °C).

Carbamate of DL-AA	α, μmole min^{-1} mg^{-1}	K_M, mM	Time, h	L-AA detected, %	
				A	B
N-MOC-Ala	0.63	8.2	78	47.5	43.0
N-EOC-Ala	0.56	8.2	70	45.5	44.0
N-MOC-Val	0.45	9.1	70	45.5	44.5
N-EOC-Val	0.40	9.1	76	42.5	34.5

Note. α is specific activity; A before chromatographic separation; B after chromatographic separation.

When considering the mechanism of the enzymic hydrolysis reaction of carbamates of amino acids the authors suggested two possible routes for the reaction.[72] The first was fission of the ester bond of the carbamate. The products of this reaction would be an alcohol and a substituted carbamic acid. Derivatives of carbamic acids are unstable and the intermediate obtained is spontaneously decomposed into an amino acid and carbon dioxide. Enzymic attack at the carbonyl atom with fission of the amide bond is a more probable route. The products of this reaction are the amino acid and a monoester of carbonic acid which decomposes to an alcohol and CO_2. In either case two volatile products are formed which may readily be removed from the reaction. This enables the reaction to proceed to completion and simplifies the isolation of the amino acid.

However the low values of the carbamates activity of acylase and acetylcholinesterase exclude the possibility of using these enzymes for the large scale resolution of amino acid racemates. In this situation there are two next steps, 1) a search for new sources of enzymes possessing high activity and 2) the selection of mutant strains. Kula and Sambale chose the first route.[73,74] They investigated 42 strains of microorganisms isolated from soil, which had previously been subjected to treatment with pesticides containing carbamate structures, and 36 strains from the German Microorganism Collection (from *Agrobacterium rodiobacter, Agrobacterium rhizogenes, Arthrobacter globiformis, Bacillus coagulans, Corynebacterium sepedonicum, Enterobacter cloacae, Mucobacterium spegmatis, Pseudomonas fluorescens, Pseudomonas putida*). Seven strains from the German Collection displayed low activity towards the alanine derivative and four towards the lysine derivative. The greatest activity was shown by the strain of *Pseudomonas fluorescens* DSM 50124 at 2.3 nmol min^{-1} mg^{-1} for *N*-MOC-Ala and 1.6 nmol min^{-1} mg^{-1} for *N*-MOC-Val.

The strains of microorganisms isolated from soil were cultured in media enriched with one of the substrates *N*-MOC-Ala, *N*-MOC-Val or *N,N'*-α,ε-bis(MOC)-Lys and the presence of carbamatase activity was then determined. It turned out that such activity was possessed by significantly fewer strains cultured in media enriched with the valine derivative than in the case of the alanine and lysine derivatives. This may be linked with the bacteriostatic properties of valine.[75] The majority of strains possessing carbamatase activity effected the hydrolysis of all three substrates but the activity towards the lysine derivative was the least. It is interesting to note that strains cultured on a medium enriched with *N*-MOC-DL-Ala possessed higher activity towards valine and lysine derivatives than those cultured on media enriched with *N*-MOC-DL-Val or *N,N'*-α,ε-bis(MOC)-DL-Lys. Six samples were isolated for further investigation (Table 11). The D-enantiomers of the substrates investigated were stable to the action of the enzyme. The hydrolysis of racemic substrates led to a product containing contamination by the D-isomer only in the case of alanine, but this is apparently linked with the presence of an alanine racemase.

Table 11. Hydrolysis of *N*-methoxycarbonyl-DL-amino acids by various strains of microorganisms isolated from soil.

Strain	α, nmole min^{-1} mg^{-1}			Hydrolysis of *N*-Moc-DL-Val				
	N-MOC-*DL*-Ala	N-MOC-*DL*-Val	*N,N'*-α,ε-bis(MOC)-DL-Lys	[protein], mg ml^{-1}	[substrate] mM	Time, h	[product], mM	Yield, %
A3 Xanthomanas maltophilia	166	126	96	0.2	180	65.5	18.5	10.6
A4 Methylobacterium extorques	318	81	45	1.2	180	65.0	29.5	16.9
L8 (not determined)	19.5	4.1	8.9	1.5	180	63.5	9.2	5.4
L10 Pseudomonas putida	59.0	8.8	0.0	0.5	180	67.0	46.0	26.3
L12 not determined	8.3	6.1	0.0	4.0	180	64.0	74.7	42.7
L18 Alcaligenes sp.	20.9	51.8	0.0	1.4	350	64.5	162.5	46.5

In the majority of cases the hydrolysis of *N,N'*-α,ε-bis(MOC)-Lys led to *N*-ε-MOC-LYs, *N*-α-MOC-Lys was not detected in the reaction products. Four strains gave unsubstituted lysine, two others a mixture of lysine and *N*-ε-MOC-Lys.

In the course of further investigations a strain was found possessing DL-carbamatase activity (121 nmol min^{-1} mg^{-1} for the alanine derivative, 170 nmol min^{-1} mg^{-1} for valine and 6.0 nmol min^{-1} mg^{-1} for lysine).[74] Two enzymes were isolated by purification, an L-carbamatase (MW 160000) and a D-carbamatase (MW 90000). Their substrate specificities towards the amino acid side chain and the alcohol component of the carbamate group were investigated (Table 12). The L-carbamatase displayed the greatest activity towards *N*-MOC-L-Phe while the best substrate for the D-carbamatase proved to be *N*-MOC-D-Ala. An increase in the number of carbon atoms in the alcohol component of the carbamate group causes a change in activity, which is extremely marked in the case of the L-carbamatase and insignificant in the case of D-carbamatase.

The stereoselective hydrolysis of *N,N'*-α,ε-bis(MOC)-DL-Lys occurs only at the α-amino group. Such a regioselective enzyme might play an important role in peptide synthesis for removing *N*-α-protecting groups.

Table 12. Specific activity of purified enzymes.

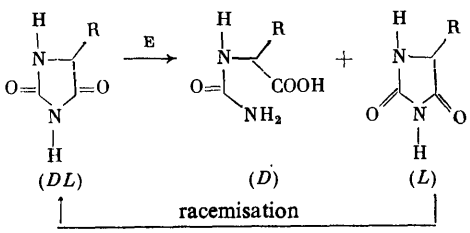
DL-Amino acid carbamate	L-Carbamatase activity, μmole min^{-1} mg^{-1}	D-Carbamatase activity, μmole min^{-1} mg^{-1}
N-(MOC)-*DL*-Val	12.1	4.5
N-(EOC)-*DL*-Val	1.1	2.1
N-(MOC)-*DL*-Ala	25.6	51.3
N-(EOC)-*DL*-Ala	8.9	26.7
N-(MOC)-*DL*-Phe	42.6	0.1
N-(MOC)-*DL*-Leu	3.3	1.0
N,N'-αε-bis(MOC)-DL-Lys	1.0	0.5

In conclusion it must be recorded that the specific activity of the strains found in the primary selection were inadequate for the development of an enzymatic process. However the fact that many microorganisms belonging to different species possess carbamatase activity raises hopes that further search and investigations will lead to the obtaining of enzymes suitable for the industrial resolution of amino acid carbamates.

6. Cyclic derivatives of amino acids

a) 5-Monosubstituted hydantoins

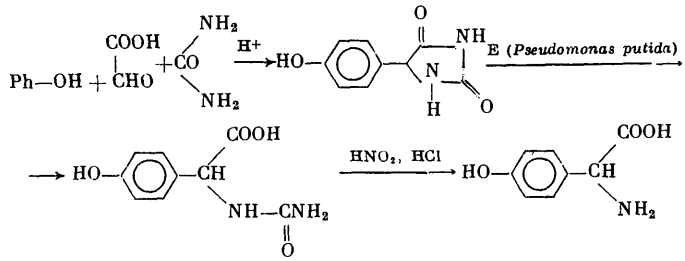
Enzymes possessing hydantoinase activity are mainly encountered in the microorganisms *Hansemula sp.*,[76] *Pseudomonas*,[77–79] *Agrobacterium*,[80] *Arthrobacter*,[81,82] *Corynebacterium*,[83] *Bacillus*,[84] etc. They catalyse the fission of hydantoins into *N*-carbamoyl-α-amino acids.



Hydantoins are intermediate compounds in the synthesis of α-amino acids from aldehydes, KCN and urea or ammonium carbonate.[85] They have an important advantage in comparison with other derivatives of amino acids. They racemise spontaneously under the conditions of the enzymic reaction and make it possible to convert practically 100% of a racemate into one of the enantiomers.

Removal of the *N*-carbamoyl group is possible chemically with an equimolar quantity of sodium nitrite in acidic medium. Complete retention of configuration was observed and the degree of conversion was close to 100%.[86]

This method enabled development of one of the most economic processes for the large scale manufacture of such amino acids as D-*p*-hydroxyphenylglycine used in the preparation of the semi-synthetic penicillin amoxicillin and the cephalosporins cephadroxil and cefatriazine.[86] Development of the process included the design of a simple and economical method for the chemical synthesis of the substrate DL-5-(*p*-hydroxyphenyl)hydantoin from phenol, glyoxylic acid and urea in an acidic medium.



The manufacture of D-phenylglycine and D-valine, which are used to the synthesis of antibiotics and pesticides, was developed in a similar manner.

The catalytic conversion of DL-5-(*p*-hydroxyphenyl)hydantoin also occurs by the action of cells of *Pseudomonas sp.* AJ-11220 however in this case the product is not the *N*-carbamoyl-D-amino acid but D-*p*-hydroxyphenylglycine.[87,88] Other similar processes have been studied.[89,90]

Yokozeki and collaborators have investigated strain AJ-11220, have optimised the conditions of expression of cells and of carrying out the enzymic hydrolysis (pH optimum 8.0, optimum T = 43 °C) and determined the substrate specificity of the enzyme (Table 13).[87]

Table 13. Substrate specificity of the enzyme from *Pseudomonas sp.* AJ-11220.

Hydrolysis produce	V_{rel}, %	Hydrolysis produce	V_{rel}, %
D-cyanoethylglycine	100	*D*-His	33
D-Met	80	*D*-Trp	21
Gly	80	*D*-Ile	19
D-Gln	72	*D*-Lys	18
D-Phg	62	*D*-Val	15
D-*p*-hydroxy-Phg	61	*D*-Glu	12
DL-Ala	58	D-3, 4-methylenedioxy-Phe	11
D-Phe	41		

All the products with the exception of glycine and alanine have the D configuration. In the case of alanine the authors linked the formation of a racemic product with the presence of alanine racemase in the cells, which was confirmed by subsequent experiments.

The possibility of obtaining D-lysine from its hydantoin precursor has been demonstrated for the first time.[87] It must also be noted that dihydrouracil is hydrolysed to a very insignificant extent by

AJ-11220 cells although it is the best substrate for the enzyme from *Pseudomonas putida*.[86] All these data suggest that the enzyme participates in the catalytic process with a different substrate specificity. To investigate this a partial purification was carried out and the substrate specificity of the fractions isolated was determined.[88] Cells of *Pseudomonas sp.* AJ-11220, suspended in 0.02 M tris HCl buffer (pH 7.5) containing either 10 mM $CoCl_2$ and $CaCl_2$ (variant I), or 10 mM dithiothreitol (variant II), were subjected to the action of an ultrasonic oscillator with subsequent fractionation on a column of DEAE-Toyopearl 650 M previously equilibrated with the appropriate buffer. Isolation by the first variant led to a 27-fold purification of the enzyme, viz. D-hydantoin hydrolyase (D-HH), with an overall activity yield of 63% (Table 14). No L-hydantoin hydrolase was detected. The hydrolase of *N*-carbamoyl-AA (CH) found in the unpurified extract was also not detected after fractionation on DEAE-Toyopearl.

Table 14. Partial purification of D-hydantoin hydrolase.

Fraction	Total quantity of protein, mg	Formation			
		D-enantiomer		L-enantiomer	
		A*, nmole min^{-1}	α, nmole min^{-1} mg^{-1}	A*, nmole min^{-1}	α, nmole min^{-1} mg^{-1}
Unpurified extract	540	36 000	67	0	0
DEAE-Toyopearl	13	22 620	1795	0	0

*A is total activity.

Purification according to variant II led to the observation that D-hydantoinase activity, found in the unpurified extract, was not detected after fractionation on DEAE-Toyopearl. The results of purifying the D and L hydrolases of *N*-carbamoyl-AA are shown in Table 15.

Table 15. Partial purification of *N*-carbamoyl-L- and D-amino acid hydrolases.

Fraction	Total quantity of protein, mg	Formation			
		D-enantiomer		L-enantiomer	
		A, nmole min^{-1}	α, nmole min^{-1} mg^{-1}	A, nmole min^{-1}	α, nmole min^{-1} mg^{-1}
Unpurified extract	475	7200	15	2290	5
DEAE-Toyopearl	10	2600	261	0	0

The data obtained enable certain conclusions to be drawn as to the mechanism of the asymmetric hydrolysis of DL-hydantoins of amino acids by *Pseudomonas sp.* AJ-11220. Only the D-isomer of the hydantoins is converted into the corresponding *N*-carbamoyl-D-amino acid by D-HH (pH optimum 8.0, optimum T 55 °C). *N*-Carbamoyl-D-amino acids are hydrolysed to the D-amino acid by D-CH (pH optimum 7.0, optimum T 50 °C). The L-hydantoins of amino acids racemise spontaneously and the D-isomers obtained are introduced into the hydrolysis process. When using preparations of D-HH and D-CH, obtained by fractionation on DEAE-Toyopearl, in the hydrolysis of DL-5-(*p*-hydroxyphenyl)hydantoin (pH 8.0) the product D-(*p* hydroxyl)phenylglycine, was obtained quantitatively. The substrate specificity of the three partially purified enzymes was also determined (Table 16).

Table 16. Substrate specificity of enzymes (D-hydantoin hydrolases and hydrolases of *N*-carbamoyl-D- and L-amino acids).

Substrate, hydantoin derivative of AA	V_{rel}, % (D-HH)	Substrate, *N*-carbamoyl-D- or L-AA	V_{rel}, %	
			D-CH	L-CH
D-Met	100	Met	100	47
DL-Met	54	Phg	94	–
L-Met	30	*p*-hydroxy-Phg	88	–
D-Phe	57	DOPA	62	0
D-Val	40	Leu	61	98
D-Phg	34	Ala	56	44*
D-*p*-hydroxy-Phg	33	Asn	48	2
DL-*p*-hydroxy-Phg	23	Phe	32	10
L-Lys	28	Glu	32	3
D-Tyr	19	Trp	31	0
DL-DOPA	18	Tyr	30	9
β-Ala	9	Val	18	100
DL-Leu	8	Gly	8	0
D-Trp	6	β-Ala	8	–
Gly	5	–	–	–
L-Glu	5	–	–	–
L-Asp	5	–	–	–
L-Ala	2			

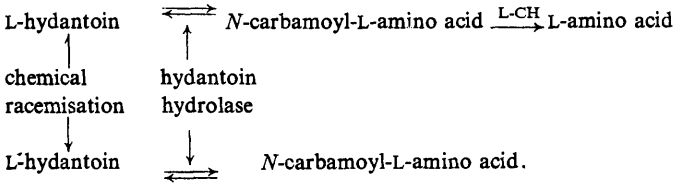
* Product was DL-alanine (due to the presence of alanine racemase in the unpurified extract).

Table 17. Substrate specificity of hydantoin hydrolase enzyme from strain AJ-3940.

Substrate, hydantoin derivates of AA	V_{rel}, %
L-Trp	100
5-Hydroxy-L-Trp	12
L-Phe	108
L-Tyr	71
L-3,4-DOPA	105
DL-3,4-Methylenedioxy-Phe	112
DL-3,4-Dimethoxy-Phe	4
L-Met	2
Gly,L-Ala,L-Ile,L-Asp,L-Glu	0

The strain *Flavobacterium sp.*-3912 was investigated in a similar manner. This enzyme hydrolyses DL-5-indolylmethylhydantoin to L-tryptophan in fairly high yield. The mutant strain AJ-3940, in which the routes decomposing tryptophan are blocked (yield of L-tryptophan was almost 100%), was also investigated.[91–93] The pH optimum for strain AJ-3940 was 8.5 and optimum T about 50 °C. Data on the substrate specificity are shown in Table 17.

Hydantoin hydrolyase activity towards both L and D substrates was observed at all stages of purifying the enzyme from strain AJ-3912 (ratio of specific activities L/D = 2.6 to 2.7). The *N*-carbamoyl-AA hydrolase activity was also detected at all stages of the purification but only towards the L substrate. Since no *N*-carbamoyl-AA racemase was detected in the strain, the following mechanism is proposed for the enzymic conversion of hydantoins of DL-amino acids into L-amino acids.[93]



The pH optimum for the hydrolysis of the hydantoin derivative was 9.7, the reverse reaction proceeds at a pH close to neutral values (7–8). The pH optimum for the action of L-CH is 8.0 and the optimum temperature for the purified enzymes is 40 °C. Data on the substrate specificity of L-CH are shown in Table 18.

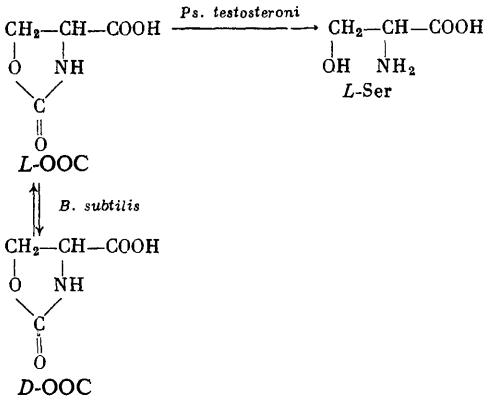
Table 18. Substrate specificity of *N*-carbamoyl-L-amino acid hydrolase.

Substrate, *N*-carbamoyl-AA	V_{rel}, %
DL-3,4-Methlenedioxy-Phe	100
L-Phe	82
L-Tyr	59
L-Trp	55
DL-3,4-Dimethoxy-Phe	24
L-Met	24
Gly	5
L-Ile	2

Another strain, *Arthrobacter sp.* DSM 3747, has been investigated.[94] This strain is able to catalyse the hydrolysis of DL-5-indolylmethylhydantoin to L-tryptophan, which showed that the conversion proceeded according to a scheme similar to that proposed previously,[93] but the racemisation of 5-indolymethylhydantoin in the presence and absence of cells of *Arthrobacter sp.* occurs in a different way (Fig. 2). This formed the basis for proposing that a third enzyme participates in the process, a hydantoin racemase, which was isolated during subsequent work.[95]

b) DL-2-Oxooxazolidine-4-carboxylic acid

A method is known for the quantitative preparation of L-cysteine from DL-2-aminothiazolin-4-carboxylic acid (ATC), an intermediate in the chemical analysis of DL-cysteine, by a combined enzymic process of hydrolysis of L-ATC and racemisation of D-ATC by cells of *Pseudomonas thiazolinophilum* AJ-3854.[96,97] The process was applied industrially and subsequently attempts were made to develop a similar process to obtain L-serine from DL-2-oxooxazolidine-4-carboxylic acid (OOC), which is an intermediate in the synthesis of DL-serine.[98] It is necessary to effect two reactions for the complete conversion of the racemic derivative into the optically active amino acid, viz. the hydrolysis of L-OOC to L-serine and the racemisation of D-OOC. In all 849 strains were investigated 12 of which proved to be capable of catalysing the first reaction and 8 the second. The strain of *Pseudomonas testosteroni* AJ-2770 was the best source of hydrolysis activity and *Bacillus subtilis* AJ-1996 of racemisation. By the combined process L-Ser was obtained from D-OOC in 30% yield with cells of *Ps. testosteroni* and *B. subtilis*. When using L-OOC as substrate the reaction proceeded in a similar manner. This enabled the conclusion to be made that racemisation is not the rate-limiting stage. L-Ser was not obtained from D-OOC if cells of one of the strains was not present. The combined process occurs according to the scheme:



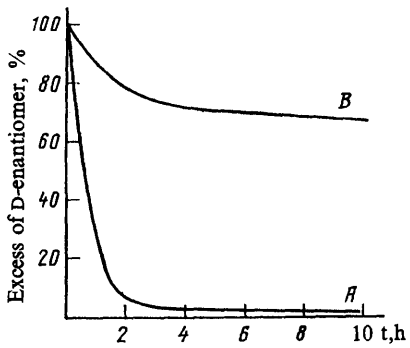


Figure 2. Racemisation of D-indolylmethylhydantoin *A*, in the presence and *B*, in the absence of cells of *Arthrobacter sp.*

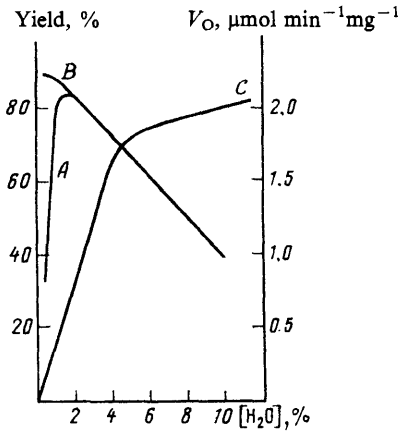


Figure 3. Effect of water content on the yield of *N*-acetyl-L-tryptophan ethyl ester (*A*, reaction time 24 h; *B*, at low H_2O concentrations the reaction time was increased to 15 d) and *C*, on the reaction rate. *N*-Ac-L-Trp 0.05 g (0.02 mmole), α-chymotrypsin 0.01 g, 0.1 M phosphate buffer pH 6.8, 30 °C.

III. Enantioselective enzymic derivatisation of amino acids and their derivatives

Reactions catalysed by enzymes are, as a rule, reversible. However by creating particular conditions (for example varying reagent concentration, removing one of the products from the reaction) it is possible to secure a shift in the equilibrium in the direction required. In practice this is achieved by carrying out the reaction in media containing significant quantities of organic solvent, such as in aqueous organic media (including alcohol–water), in two-phase systems (water–immiscible organic solvents), in systems of reverse micelles and in two-phase aqueous polymeric systems. The enzymic synthesis of aminoacid derivatives is in the development stage. The greatest number of studies in this area is devoted to the synthesis of α-amino acid esters.

1. Synthesis of amino acid esters

One of the first reports on the ability of enzymes to catalyse the synthesis of amino acid esters was made in 1965.[99] The rate of the enzymic reaction and the yield of product depends on many factors, among which are the decisive role played by the state of the enzyme, the properties of the carrier (including the specific surface) when using immobilised catalysts, the composition and pH of the aqueous phase, the concentration of amino acid and alcohol, the composition of the organic phase, the rate of the volumes of the organic and aqueous phases, etc. The synthesis of *N*-acetyl-L-tyrosine ethyl ester using immobilised α-chymotrypsin in a two-phase system has been optimised with respect to these parameters (yield of product was 85–90%).[100] *N*-Acetyl-L-tryptophan ethyl ester was obtained in 86–95% yield under similar conditions (two-phase water–chloroform system, time 2–8 h),[101] which enabled the process to be used for separating racemic *N*-acetyltryptophan (time 48 h, yield of L-enantiomer 45%).[102] The esterification of acyl derivatives of aromatic amino acids in two-phase systems and in aqueous organic media has been investigated.[103,104] The ratio of aqueous and organic phase proved to have a significant effect on the extent of conversion. On changing this ratio from 1:10 to 1:80 the yield was increased from ~38 to ~92%. In a water–chloroform system at constant V_{aq}:V_{org} ratio (1:40) the effect of ethanol concentration on the yield of product was fairly weak (Table 19). The yield of product in ethanol was satisfactorily high. The reaction system was a suspension of hydrated α-chymotrypsin which may easily be removed by filtration. Another important virtue of the one-phase system was considered to be the significantly less noticeable inhibition by the substrate concentrations (Table 20).

Table 19. Effect of ethanol concentration on yield of product.

[EtoH] in $CHCl_3$, M	Yield of *N*-Ac-L-Trp ethyl ester, %
1	83 *
3	86 *
5	77 **
8.6 (50 об.%)	79 **
17.1	78 **

* Two-phase system.
** One-phase system.

Table 20. Effect of substrate concentration.

N-Ac-L-Trp	Reaction time, h	Yield of *N*-Ac-L-Trp ethyl ester, %	
		EtOH	$CHCl_3$ (1 M EtOH)
0.05	24	81	78
0.10	24	86	78
0.15	24	75	78
0.20	24	70	78
0.20	48	85	78
0.20	72	83	78
0.20	96	85	4.4
0.25	96	58	3.0

The dependence of the ester yield on the water content of the system when carrying out esterification for 24 h has a maximum in the region of 2–4% H_2O (Fig. 3, curve *A*), however the shape of the curve is changed on increasing the synthesis time (at these and lower H_2O concentrations) to 15 d (Fig. 3, curve *B*). This is seemingly linked with the significant reduction in reaction rate (Fig. 3, curve *C*) due to the reduction in the extent of hydration of α-chymotrypsin. It is possible that the negative effect may be reduced by using the modified enzyme, hexylchymotrypsin, for the synthesis of esters.[105] The size of V_{max} for such an enzyme is increased.

Another possible method of increasing the reaction rate at low H_2O concentrations is immobilisation of the enzyme, such as the adsorption of α-chymotrypsin into chitin.[106] When carrying out

esterification in ethanol containing 3.4% water the yield of *N*-acetyl-L-tryptophan ethyl ester was 28% for the free enzyme (reaction time 24 h) and 85% for α-chymotrypsin adsorbed onto chitin (reaction time 12 h). The use of other polysaccharides, such as microcrystalline cellulose and aminoethylcellulose, led to a lower yield (20 and 23% respectively after 24 h) than for the free enzyme. It is known that α-chymotrypsin in solutions containing hydrophilic solvents at high concentration loses its catalytic activity to a significant extent due to partial unfolding of the polypeptide chain. The enzyme bound to chitin probably retains the native conformation at H_2O concentrations below 5%. It is possible that a significant portion of the water in such solutions is also adsorbed by the chitin and contributes to the stabilisation of the native conformation.

Investigation of the esterification at various temperatures showed that the yield was practically unchanged in the temperature range 10–35 °C and at higher temperatures it fell sharply.[104] Under the conditions described above esterification was effected for aromatic *N*-acetyl-L-amino acids (tryptophan, tyrosine and phenylalanine), the analogous derivatives of L-alanine and L-leucine did not react. The yields of the ethyl esters of *N*-acetyl-D-tryptophan and -phenylalanine were extremely insignificant. This indicates the retention of substrate specificity and enantioselectivity under the given conditions. However the specificity towards the alcoholic component of the reaction was other than in the case of hydrolysis. Methanol and 2-methylpropan-2-ol (t-butanol) did not react, the other primary and even secondary alochols investigated gave a product in high yield (Table 21).

Table 21. Effect of structure of the alcohol component on the synthesis of *N*-acetyl-L-tryptophan esters.

Alcohol	Yield after 24 h, %	Alcohol	Yield after 24 h, %
Methanol	0	Butan-2-ol	83
Ethanol	81	Butan-2-ol	65
Propan-1-ol	83	2-Methylpropan-1-ol	80
Propan-2-ol	78	2-Methylpropan-2-ol	0

Table 22. Initial esterification rate (V_0) and yield of acetylamino acid ester.

Solvent	*N*-Ac-L-Trp-OEt		*N*-Ac-L-Tyr-OEt	
	$V_0 \cdot 10^2$, μmole $min^{-1} g^{-1}$	Yield % (24 h)	$V_0 \cdot 10^2$, μmole $min^{-1} g^{-1}$	Yield %(24 h)
Acetone	6.1	71	18	74
Nitromethane	4,3	60	31	89
Acetonitrile	2.3	56	13	80
Propylene carbonate	1.1	45	6.8	66
Tetrahydrofuran	0.88	30	4.5	44
1,4-Dioxan	≪0.5	12	6.5	46
Ethanol	12	81	15	82

Attempts were also made to conduct the synthesis in other hydrophilic solvents containing 1.7 M ethanol (Table 22).[107] Esterificaiton of *N*-acetyl-L-tryptophan did not take place in dimethylformamide, dimethylacetamide and dimethylsulphoxide.

An investigation was also conducted on the effect of aqueous phase composition, buffer concentration and pH (Table 23) which showed that the yield was extremely insignificant (5%) in pure H_2O. When using phosphate buffer the optimum concentration was 0.1 M. At higher concentrations the activity of the enzyme was reduced. This may be linked with a reduction in the quantity of water available for the stabilisation of the enzyme due to the increase in the quantity bound to phosphate. It is interesting that other buffers at the same molar concentration at other pH (5.0 and 9.0) gave results (70 and 74%) similar to that obtained when using phosphate buffer (pH 6.8). The minimal effect of pH may be explained by the inorganic salts playing the role of adsorbents of the enzyme after mixing the solution of α-chymotrypsin with a large excess of organic solvent.

Table 23. Effect of buffer on the synthesis of *N*-acetyl-L-tyrosine ethyl ester.

Buffer	pH	*M*	$V_0 \cdot 10^2$, μmole $min^{-1} g^{-1}$	Yield, % (24, h)
Phosphate	6.8	0.05	4.1	78
	6.8	0.1	4.9	78
	6.8	0.2	2.4	49
	6.8	0.5	2.3	24
Acetate	5.0	0.1	4.4	70
Borate	9.0	0.1	4.7	74
H_2O	–	–	*	5

* Not determined.

Table 24. Esterification of *N*-t-butyloxycarbonyl-L-amino acids using papain (37 °C, 8 h).

Substrate, *N*-Boc-AA	Volume ratio buffer: CH_2Cl_2: alcohol	Yield, %	Substrate, *N*-Boc-AA	Volume ratio buffer: CH_2Cl_2: alcohol	Yield, %
Leu	3 : 1 : 1	75	Tyr	3 : 5 : 1	90
Phe	3 : 1 : 1	76	Ser	3 : 5 : 1	75
Trp	3 : 1 : 1	78	Thr	3 : 5 : 1	40
Met	3 : 1 : 1	76	Glu	3 : 50 : 1.5	90
Cys(Bzl)	3 : 1 : 1	74	Glu *	3 : 50 : 1.5	78
Val	3 : 0.5 : 1	27	Gln	1.5 : 50 : 1.5	85
Ile	3 : 0.5 : 1	22	Asp	3 : 50 : 1.5	83
Gly	3 : 5 : 1	82	Asp *	3 : 50 : 1.5	70
Ala	3 : 5 : 1	88	Asn	1.5 : 50 : 1.5	82

* Benzyl alcohol was used as the alcohol component.

Papain is another enzyme widely used for obtaining optically active esters.[108–113] Attempts were undertaken to separate enantiomers of *N*-t-butyloxycarbonylamino acids by the enzymic synthesis of esters. Methylene chloride was used as the organic phase and 1 M citrate–phosphate buffer (pH 4.2) as the aqueous phase. By varying the ratios of buffer : methylene chloride : alcohol, esters were obtained for the majority of amino acids in high yield (Table 24). Yields were not high in the case of sterically hindered valine, isoleucine, threonine) and basic (lysine, arginine, histidine) amino acids.

As is seen from Table 24 the optimum ratio of organic and aqueous phases $\beta = V_{org}/V_{aq}$ varied from $\beta = 17$ for hydrophilic amino acids (aspartic and glutamic acids) to $\beta = 0.3$ for the hydrophobic (phenylalanine, leucine, tryptophan and methionine). Esterification of the dicarboxylic acids occurred at the α-carboxyl group to the monoester. The possibility of using enzymic synthesis for the separation of amino acid racemates was demonstrated by the synthesis of *N*-t-butyloxycarbonyl-L-aspartic acid from the racemic *N*-protected amino acid and benzyl alcohol. No D-ester was detected in the product and it was shown that the D-enantiomer was not esterified by papain. In subsequent investigations the possibility was shown of obtaining esters from the analogous *N*-derivatives of alanine and aliphatic alcohols $C_nH_{2n+1}OH$ (n = 2, 4, 6) and diols $HO(CH_2)_{2m}OH$ ($1 \leqslant m \leqslant 5$).[109] Immobilisation of papain itself on XAD-7 (neutral cross-linked polymethylacrylate) or Sepharose enabled the reaction to be carried out for n = 8, 10, 12, 16 and m = 6 as well. When using the immobilised enzyme the amount of alcohol was reduced 5-fold and the enantioselectivity of papain action towards α-amino acids was retained. The process may be used for resolving racemic *N*-t-butyloxycarbonylamino acids (alanine and aspartic acid).[110] As in the cases of α-chymotrypsin the enzymic synthesis using papain may be conducted in an aqueous alcoholic medium.[111–113] Esterification of *N*-benzyloxycarbonylamino acids catalysed by papain was carried out in an alcohol–water system with a minimum quantity of water (4–5 eq. H_2O/eq. AA). Ethyl, methyl, n-propyl and n-butyl alcohols were used as the alcohol component of the reaction (Table 25).[112]

Table 25. Synthesis of *N*-protected amino acid esters.

N-Protected-DL-AA	Product, *N*-Z-L-AA-OR		*N*-Protected-DL-AA	Product, *N*-Z-L-AA-OR	
	R	Yield, %		R	Yield, %
Ala	Et	48.5	Ser	Et	26.5
Ala	Me	42.5	Met	Et	47.5
Ala	n-Pr	37.5	Asp	Et	31.5
Ala	N-Bu	40.0	Gln	Et	44.5
Ala *	Et	36.5	Trp	Et	46.0
Ala **	Et	17.5	Phe	Et	43.5
NorVal	Et	49.0	Tyr	Et	47.5
NorLeu	Et	48.5	4-F-Phe	Et	41.0
Val	Et	19.0	4-NO_2-Phe	Et	37.5
Leu	Et	45.0	3,4-Cl_2-Phe	Et	45.5

Note. Reaction conditions in example 1: 50 °C, 10.7 g Z-DL-Ala in 80 ml abs. EtOH containing 2 ml citrate buffer (pH 4.5), time 24 h. Yield of Z-D-Ala was 42.5% (enantiomeric excess > 95%).

* *N*-Boc-L-Ala-OEt.

** *N*-Fmoc-L-Ala-OEt.

Immobilised papain was used in another study for esterification.[113] Of eight carriers investigated the best proved to be Sephadex G-50 (yields of esters of *N*-t-butyl- and *N*-benzyloxycarbonylamino acids were 40 to 93%). Investigation of the effect of volume, concentration and pH of the aqueous phase showed that the maximum yield was achieved at a water content of about 5%. The dependence of yield on pH had a sharp maximum at pH 4.2 and on increasing the concentration of citrate buffer from 0 to 3 M the yield was increased from 0 to 93%.

Some studies have appeared recently demonstrating the possibility of carrying out enzymic reactions in anhydrous organic solvents.[114–116] It has been shown[117] that α-chymotrypsin precipitated from n-propanol is capable of catalysing the synthesis of *N*-acetyltryptophan ethyl ester in cyclohexane with a high enantioselectivity which may be adjusted by varying the precipitation conditions. On precipitating in the presence of *N*-acetyl-D-tryptophan the ratio of the initial rates of the enzymic reactions $V_0^L/V_0^D = 70$ (V_0^L = 0.5 μmol mg^{-1} h^{-1}, V_0^D = 7.1 mmol mg^{-1} h^{-1}). When precipitating in the presence of *N*-Ac-L-Trp the enantioselectivity was strongly increased (V_0^L = 2.7 μmol mg^{-1} h^{-1}, no synthesis of D-ester was observed after 120 h).

2. Synthesis of amino acid amides

It was found that the D-enantioselective aminopeptidase from *Ochrobactrum anthropi*, which is able to hydrolyse the amides of D-amino acids and the *p*-nitroanilides and esters of amino acids and certain peptides, catalyses the aminolysis of D-amino acid esters under certain conditions.[118,119] D-Alanine-3-pentylamide was synthesised quantitatively in 1 h from D-alanine methyl ester and 3-aminopentane in various organic solvents saturated with water (Table 26).

Table 26. Enzymic aminolysis of alanine methyl ester by 3-aminopentane.

Substrate	Solvent	Yield, %
D-Ala-OMe	n-Butyl acetate	98
DL-Ala-OMe	n-Butyl acetate	48
L-Ala-OMe	n-Butyl acetate	0
D-Ala-OMe	Benzene	98
D-Ala-OMe	1,1,1-Trichloroethane	91
D-Ala-OMe	Toluene	67

When using a DL-substrate the product contained no L-amino acid amide. The enzyme possesses a wide specificity towards the acceptor of the acyl group. Products were syntheised in high yield from D-alanine and n-butylamine, benzylamine and neopentylamine in a similar manner. At the same time the specificity of the enzyme towards the acyl group proved to be appreciably worse. Only esters of D-alanine, glycine and D-α-aminobutyric acid gave a product in high yield (98, 80 and 40% respectively). The methyl esters of 19 other D-α-amino acids, β-alanine and various carboxylic acids were not substrates in this enzymic reaction. In water the aminolysis of

D-alanine methyl ester occurs in 78% yield after 7.5 min with subsequent complete hydrolysis to D-alanine in 30 min.

The information presented in the review on the enzymic methods of resolving racemic amino acids and their derivatives demonstrates the intense development of the sphere of science and manufacturing activity. The widespread use of enantioselective enzymic processes together with processes for the enzymic synthesis of amino acids from achiral substrates enables the need for optically active amino acids to be satisfied to a significant extent.

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Translated from *Uspekhi Khimii* **60** 2292–2331 (1991) U.D.C. 541:574;550;551;556;523;524;533.9

The role of chemical factors in the evolution of natural systems (chemistry and ecology)

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ABSTRACT. Certain trends in the development of chemical and related sciences as regards the solution of ecological problems are described. Apart from the discussion of traditional chemical problems associated with the development of resource-saving and low-waste technologies and sensor systems for the monitoring of the natural environment, the physicochemical aspects of the dynamics of a wide variety of natural systems are analysed and the role of the chemical factor in their evolution is elucidated. The idea of parameters defined as limiting permissible amount of waste and limiting permissible concentrations, characterising respectively the self-protecting properties of the environment and individual organisms was introduced on the basis of non-linear models of non-equilibrium thermodynamics. The dynamic equations describing the states of eco-systems in the presence of external stochastic chemical factors are discussed. Problems concerning the influence on the evolution of natural communities of mass transfer processes in the interior of the Earth and in various layers of the atmosphere are analysed. The idea that the Earth–atmosphere system as thermodynamically open is developed and the possible role of anthropogenic factors in the initiation of natural catastrophies is discussed.

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I. Introduction

The Earth's biosphere, which embraces the lower part of the atmosphere, the hydrosphere, and the upper part of the lithosphere with its rich and wide variety of ecological localised regions and eco-systems, was formed under conditions where the Earth was strongly acted upon both from space (electromagnetic radiation over a wide frequency range, solar and stellar wind, gravitational effects of the sun, the moon, and the planets, and collisions with macroscopic objects—asteroid fragments and comets), and from the inner regions of the Earth (terrestrial magnetism, movements of the lithospheric plates and of the Earth's core, material ejected in major volcanic eruptions). The unity (physicochemical, biochemical, geochemical, and cosmochemical) between eco-systems and their environment arising under these conditions[1–5] was responsible for the modulating and modifying variability[6] of organisms subjected to variations in the intensity and form of extraneous factors. The evolution of terrestrial communities provided examples of the stability of living matter accompanied by the variability of its forms even under the conditions of global catastrophies. Since the 30's of the present century and especially during the last decades, the biosphere has been subjected to the influence of anthropogenic factors having anomalously high (compared with those obtained previously) local intensities and sometimes exhibiting new essential features. According to Matros and Noskov,[7] in terms of the amount of sulphur dioxide (~150 million tonnes annually) and hydrocarbons (~70 million tonnes annually) evolved, industry has already become comparable to natural sources and as regards carbon monoxide (~300 million tonnes annually) it surpasses them. The parameters of other types of anthropogenic contaminants ejected into the natural environment and their amounts are also not encouraging.[8] The greatest risk associated with anthropogenic contaminants and influences (in contrast to the natural ones) involves their locally high concentrations, harmful to living matter, or their locally enhanced levels (for example, radioactive and elecromagnetic radiation). Indeed, despite the large integral radiation dose received by the biosphere from cosmic rays and the natural breakdown of radioactive elements in the Earth's core, the overall background of damaging radiation is low and is not dangerous to eco-systems. Whereas the material ejected by volcanoes contains large amounts of harmful components (for example, SO_2), it is usually scattered over large areas because, these components reach an extremely great height. Thus, the relationship between the appearance of silvery clouds at a height of approximately 80 km and the powerful eruption of Vesuvius preceding this phenomenon led to the conclusion that large amounts of water vapour are ejected into the mesopause by the eruption.[11] Sulphur compounds have also been detected in the silver clouds.[12]

In the anthropogenic evolution of harmful components, their scattering in the atmosphere, the hydrosphere, and in the soil does not occur on such a scale and the local concentrations (or harmful radiation) can exceed by many orders of magnitude the natural background. An even greater danger is associated with the ejection into the biosphere of substances foreign to living organisms—xenobiotics, including those which did not exist previously in nature. Such substances are dioxins, formed in the manufacture of organochlorine derivatives.[13] They already constitute a global risk to humanity and civilisation as a result of the possibility of the long term contamination of the entire biosphere by these substances.

Under these conditions, ecology and other sciences which may participate in the solution of complex ecological problems assume first class importance.[14] In this communication, an attempt is made to present the principal relationships through which such interaction between chemistry and ecology can occur and is already occurring. However, before proceding to the discussion of the essential features of the problems, certain general explanations are necessary.

In connection with the development of acute ecological problems, during the last decade the concept of "ecology" has been extended and it is now regarded as an interdisciplinary synthetic science and protection of the environment from pollution, the development of low-waste resource-saving technologies, the construction of purifying equipment, and planned utilisation of the Earth's resources are included in it. Naturally, ecology employs data from most varied disciplines, but this refers to the methodological and not the idealogical aspects of the science.[15,16]

Ecology is a component of biological science, dealing with the study of the structure and functioning of systems at a superorganism level (eco-systems or biogeocenoses) as regards their relationship with one another and with the environment.[1-5,15-17] This means that any ecological development should include the analysis of the state or dynamics of biological communities in their living environment. Separate components are traditionally investigated in this connection within the framework of genetics, physiology, and anatomy; the level of individual cells is investigated in cell biology; the mechanisms of the interaction of molecular components in the environment and various types of radiation with submicroscopic elements of living systems (biological membranes and their fragments), a wide variety of enzymes, parts of the heredity apparatus, etc. are studied in biochemistry and molecular biology; the state of the environment, including the effects of radiations and particles of different kinds on such environment (liquid, gaseous) is investigated in various branches of chemistry (analytical, inorganic, organic, chemistry of macromolecular compounds, colloid, physical, and radiation), physics (chemical, the physics of the condensed medium, nuclear, molecular, biological), and mathematics.[18] Thus the effecive solution of ecological problems implies that specialists in adjacent disciplines possess the necessary professional knowlege and that each executes his own concerted "manoeuvre".

In particular, in the construction and analysis of models of the evolution of eco-systems—ecological modelling,[19] there arises, together with the formulation of the problem and the elucidation of the main factors to be taken into account in the model (the ecological problem), a set of physicochemical, physical, and biochemical problems associated with the determination of the essential features (genesis) of the parameters in the equations and their dependences on the state of the environment, which may change, as well as mathematical problems associated with the necessity to analyse the corresponding systems of equations (in the general case non-linear), the determination of stationary states of the eco-system and the conditions of bifuraction transitions,[20] etc.

The aim of the present article is to present in a general form (accompanied by specific examples with which the author is most familiar) the possible relations between chemistry and ecology in order to elucidate the aspects of chemical science, of greatest current interest, which assist in the solution of ecological problems. Evidently in such formulation of the problem the role of chemical science should consist primarily in the development of nature-protecting and resource-saving technologies with analytical monitoring of the composition of the entire industrial waste and of the quality of the final products and articles. The ecological problems then involve the study of the influences of such waste on eco-systems with the elucidation of the possible ecological modulations and modifications[6] to prevent the possible eco-system degradation process. Naturally, it is essential to describe adequately the self-protecting possibilities of the eco-systems themselves, the buffer properties of their environment, the ecological resources of the biosphere as a whole, and its "tolerance of abuse".[21,22] This is particularly important bearing in mind the objectively existing tendencies to expand industrial manufacturing processes, to develop further the exploitation of useful mineral products, and to influence actively the biosphere.

The ecological resources are usually estimated empirically and are characterised by experimental (for the given region, a specific season, etc.) limiting permissible amount of waste (LPW) and limiting permissible concentrations (LPC). However, the discovery of the genesis of these parameters and the elucidation of the responses to various anthropogenic influences of the living systems themselves as well as the purifying possibilities inherent in inorganic nature make it possible to forecast on a sounder basis and more comprehensively the consequences of harmful influences of anthropogenic factors on eco-systems and to prevent these influences. As shown below, chemical science can analyse successfully and partly solve such problems.

II. Nature-protecting chemical technologies

The scale and nature of man's industrial activity has to be interrelated with the possibilities of modern science and technology and cannot permit a disturbance of the state of the environment of the planet's eco-system. This means that technological waste (gaseous, liquid) from industry must be sufficiently diluted as regards corrosive components and components harmful to living systems, so that, despite the wide variety of substances of anthropogenic and non-anthropogenic origin constantly ejected into the natural environment, the "buffer capacity" of the environment is maintained, i.e. the rates of degradation or elimination from turnover cycles (accompanied by irreversible "storage") should ensure the conversion of harmful substances into safe ones, which participate in natural turnovers. At the same time certain stationary concentrations of corrosive components not exceeding the LPC should be established in the environment (see Section IV).

The discovery of the mechanisms of the binding, detoxification and transformation (chemical, radiochemical, photochemical, microbiological) of harmful substances in the environment and also their elimination (filtration, micro-and ultra-filtration, reverse osmosis[23,24]) or their decomposition products constitutes an important problem in the protection of nature, since requirements as regards the LPW and the anthropogenic contaminants of the environment (LPC) in each specific region must be worked out on precisely this basis.

High local pollution of the environment by heavy metals, in the first place lead, cadmium, mercury, and arsenic,[25] accumulating in living organisms, is especially dangerous. Metals and metalloids enter the atmosphere with aerosol and vapour-phase industrial waste, as a result of dust rising from the soil, as a consequence of the arrival of dust from space, during volcanic eruptions, etc.[26] At the same time the metals present in rain water enter the soil and open water containing areas where the vast majority of heavy metal ions are adsorbed on microscopic suspensions of mineral origin which form part of the composition of medium and fine silt particles

0.05–0.005 μm in size (up to 70–80% of the total content in water).[27]

There are a wide variety of technological processes for the elimination of heavy metals from industrial aqueous waste and water in open water containing areas. Membrane (including membrane-sorption[23,24] and membrane-extraction[28]) and radiation-sorption methods for the detoxification of contaminated waters are effective. Such procedures are frequently used in combination with traditional chemical treatments with active agents (Cl_2, NH_3, O_3) and physical treatment (heating, UV radiation). There is now a possibility of synergism in the action of the above factors.[29] Irradiation alters the chemical (microbiological) composition of the system, i.e. leads to the disruption or conversion of the contaminants in water, which makes it possible to remove them subsequently from the medium being purified.

The solutions of the problem of the detoxification of aqueous waste by the removal of heavy metals may also be based on the use of the characteristic features of their complex formation reactions with a wide variety of ligands in the given medium. The formation of the so called secondary bonds,[30] whose strength is intermediate between covalent and van der Waals bonds, frequently plays an important role in such complex formation. The formation of secondary bonds by heavy organometallic cations with the functional groups of biopolymers is responsible for the poisoning of living organisms by heavy metals [for example, Hg(II)]. At the same time, the secondary bonds between Au(I) and organic ligands are formed in many medicinal drugs exhibiting a high therapeutic effect.

Other examples of the use of modern advances in chemical science for the detoxification of natural and technological waters may be found in other reviews of the present issue (see also Refs. 31 and 32). Naturally the number of unsolved problems is still very large. Cellulose-paper industries, non-ferrous metallurgical undertakings, power engineering, and the industrial manufacture of caustic soda and chlorine are serious sources of the pollution of the environment. The ejection into the atmosphere of Freons, which help to disrupt the Earth's ozone layer protecting the biosphere against the harmful effects of UV radiation, is a well known ecological danger.[33,34]

It is important to note that the advances achieved in chemical technologies makes it possible to reduce the amount of waste and achieve a saving of energy and materials in many industries. In particular, the harmful components discharged into the atmosphere (under conditions where they become highly concentrated during the purification process) may become sources of a valuable raw material for other industries. At the present time, large streams of effluent gases, containing admixtures of harmful components (SO_2, NO_x, HF, H_2S, CO) are ejected into the atmosphere in many industries.[35] In particular, the amount of sulphur dioxide discarded into the atmosphere in individual copper-zinc undertakings exceeds 1000000 tonnes per year. Nevertheless in the processes involving the neutralisation of gaseous waste containing SO_2, H_2S, and HF in small amounts (<1%) the sulphur- and fluorine-containing waste is hardly utilised.

One of the possible schemes (Fig. 1) for the detoxification of local gaseous waste (their volume is relatively small), which contains harmful components (SO_2, HF, HCl, NO_x, CO, H_2S), is described below. It involves their neutralisation with ammonia and the utilisation of the useful components, using a membrane unit whereby the excess ammonia is returned to the cycle. In the presence in the initial gaseous stream of the least reactive components (NO_x, CO, H_2S), it is necessary to introduce a catalytic reactor into the scheme[35] in order to neutralise these components with ammonia.

This scheme provides for the absorption of the excess ammonia (usually the amount of the excess ammonia may be approximately 10–20% of that supplied for neutralisation) by dilute aqueous ammonia solutions followed by the extraction of the absorbed ammonia and its return (with regulated amounts of water vapour) to the neutralisation reactor. Ammonia is extracted from the ammonia solution by passing a small proportion αI ($\alpha \ll 1$)

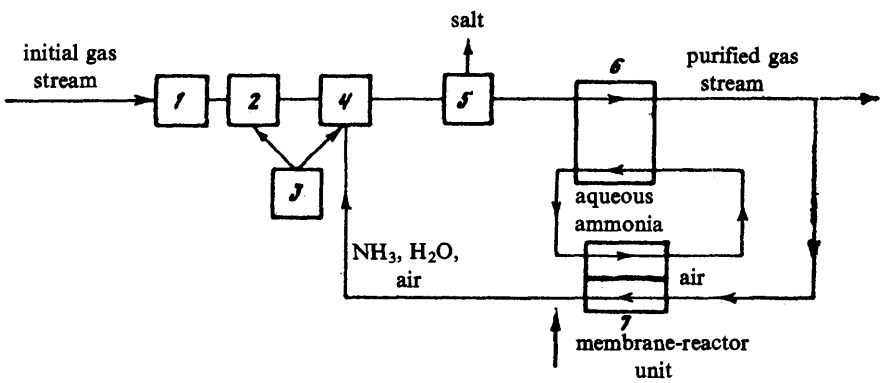


Figure 1. Schematic illustration of the process involving the neutralisation with ammonia of the corrosive components of gaseous waste in the membrane unit for the return of ammonia to the cycle.[36] The principal components of the block scheme: *1*, filter for preliminary purification of the gas mixture; *2*, catalytic purification unit (in the presence of NO_x, CO, and H_2S in the gas); *3*, source of ammonia; *4*, turbulent reactor for the neutralisation of corrosive components with moist ammonia supplied in stoichiometric excess; *5*, system for the trapping of the aerosol formed with isolation of the salt product; *6*, system for scrubbing with water to remove excess ammonia from the effluent gas stream, including a water absorber with supply to the latter of dilute aqueous ammonia (2–4%) (at the outlet the ammonia concentration is 4–5%); *7*, membrane unit (aqueous ammonia at a concentration of 4–5% is supplied to the interfibre space).

of the purified gas stream *I* through hollow fibres,[36–38] the ratio of the concentrations of ammonia and water at the outlet from the membrane unit being regulated by the gas-dynamic gas flow regime within the fibre.[36,37] For gas flow rates of approximately 10^2-10^3 $m^2\ h^{-1}$ and for a content of acid components of about 1 vol. %, the membrane elements should return ammonia in an amount $\lesssim 1.0$ m^3 $NH_3\ h^{-1}$, which is an entirely acceptable task in view of the functional characteristics of the hollow fibre membranes developed for this purpose on the basis of a perfluorinated sulphonic acid cation-exchange material of the Nafion type.[38]

The salt compounds removed from the mixing reactor (trapped in the form of aerosols) may be of interest as a raw material. In particular, the neutralisation of sulphur dioxide with ammonia in the presence of water vapour results in the formation of salts of sulphurous and sulphuric acids, which can be used either for the preparation of mineral fertilisers or for the liberation of ammonia (on thermal decomposition of the salts, on electrolysis of their solutions) with return of the ammonia to the cycle. This imparts to the given technology a low-waste character. Naturally, problems associated with the development of the optimum design of the mixing reactor with a system for the trapping of aerosols and for the removal of solid or highly concentrated liquid products arise in the application of this type of technology.

In fact, each liquid or gaseous industrial waste can be and should become a source from which valuable components can be extracted (or returned to the cycle): scarce heavy metals (Cu, Cr), organic components, acids, and alkalies. The advances in chemical science give grounds for the hope that new highly effective nature-protecting and resource saving technologies will be achieved:[39,40]

In discussing problems associated with the ejection of harmful components into the environment, it is important to discover whether these components are scattered uniformly throughout space (as molecular or ionic impurities) or are concentrated on some type of carriers (for example, aerosols, a wide variety of submicroscopic colloid particles, etc.). It is well known that simple knowledge of the chemical composition of the environment does not permit the understanding of many of the phenomena in inorganic nature. The combination of even small fractions of certain components of the environment (water molecules, other inorganic molecules or atoms, organic molecules) into colloid formations influences fundamentally a wide variety of physicochemical processes in the environment. Aerosols, the amount of which (in terms of weight) in the atmosphere is small (microgramme amounts in a cubic metre of air) and are at the level of the content of rare gases (xenon, krypton), determine not only many properties and phenomena (including the generation of sky glow, rainbows, and false suns as well as the climate in different regions of the Earth) but also the forms and rhythms of life on our planet, which we are witnessing.[41]

Furthermore, aerosols as well as colloid impurites in aqueous media can sorb harmful components in the environment, giving rise thereby to their anomalously high concentration: the concentrations of these components averaged over the volume of the aerosols can exceed by many orders of magnitude the corresponding average values in the environment. Such concentration processes play a dual role. On the one hand, the environment is freed from harmful components (including carcinogenic, radioactive, etc. components) with their "storage" in a relatively small number of macroparticles. On the other hand, these "depositories" represent a serious danger to individual persons so that development of methods for the individual protection of organisms against the harmful effect of active aerosols[42] and other colloid particles has acquired great importance as regards the protection of nature.

The development of methods for exerting controlled chemical, physical, and physicochemical influences on the environment in order to initiate such processes leading to the storage of individual components of the environment in a colloid-chemical depository is extremely urgently required. One can, for example, spray into the atmosphere special aerosols or introduce into an aqueous medium specific complex forming agents, after which the resulting complexes can be concentrated by ultrafiltration.[43] Various flocculation,[44] coagulation, etc. procedures are effective.

One of the methods whereby aqueous systems can be specifically acted upon may be the so called "magnetic treatment". Although this type of preparation of water for use in steam boilers in order to diminish the amount of scale formed during their functioning has long been known,[45] the attitudes to various procedures for the magnetic treatment of aqueous systems (the establishment of a flow of water through a permanent magnet with an induction of approximately $1-10^3$ Oe,[46,47] exposure to a variable electromagnetic field in the frequency range $1-10^3$ Hz [24]) have been extremely cautious in view of the controversial nature of the theoretical interpretations of the effects of such treatments.

Nevertheless, certain ideas about the results of the action of magnetic fields on real aqueous systems have already been formulated. According to Michelson,[46] when a moving solution supersaturated with hard salts is exposed to a magnetic field, crystallisation results in the formation of particles with a crystallographic structure differing (looser) from that arising in the absence of the magnetic field, so that there is a change in the ratio of the rates of crystallisation in the bulk of the solution and on the inner surface of the thermal apparatus (the latter is undesirable).

Further progress in the discovery of the mechanisms of the action of magnetic fields on aqueous systems will be associated with the formulation of experiments with the necessary analytical backup, including the monitoring of the content of ionogenic impurities (starting from water with a specific resistance of 18 N Ω cm) and of the number of colloid particles (for example, when microfiltration membranes with a pore size of approximately $0.1-0.2$ μm are used) in the aqueous medium.[48] Various hypothetical models of the mechanisms of such influences can have undoubted heuristic value in this connection.[49]

III. Chemical membrane sensors

The application of nature-protecting and resource-saving technologies is possible only when special systems for the industrial monitoring of the quality of the products and waste and also for continuous monitoring of the environment with analysis of specific industrial gaseous and liquid waste (for chlorine-containing hydrocarbons, organic solvents, pesticides, heavy metals, etc.) are present at all the stages and cycles of the manufacturing processes. A wide variety of systems for the detection of chemical signals are usually employed; traditional, analytical systems (based on specific chemical reactions, in particular colour reactions) and modern sensor systems which permit high-speed and continuous monitoring of the chemical composition of the medium up to the determination of the lowest possible concentrations of the components.[50–52] The sensitive elements in the recording system of the sensor are usually sputtered layers of metal oxides (ZnO, TiO_2, NiO, etc.) whose

resistance changes on chemisorption of electron-donating or electron-accepting components,[53] field transistors sensitive to chemisorption processes on the locking valve,[50] ceramic layers formed from mixtures of oxides ($Cr_2O_3-Al_2O_3-V_2O_3-Ti_2O_3$, α-$Fe_2O_3-SnO_2$, etc.)[54] whose electrical conductivity changes on sorption of certain components, light guides where conditions for total internal reflections are altered on sorption of specific components on the surface which thereby influences the propagation of the light signal,[55,56] and thin metallic layers (Al, Cu) in which surface plasmons, sensitive to the adsorption of specific components, may be excited in the IR range.[57]

The characteristic concentrations of the components measured by the above procedures depend on the type of molecules, the method of measurement, and the composition of the medium and lie in the range $10^{-8}-10^{-4}$ M. In individual cases, a higher sensitivity can be attained: antigen concentrations of approximately 2.5×10^{-9} M have been measured[57] with the aid of an IR biosensor; proteins in solution at a concentration of approximately $10^{-11}-10^{-12}$ M have been detected using opto-biosensors with excitation of surface plasmons;[58] using in the recording system sensitive bioelements (of the blue crab) in which electrical pulses are generated during the "recognition" process, an aminoacid concentration of approximately 10^{-13} M has been measured.[59] For comparison, we may point out that insects can distinguish the molecules of sex attractants when their content relative to other molecules in air is in the proportions $1:10^{17}$.[60]

The use of solid state systems for chemical sensors makes it possible to diminish greatly the size of the latter by accommodating on a single crystal or transistor several sensitive elements together with electronic circuits for the preliminary treatment of the signal and the storage and processing of information. Highly sensitive electrochemical sensors,[61,62] in which electrocatalytic reactions of components adsorbed on the electrodes take place, are widely used.

The progress in the creation of chemical and electrochemical sensors is at present very appreciable.[50-52] Sensors for the determination of the concentrations of ions (H^+, K^+, Na^+, Ca^{2+}, Ag^+, NH_4^+, Fe^{2+}, Cu^{2+}, Ni^+, Cd^+, Pb^+, F^-, Cl^-, Br—, NO_3^-), gas molecules (H_2, O_2, NH_3, CO_2), and biologically active substances (glucose, urea, quaternary ammonium compounds, sucrose, lactose, lysine, ethanol, penicillin, pyruvate, lactate, organophosphorus compounds, carbolates, psychotropic substances) have been developed and are widely used.[63-66] Thus semiconductor sensors based on metal oxides (ZnO, TiO_2, NiO) make it possible to measure microamounts of oxygen in gases ($10^{-5}-10^{-1}$ vol. %), to determine the concentrations of organic and inorganic gases and vapours (alcohol, acetone, ammonia, nitrogen oxides, carbon monoxide), and to detect free atoms and radicals (H, O, N Cl, OH, CH_3, C_2H_5, NH, NH_2) with a sensitivity up to 10^6-10^8 of active species in 1 cm^3.[53] Nevertheless the requirements (decrease in the levels of measurable concentrations of the components in liquid and gaseous media, greater selectivity, high speed, stability of characteristics) which must be met by such systems are continuously becoming more stringent, which is associated with the creation of new industries where components dangerous to eco-systems may be synthesised and also with some progress in establishing the harmful influence of components which had been previously regarded as safe. This entails the appearance of new virtually uninvestigated problems associated with the possible observation of synergistic effects when the eco-system is acted upon simultaneously either by a mixture of harmful components or by individual components against the background of fields of different nature (electromagnetic fields in different frequency ranges, low-frequency sonic fields).

The study of effects of this type will probably lead to a revision of the established values of the LPC (for different regions of the Earth and for different times of the year). This means that work on the improvement of chemical sensors should continue and chemical science should help in progress in this field. Together with the problem of the chemical composition of the environment (in the first place the determination of the content of harmful components), it is necessary to formulate the problem of the adequate description of the state of the environment—the provision of a more complete set of its characteristics influencing the evolution of an individual person and the eco-system as a whole. Therefore, apart from purely chemical sensors which permit the determination of the chemical composition of the environment as well as temperature and pressure sensors, it is necessary to employ other procedures for monitoring the state of the environment (for example counters for aerosol particles and radioactive radiation, sensitive receivers for electromagnetic radiation).

In this section, we shall discuss only problems associated with the increase in the sensitivity of the action of chemical sensors. Problems involving an increase in the selectivity of the detection of individual mixture components by solid state sensors are of extremely great current interest because the selectivity of many of the existing systems is low. Thus the change in the resistance of semiconducting oxide films depends only on the electron-donating or electron-accepting properties of the chemisorbed components. Therefore the overall change in resistance on sorption of several components makes it difficult to reach unambiguous conclusions about the contributions of individual components. The causes of the change in the charge on the gate of a field transitor on chemisorption of several components simultaneously are also difficult to analyse. The selectivity of such sensor devices can be significantly increased using as one of the elements special layers, partitions, or coatings which separate the medium being analysed from the recording system. Such composite devices are usually referred to as membrane sensors. If the partition (in particular, a porous one) contains biologically active compounds, enzymes, fragments of individual cells, immobilised antigens for the detection of the corresponding antibodies, fragments of membranes with chromophoric groups, etc., one refers to membrane biosensors.[55,56,67]

Coatings modifying the surface of the recording system increase the efficiency of the analysis in cases where the transfer of the components through the membrane layer is the rate-limiting stage of the overall irreversible process involving the detection of these components, namely in the appearance of stationary currents associated with electrochemical reactions of the components of the mixture analysed (O_2, H_2, alcohols, etc.),[68] in transient processes during the establishment of the state of equilibrium on sorption of components by the sensitive elements of the device, in enzyme-catalysed chemical and biochemical reactions,[66] in the generation of photocurrents whose magnitude may depend on the sorption of the components of the medium,[69] on irreversible "storage" or chemical binding of the permeating components in information accumulating systems, etc. Materials (organic and inorganic) usually employed in the membrane technology can be used for the formation of membrane coatings on the surfaces of sensor elements. The main difficulty then consists in the deposition of membrane coatings with an optimum thickness: sufficiently thin so that the response time does not exceed a certain required value and at the same time sufficiently thick so that the transfer through the coating (or the

transient processes in it for non-stationary analytical methods) should remain the rate-limiting stage of the entire irreversible process leading to the detection of the component with its chemical or electrochemical transformation. One of the optimum solutions apparently involves the creation of fairly compact submicroscopic barrier membrane layers with $d \simeq 0.01\,\mu m$.[70]

In this case it is possible to achieve anomalously high selectivities with respect to the target components for a relatively short delay time τ ($\tau \simeq d^2D \simeq 1$ s for diffusion coefficients D characteristic of vitreous polymeric materials) in the detection of a chemical signal. The possibility of attaining high selective detection parameters will be demonstrated on a model example.[71] We shall assume that the barrier layer is formed on the basis of a film with a thickness d and consisting of a material with a permeability constant $\Pi_{0i} = \gamma_{0i}D_{0i}$ in which repelling (for the permeating component i) force centres are distributed at random. We shall represent the repulsion potential of this species i, at a distance r from the centre, by the expression

$$U_i(r) = U_{0i}(b_i/r)^{m_i},$$

where b_i is the characteristic distance and m_i is a numerical parameter. Suppose that n is the concentration of such centres, whereupon, under conditions such as $d \ll d_{0i}$,

$$d_{0i} = [(U_{0i}/k_BT)^{1/m_i} b_i n^{1/3}]^{m_i-2} n^{-1/3},$$

we have the following expression for the permeability constant:[71]

$$\Pi_i \simeq \Pi_{0i} \exp\left[-\pi\Gamma\left(1-\frac{2}{m_i}\right)(U_{0i}/k_BT)^{2/m_i} b_i^2 nd\right]. \qquad (1)$$

A similar situation occurs also in other model representations of the potentials of the repelling centres.

The case considered corresponds to the transfer process (below the permeation threshhold) of the components i.[24] For a lower density of the scattering centres, where the transfer process "above the permeation threshold" obtains (for further details, see Refs. 24 and 71), we have the following features:

(1) for $d \lesssim L_i$ (L_i is the correlation length characterising the topology of the path followed in the transfer of the species i in the given material[24]), we have $\Pi_i \simeq d^{3-D_{fi}}$ — fractal transfer (D_{fi} is the fractal dimension);

(2) for $d \gg L_i$, we have $\Pi_i = \text{const.}$ — diffusional transfer.

The significance of the theoretical relations (1) for low values of d is that at high repulsion potentials the species effectively pass through the membrane only in those regions where the fluctuating force field is weakened by the lower local concentration of repelling centres (in the region of a "defect" in the packing of the centres. Since the parameters of the repulsion potentials for species of different nature are different, the selectivity of such a membrane depends exponentially on its thickness. Therefore it is possible, in principle, to achieve for the target component an anomalously high selectivity combined with a high (owing to the small thickness) permeability. So far this is merely a theoretical prediction of the unique possibilities for the selective isolation of mixture components with the aid of submicroscopic barrier membrane structures. These may be layers of organic or inorganic (for example, polyphosphazenes) materials obtained in different ways (the Langmuir–Blodgett method, plasma-chemistry, photochemistry, electrochemistry, alkoxo-technology, etc.). The Langmuir–Blodgett method, which makes it possible to achieve in the layer a specified array of individual molecules (for example, the formation of alternating oriented donor and acceptor layers separated by a distance of 2–3 nm) is especially promising.[72–75]

The technology used for the creation of such barrier structures and ultrathin layers should be at the highest level of sophistication. Such ultraclean technology (as regards materials and the concentrations of impurities and aerosols in the preparation chamber) should employ the experience and methods of the electronic industry. The sensitivity of such membrane systems with respect to the component being detected can probably be increased if the signal is recorded with one-sided excitation of the recording system (on photoexcitation of a semiconductor film, on transition of the membrane to the conductivity switching state,[24] etc.).

In the case of electrochemical sensors, the electric field behaves as an additional controlling factor, which determines the transfer of species, by altering its strength in the layer, one can apparently regulate the "permeation" regime for individual components — below or above the threshhold. Analysis of the voltage–current characteristics of such electrochemical systems with barrier membrane layers over a wide range of potentials can therefore yield exhaustive information about the impurities present in the electrolytic medium.

IV. Physicochemical principles of the modelling of the state of eco-systems

One of the main tasks in ecology consists in the discovery of the dynamic changes in the eco-systems taking into account the wide variety of life cycles, complex interactions, and internal controls (including positive and negative feedback) in food chains.[76] The classical deterministic models characterise the simplest of the situations, such as the dynamics of the growth of population in a closed environment, taking into account the fertility parameters, the real living area, etc., described by a logistic equation,[77–79] the dynamics of the mutual relations between the predator and prey taking into account the "search efficiency", the "successful" encounters between the predator and the prey, etc., described by the Lotka–Volterra equation.[76,80]

Such models make it possible to discover the main principles governing the existence and coexistence of consumers in eco-systems and to understand in what way and how rapidly anthropogenic factors can interfere in the natural characteristic features of the development of populations. The possibilities of modern computers have made it possible to expand significantly and increase the sophistication of deterministic models and to introduce into the latter various functional relationships, including a wide variety of food chains,[81,82] and to elaborate the interactions between consumers and the environment, including the situation when the latter contains toxicants.[83–85] There has also been a growth of the spatial scale of eco-systems susceptible to modelling: from levels corresponding to individual lakes[86] to the level corresponding to large regions (with dimensions up to 500 km).[84] The results of such model calculations make it possible to plan and prosecute more purposefully on a well-founded basis man's economic activity and to develop a strategy for saving ecologically endangered regions.

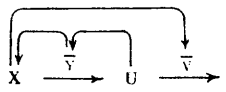
However, a number of fundamental problems arise in such modelling.[78] Each investigator is faced by the necessity to select certain arbitrary boundaries of eco-systems and boundary conditions, which influences the characteristic features of the evolution of the system, its stationary states, and naturally

introduces elements of subjectivity. The second more fundamental problem consists in the non-linearity of deterministic equations for the dynamics of eco-systems, which gives rise to the virtual unpredictability and the pseudo-random nature of the behaviour of such systems over a long time interval owing to the exceptional sensitivity of the solutions to the selection of the initial conditions, which can never be fixed or measured with sufficient accuracy. High-dimensional systems, such as the real eco-systems with a wide variety of internal feedbacks (positive and negative, including feedbacks with lag) and external influences, exhibit a random behaviour to a large extent with transitions between various stationary states. An impression is created that the greater the number of real factors underlying the model, the greater the chance of a transition during analysis to chaos or at least to instability.[78]

All the foregoing means that the very formulation of the model must be designed not so much to discover the multifactor influences on eco-systems but rather to establish the possibilities of the eco-system (with all its complex inter-relationships) as regards its preservation and its reponse to individual factors. In particular, these can be the response of eco-systems to changes in the state of the environment, for example, under the influence of electromagnetic radiation and on introduction of toxicants and sources of radioactive contamination. In the latter cases, the analysis of ecological models makes it possible to represent more effectively the physicochemical and biochemical significance of the LPC and LPW, including the nature of the change in the states of consumers at concentrations of harmful substances exceeding the LPC and of the "ecological reserves" of the system which determine the values of the LPW. Evidently the equations describing the evolution of eco-systems must take into account the possibility of the transfer of consumers to new states with altered properties (in particular with an altered content of harmful substances). We shall examine all these problems in somewhat greater detail.

1. Models of the evolution of eco-systems subjected to the action of toxic substances. The limiting permissible amounts of waste

To illustrate the general principles governing the allowance for the effect of toxic components on the evolution of eco-systems, we shall examine, following Kreikenbohm and Bohl,[83] a model example of a system comprising two interacting populations Y and V of microbions in the food chain:



Here X is the substrate of the organism Y which is a toxicant of the organism V, this being reflected in the above scheme by the direction of the arrow from X to V. It is assumed that, at low concentrations of the substrate, the latter undergoes degradation (consumption by the organism Y), i.e. the "environment is purified" by the removal of the substance X. However, with increase in its concentration, the substrate suppresses the functional activity of Y and thereby limits the formation of the product U, which in its turn inhibits the activity of Y. The scheme presented can, for example, describe the functioning of the phenol degrading bacteria (X = phenol, toluene, unsaturated hydrocarbons, aliphatic acids),[83] which are inhibited by the substrate X itself at its elevated concentrations (in the case examined by the above workers,[83] for $x \gtrsim 5$ mM). Their metabolic partners—the bacteria V (methanogens)—completely cease to form the products of the conversion of their substrate U (methane) at concentration $x \gtrsim 20$ mM.

The evolution of such microbiological populations can be described by the following dynamic system of formal chemical kinetic equations:[83]

$$\dot{x} = -\frac{\mu_1(x, u)}{\gamma_1} y + \tilde{D}(x_R - x), \tag{2a}$$

$$\dot{y} = [\mu_1(x, u) - \tilde{D}]y, \tag{2b}$$

$$\dot{u} = \frac{\mu_1(x, u)}{\gamma_1} y - \frac{\mu_2(x, u)}{\gamma_2} v - \tilde{D}u, \tag{2c}$$

$$\dot{v} = [\mu_2(x, u) - \tilde{D}]v, \tag{2d}$$

$$\gamma_1 > 0,\ \gamma_2 > 0,\ \tilde{D} > 0,\ x_R > 0,$$

where x and u are respectively the concentrations of the substrates X and U in the given medium, x_R is the concentration of the substrate on the surface of the source (we postulate that the substrate enters the medium by dissolving at a rate $\tilde{D} = \alpha S$, α being the rate constant for the dissolution of the substrate X and S the surface area of the substrate), y and v are respectively the densities of the populations of Y and V in the culture medium, $\mu_1(x, u)$ and $\mu_2(x, u)$ are parameters (for their model representation, see Kreikenbohm and Bohl[83]) which determine the rates of change of the densities of the populations of Y and V, and γ_1 and γ_2 are parameters relating the changes in the concentrations of the populations of Y and V to the concentrations of the substrates X and U. The second terms in Eqns. (2b) and (2d) model the effects of inhibition by the substrate X. We may draw attention to the fact that in the scheme described by Eqns. (2a)–(2d) purely concentration effects are considered without taking into account the possible changes (see below) in the functional parameters of the kinetic scheme in an evolutionary dynamic process.

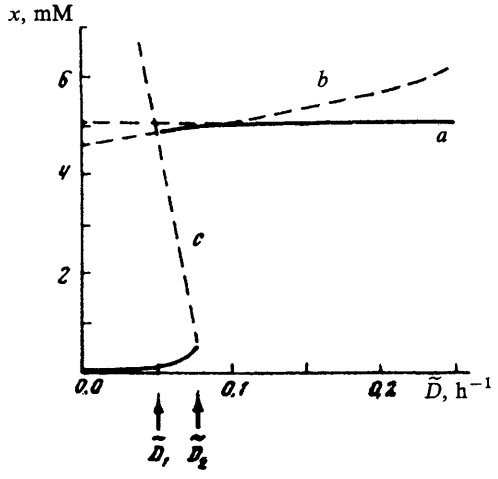


Figure 2. Bifurcation diagram for Eqns. (2a)–(2d).[83] The continuous lines along branches *a*, *b*, and *c* characterise the stationary states of the substrate.

Kreikenbohm and Bohl[83] analysed the stability of various stationary states of the system of non-linear equations (2a)–(2d). The rate of introduction of the substrate-toxicant X into the medium was examined as the controlling parameter. Fig. 2 presents the bifurcation diagram in the plane $(\tilde{D}, x)$ corresponding to the system (2a)–(2d) and constructed using a certain set of parameters.[83] The continuous lines on all three branches *a*, *b*, and *c* characterise the stationary states of the substrate X attained for any evolution of the system beginning in the vicinity of these states (stable states). The range $\tilde{D}_1$, $\tilde{D}_2$) represents the region of bistability. From the ecological point of view, the "bacteriological reactor" described functions well, provided that the system is in the region of stability of the branch *c*. The magnitude of the perturbation forcing the system components to evolve to the standard state on the branch *b*, in which the system is no longer capable of ensuring to the required extent the degradation of the toxic substance X, is thereby determined in the model.

Evidently, in a comparative analysis the parameter $\tilde{D}$ may characterise different types of toxicants added to the medium by sources with the same area of dissolving surface but with different rates of dissolution. At the same time, the differences in the value of $\tilde{D}$ can be caused by the different amounts of a definite toxicant present in the medium, i.e. by different areas of the source adding the toxicant at a specific rate. When the medium contains only one kind of toxicant, this provides grounds for relating the parameter $\tilde{D}$, for which there is a transition from the stable branch *c* to the stable branch *b*, to LPW—the limiting permissible amount of waste component injected into the medium, which is determined by the area S_{lim} injecting the toxicant. When the output of the source of the harmful component exceeds the limiting value, so that $S > S_{\text{lim}}$, the bacteria Y are no longer able to cope with the "processing" of the toxicant. In this case irreversible changes may occur in the eco-system (see below).

2. Models of the functioning of protetcing systems of the organism. Limiting permissible concentrations

As mentioned in the Introduction, living systems have been subjected throughout the entire course of evolution to powerful one-sided influences of different kinds. Under these conditions, specific protecting systems should have arisen in organisms, preventing the lethal effect of at least low concentrations of xenobiotics and other harmful components and small doses of a wide variety of harmful radiation.

Evidently such stability of biosystems in relation to changes in the parameters of the environment is possible up to a certain limit. When this is exceeded, the functional stage of the organism changes and there is then a possibility of ecological consequences for the entire eco-system owing to the existing interrelations, including food chains. Such deviations of the states of individuals from the norm can be naturally attributed to structural rearrangements in individual components or systems of the organism (enzymes, membranes, respiratory or photosynthetic chains). The Ageev–Vershubskii model,[87] proposed previously to describe the cooperative phenomena associated with the rearrangement of the polymer matrix in uptake–release processes in binary media containing surface-active and inactive components, may prove useful in this instance.

We shall consider the evolution of the structural changes in certain components of the living system occurring on uptake of a toxicant by this component. In conformity with Ageev and Vershubskii,[87] we shall consider the equations governing the evolution of two coupled quantities characterising the state of the component being examined: the concentration $c(t)$ of the toxicant component taken up by the component and the structural parameter $a(t)$ defined as the current values of the fraction of the total volume V_0 of the component undergoing structural rearrangements on uptake. We assume that $0 \leqslant a(t) \leqslant a_{\max} < 1$, where $a_{\max}$ is the fraction of the volume of the component in which the given structural changes can occur on uptake of the toxicant. We assume further that the volume $(a_{\max} - a)V_0$ which has still not been transformed and the volume $V_0(1 - a_{\max})$ which does not undergo structural rearrangements participate in the uptake process (the rate constants for the corresponding uptake processes will be designated by γ and η), while the release of the toxicant into the medium takes place via the volumes $(a_{\max} - a)V_0$ and a_0V_0 with release rate constants β and α respectively. Let k be the rate constant for the structural rearrangements which may occur in the volume $a_{\max}V_0$ of the component on uptake of the toxicant. Evidently the physical significance of the constants α, β, γ, η, and k can be discovered by constructing models at a more elementary level, taking into account the nature of the influence of the toxicant molelcules on components of the living system and specifying in detail the characteristics of the mechanism of the structural transformations occurring in the components.

According to Ageev and Vershubskii,[87] the system of equations for the evolution of the parameters $c(t)$ and $a(t)$ can be expressed as follows:

$$\dot{c} = \gamma\left[1 - \left(\frac{c}{c_s}\right)^n\right](a_{\max} - a) + \eta(c_{0s} - c)(1 - a_{\max}) - \\ - \beta c(a_{\max} - a) - \alpha c a, \tag{3a}$$

$$\dot{a} = -ka\left[a^2 - a_{\max} \cdot a + \frac{1}{4}a_{\max}^2 \frac{c_{\max} - c}{c_{\max} - c_{\min}}\right] \\ \text{when } c \leqslant c_{\max}, \tag{3b}$$

$$\dot{a} = 0, a \equiv a_{\max} \text{ when } c > c_{\max}, \tag{3c}$$

where c_s and n are respectively the uptake saturation concentration and the parameter of the dynamics of the uptake of the toxicant by components of the system which can undergo a change in their structure on uptake, c_{0s} is the uptake saturation concentration of the fragments whose structure does not change on uptake of the toxicant, and $c_{\max}$ and $c_{\min}$ are the critical concentrations of the toxicant at which abrupt transitions of the system to the state with a rearranged structure (from the initial non-rearranged state) and to the state with the initial structure (from the state with a rearranged structure) respectively begin.

In order to determine the entire set of the possible stationary states of the system (3a)–(3c), it is necessary to analyse the phase diagram of the model (Fig. 3) in the states space (a, c).[87] The intersection of a zero isocline $c = 0$, which is unique for the specified system of parameters α, β, γ, and η family of the possible curves I–IV of this type with various branches of the zero isocline $a = 0$ (the equation of state of the structure) corresponds to the stationary solutions on the phase plane. There is a possibility of the intersection of the three stable branches of the equation of state MA, GB, and BE with curves I, III, and IV respectively. An unstable solution of the system with the generation of the limiting cycle DABG and the appearance of an auto-oscillatory state in the alteration of the structure corresponds to the intersection of curve II with the unstable branch GA. Fig. 4 illustrates the kinetics of the attainment of a stationary state in the regions MA, GB, and BE by the toxicant concentrations.

Within the framework of this model, the contact between the component of the living system and the environment does not alter its structure provided that the uptake concentration of the toxicant does not exceed c_{max}. Following the dynamic attainment of the critical concentration of the toxicant taken up ($c = c_{max}$), processes inolving a rearrangement of the structure of the component begin and either reach an oscillatory state (for system parameters giving rise to the type II zero isoclines) with periodic variation (from 0 to a_{max}) of the structure of the component and of the concentration of the toxicant taken up (from c_{min} to c_{max}) or are completed by the establishment of a stationary state (a_{st}, c_{st}) of the system. For parameters giving rise to the zero isocline I, the system returns to the initial non-rearranged structural state (0, c_1), in the case of the zero isocline (III) the state (a_3, c_3) is generated, while in the case of the zero isocline (IV) the state produced is a_{max}, c_4).

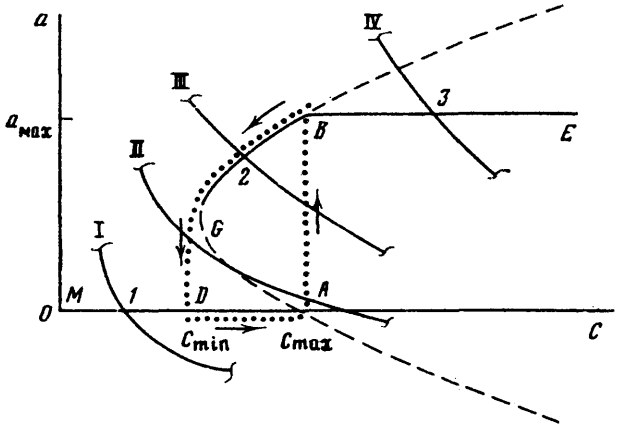


Figure 3. Phase portrait of the model.[87] Dashed lines—unstable or non-realised branches; circles—possible location of limiting cycle. The arrows indicate the direction of motion of the representative point. The numbers of solutions *1*–*3* correspond to the numbers of the regions of existence of the stationary regimes (see also text).

Thus, if the concentration c_{max} is attained in the component of the system considered for certain concentrations ρ_{lim} of the toxicant in the external environment, then it is natural to relate ρ_{lim} to the limiting permissible concentration LPC. In other words, the LPC for different individuals may be defined as the concentrations of harmful components of the external environment for which the organism undergoes a transition to another state which is different from the normal state. Such changes in states can be either reversible or irreversible depending on whether the state returns or does not return to the initial state when the harmful components are removed from the medium. In the former case, one may speak of ecological modulations, while in the latter we have ecological modifications and degradation of the system.[6] The state of the organism can then be characterised in terms of different features (the contents of the harmful component, the rate of metabolic processes, the changes in the functional activities of various systems of the organisms, disturbances in the hereditary apparatus), etc. Evidently the deviations of the states of individuals from the norm give rise to general changes in the evolution of eco-systems. In particular, an increase in the content of the harmful component (carcinogen) in certain individuals can constitute a risk to predators feeding on the given individuals, etc. This should be reflected in the system of equations for the evolution of the eco-system as a change in the "level of quality" of the predator's food. A possible scheme for the construction of equations for the evolution of eco-systems taking into account the modulating or modifying changes occurring in them under the influence of fluctuating external factors is presented below.

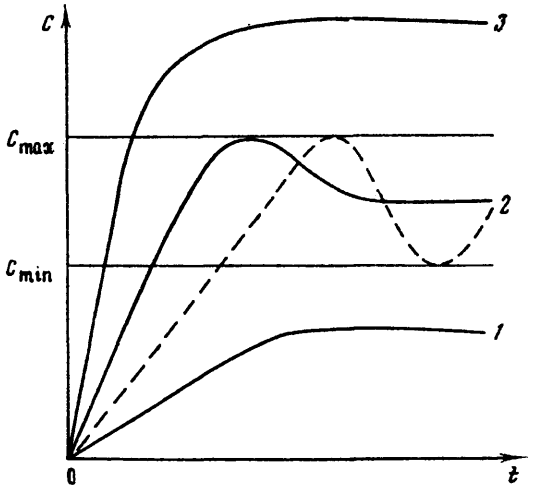


Figure 4. Characteristic form of the kinetic curves for the attainment of a stationary regime by the toxicant concentrations.[87] The numerals opposite the curves correspond to the numbers of the regions of existence of the stationary regimes; the possible occurrence of oscillatory kinetics is indicated by the dashed line.

3. Equations of the dynamics of eco-systems with allowance for various states of individuals

A general approach to the modelling of ecological modifications can be formulated on the basis of kinetic equations for space–time distribution functions of the subsystems in the overall space of the characteristic parameters with introduction of functions of random sources and sinks modelling the characteristics of the changes in state both as a result of the internal activity of the above subsystems and due to factors external to the systems.[20] The deterministic nature of the kinetic equations makes it possible to determine beforehand the nature of the possible states and to estimate their relative stabilities, while the fluctuation influences on the system determine the occurrence of one of several possible states in the vicinity of the bifurcation point.[77]

Since biological systems are highly non-equilibrium and open systems, in the analysis of their evolution it is necessary to take into account two fundamental factors. Firstly, the probability of the transition of the system to one of the stable states beyond the bifurcation threshhold of the thermodynamic branch when some

kind of controlling parameter λ is altered depends on the specific state of the system in the given time interval. The population of the species, the solar activity, the ionisating radiation dose, the amount of dissolved organic matter of allochthonous or autochthonous origin (if one is dealing with aqueous systems) etc. may be considered as the controlling parameter.

Secondly, the evolution of the highly non-equilibrium eco-systems can be effectively acted upon by weak external factors. In principle, without exerting any effects on equilibrium systems, such factors can determine the preferred selection of a particular stationary state beyond the bifurcation point ("forced bifurcation"[20]). Such factors may be, in particular, electromagnetic radiation in different frequency ranges (starting from weak low-frequency influences[88]), changes in the qualitative composition of the environment, etc. The accumulation of the changes occurring under these conditions and the subsequent fluctuation influences of diffeent kinds may lead either to slight but fundamental changes in eco-systems or to new bifurcation transitions.

Evidently the modelling of the evolution of eco-systems involves major fundamental and mathematical difficulties. Each eco-system is a multicomponent object with a multiplicity of internal feedbacks (including negative feedbacks) and subjected to multifactor influences of a wide variety of different types. The state of each system can be described by the distribution function $f(t, \mathbf{r}, \Gamma)$, where t is the time, $\mathbf{r}$ the radius-vector, and Γ the set of parameters determining the state of the given system. For a quantitative analysis of the equations for the evolution of the system (kinetic equations for the function f), complicated in many instances *a priori* by the uncertainty and the ambiguity in the overall parameters Γ, it is convenient to employ characteristics introduced in the mathematical description of random motion in mechanical and hydrodynamic systems.

Conservative systems are usually considered for which an element of the phase space undergoes a change in shape after a time but retains its volume, and dissipative systems for which the volume of the element of the phase space contracts during motion, i.e. structure formation in the system takes place as a result of an external excitation with increase in the controlling parameter. Dissipative systems are coherent. They behave as a single whole as if each species were "informed" about the state of the system as a whole. Under these conditions, a decrease in the controlling parameter in classical dissipative systems leads reversibly to the initial state of the conservative system.

In eco-systems the situation may be fundamentally different. The changes occurring in communities under conditions of the reversible alteration of certain controlling parameters may be reversible and irreversible, i.e. may be characterised by a kind of "hysteresis". The irreversible changes in eco-systems, including those characterised by a decrease in the volume of elements of a generalised phase state $(\mathbf{r}, \Gamma)$ will be defined here as ecological modulations. The irreversibility of the changes occurring in the eco-system shows that the magnitude of the controlling parameters has exceeded the adaptive possibilities of the biocenosis. Here one should refer to ecological modifications and, when metabolic and ecological regression processes have developed,[6] to eco-system degradation processes. Evidently in each specific case it is necessary to determine in addition the minimum level of irreversible changes, indicating the occurrence of ecological modulations and modifications and of ecological regression. In particular, one can detect changes in the genetic apparatus.

So far several systems are known (mechanical, hydrodynamic, etc.) for which it is possible to describe analytically the phenomena involving the appearance of dissipative structures under the influence of controlling factors (the constraining force on excitation of the motion of a pendulum, the temperature difference in the Benard system, the energy introduced into the Henon–Hales system,[77] etc.). In ecological systems one cannot even be certain about the adequacy of the description of stationary states and difficulties arise even in the modelling of the deterministic behaviour of such systems. We shall therefore refer only to qualitative analysis of the characteristics of the evolution of communities.

The nature of the transition to bifurcation points and the factors which determine such transitions to new levels of organisation of communities are of interest. In this case, it may prove sufficient to analyse a relation for the correlation function of fluctuations ("correlator") which is simpler than for the distribution functions $f(t, \mathbf{r}, \Gamma)$:

$$\delta g_a = \int \langle \delta f_a(t_1; \mathbf{r}_1, \Gamma_1) \delta f_a(t_2; \mathbf{r}_2, \Gamma_2) \rangle \mathrm{d}\Gamma_1 \, \mathrm{d}\Gamma_2 \,, \tag{4}$$

where $\delta f_a = f_a - \bar{f}_a$, where $\bar{f}_a$ is the stationary distribution function for the subsystem a. The symbol $< \ldots >$ denotes averaging over all possible states of the subsystem. In the case of spatially homogeneous systems, the averaging involves integration with respect to one of the radius-vectors and one of the times. Here one introduces the variables $\mathbf{r} = \mathbf{r}_1 - \mathbf{r}_2$ and $\tau = t_1 - t_2$. In particular, the average residence time of substances in a flow reactor is the external controlling parameter for the classical Belousov–Zhabotinskii reaction—the oxidation of malonic acid in the presence of cerium sulphate and potassium bromate where spectroscopic methods detect oscillations in the concentrations of Ce^{3+} and Ce^{4+} as a function of time. In this case the function $\delta g(\mathbf{r}, \tau) = \delta \bar{g}(\tau)$ introduced is a measure of the correlation between the successive changes in the Ce^{4+} concentration detected from the selective light absorption by these ions. For a regular motion, the function $\delta \bar{g}(\tau)$ is constant or oscillates, while in the chaotic regime $\delta \bar{g}(\tau)$ decreases rapidly (frequently exponentially) with time.[77,89]

Naturally the equations describing the evolution of the function $\delta g(\tau)$ are in general complex and difficult to analyse but the use of the phenomenological approximations to the correlation times, usually employed for such equations, may become a basis for the qualitative analysis of the models of eco-systems. Indeed, solutions of the equations for the function f when the system is acted upon by stochastic factors should be treated either in terms of generalised functions[90] or, following the Langevin method,[91] in terms of probabilities—as functions of the density of the probability of the occurrence of various values of f. At the same time, analysis of the relaxation equations, which are naturally not as informative as the equations for f, may prove an easier task. Here it is more convenient to analyse the equations for the Fourier components:

$$\delta \varphi_a(\mathbf{k}, \omega) = \int_{-\infty}^{+\infty} \int \delta g_a(\mathbf{r}, t) \exp[-i(\mathbf{kr} - \omega t)] \, \mathrm{d}\mathbf{r} \, \mathrm{d}t. \tag{5}$$

This is partly associated with the simple analytic form of the Fourier components of external stochastic influences.

We shall now quote the simplest example of the introduction of relaxation equations for correlators in a linear approximation, where the "equation of motion" for the function $\delta \tilde{f}_a(t)$ assumes the form

$$\frac{\mathrm{d}}{\mathrm{d}t} \delta \tilde{f}_a = -\sum_b \lambda_{ab} \delta \tilde{f}_b, \tag{6}$$

where λ_{ab} are constant coefficients. Correlators of the quantities $\delta\tilde{f}_a$ satisfy the same linear equations:[92]

$$\frac{d}{dt}\langle\delta\tilde{f}_a(t)\delta\tilde{f}_c(0)\rangle=-\sum_b\lambda_{ab}\langle\delta\tilde{f}_b(t)\delta\tilde{f}_c(0)\rangle,\quad t>0 \quad (7)$$

(the subscript c in this system of equations is of arbitrary significance). When the system departs appreciably from equilibrium and also when it is acted upon by random factors capable of displacing it from the initial stationary state, the equations describing the devleopment of the system prove to be non-linear.

The simplest non-linear equations with feedback,[76,93,94] in which account is taken of interspecies interactions and also of influences of abiotic factors on the system, are usually analysed in relation to the evolution of eco-systems. A way of describing the state of the system, differing somewhat from that in the literature,[76,93,94] is described below. It makes it possible to use the above synergistic approaches[20,77] for the analysis of the evolution of eco-systems taking into account all the existing internal interrelations (including positive and negative feedbacks) and external factors.

The state of eco-systems may be characterised by the presence of a definite number of trophic levels. We shall attribute to each organism of the given eco-system two numbers (ij). The order of the trophic level will be designated by the index i ($i = 1, 2, \ldots, l$), starting from the highest-order level of consumers ($i = 1$) and ending with the level of producers ($i = l$). The numbering of individuals in each trophic level i will be specified by the index j ($j = 1, 2, \ldots, N_i$), where N_i is the number of individuals in the level i. We shall assume that each individual is in one of several possible states (these states s may be characterised from the standpoint of physiology, biochemistry, etc. depending on the formulation of the problem and the level of the problem considered).

Let θ_{ij}^s represent the relative populations of each of the states $s(ij)$ for individuals (ij) subject to the normalisation condition

$$\sum_s\theta_{ij}^s=1.$$

Under these conditions, certain stationary states of the population $\theta_{ij}^{s_0}$ correspond to the state of the eco-system in the norm. The states s_0 and the corresponding values of $\theta_{ij}^{s_0}$ depend in the general case on the natural age of the entire eco-system and on its previous history and vary with fairly large characteristic times in conformity with the programmed most probable evolution of the given eco-system up to its significant modification with transition to a climatic state. Since we are interested in evolutionary changes associated with the influence of external factors of the community and occurring over a much shorter time than that of natural succession, we shall consider the evolution of an eco-system as a quasi-stationary process and shall not introduce explicitly the time variation of s_0. We shall represent the equations for the evolution of the eco-system in the form

$$\frac{d\theta_{ij}^S}{dt}=\sum_{i'j';s'}\hat{D}[\theta_{ij}^s|\{\theta_{i'j'}^{s'}\}]+$$

$$+\sum_{s'}\hat{L}[W(ij;s'\to ij;s)\theta_{ij}^{s'}-W(ij;s\to ij,s')\theta_{ij}^s]+(g_{ij}^s-r_{ij}^s), \quad (8)$$

where $\hat{D}$ is a non-linear operator defining the evolution of the eco-system as a consequence of the internal interrelations present in it under standard external conditions ensuring natural evolution. The second term, characterised by the action of the linear operator $\hat{L}$, defines the influence on the evolution of the system by the fluctuations of external factors in time and the influence of factors of a new kind (for the given eco-system) expressed in terms of the probabilities W of the transition of the system from the state s to adjacent states s' and the reverse transition from the possible state s' to the state s.

For example, when biocidic ionogenic additives are introduced into the environment, ionic impurities are incorporated into a wide variety of components of the organism, in particular into the active ion transport systems, which can influence fundamentally the kinetics of their functioning as a consequence of changes in the initial distributions of local electrostatic fields in the vicinity of ionic channels in a biological membrane and also the possible conformational rearrangements in the protein–lipid complexes.[24] This factor may be taken into account by altering the probabilities $W(ij;\ s\to ij,\ s')$ in Eqn. (8) and it should influence the populations θ_{ij}^s and hence the evolution of the entire eco-system. Evidently the influence of ionising radiation on the structural elements of biological systems can be described similarly [in terms of the change in the probabilities $W(ij;\ s\to ij,\ s')$].

The time-variable quantities such as the pH, intensity of the thermal and UV radiations, concentration of nutrient substances (if one is dealing with aqueous cenoses), etc. may behave as the fluctuating factors in Eqn. (8). The inclusion of "new" factors in the second term implies the possibility of a significant influence by the latter on the evolution of the eco-system. The third term in Eqn. (8) characterises the rate of change of the population θ_{ij}^s as a consequence of external sources (g_{ij}^s) and sinks (r_{ij}^s) and contains a component rapidly fluctuating in time. Therefore, in the second and third terms it is sometimes convenient to differentiate fluctuation components and to represent them by generalised functions, for example:

$$g_{ij}^s-r_{ij}^s=\sum_k a_{ij;k}\theta(t-t_k),\quad \theta(x)=\begin{cases}1 \text{ when } x>0\\ 0 \text{ when } x<0\end{cases} \quad (9)$$

or

$$g_{ij}^s-r_{ij}^s=\sum_k b_{ij;k}^s\delta(t-t_k). \quad (10)$$

Here $\delta(x)$ is a delta-function.

Assuming that the second and third terms are perturbing factors, it is possible to analyse the devleopment of the eco-system under the conditions where these factors operate, provided that the evolution of the unperturbed system, expressed in a general form by a system of non-linear equations for the populations $\overline{\theta}_{ij}^s$, is assumed to be known, i.e. the relations $\overline{\theta}_{ij}^s=\overline{\theta}_{ij}^s(t)$ are known. In order to obtain these relations in each specific case, it is necessary to set up and solve the corresponding model system of non-linear equations whose parameters can be obtained in the course of special studies. As pointed out above, we shall be interested in the variation of the differences $\delta\theta_{ij}^s=\theta_{ij}^s-\overline{\theta}_{ij}^s$ as a function of time. We do not assume that these changes are small in the general case ($\delta\theta_{ij}^s\lesssim 1$). As a consequence of the non-linear inter-relations in the system, the change in the populations of states s (with the transition $s_0\to s_1$) for the individuals (ij) may influence significantly the evolution of the entire system as a consequence of the influence of "weak" factors.

Evidently a fully defined state s_0^ξ should correspond to each set ξ of external factors (natural for the given eco-system). If one may formulate the concept of a mutually unambiguous correspondence between the states s_0^ξ and the state of the environment, then the

changes in the values of s_0^{ξ} (transition to adjoining states s from the state s_0) will be qualified as a modulation transition. On the other hand, if irreversible changes in the states s_0 take place (for example, there is a transition to the state s' accompanied by a change in hereditary structures), then we shall refer to the modification or degradation of the states of (ij). In this case fundamental changes may occur in the entire eco-system owing to the existence in the latter of internal interrelations. The problems of the evolution of the eco-systems involve precisely the discovery of the possibilities of such irreversible changes detected via the functions $\delta\theta_{ij}^{s}(t)$. As mentioned above, it is more convenient to analyse the evolution of correlators

$$\delta g_{ij}^{ss'}(t)=\langle\delta\theta_{ij}^{s}(t)\delta\theta_{ij}^{s'}(0)\rangle,$$

where s' is any of the possible states or components of the specific spectrum $\delta\varphi_{ij}^{ss'}(\omega)$.

V. The influence of mass transfer processes in the earth–atmosphere system on the state of the biosphere

The preservation of life on Earth under the conditions of continuing intense anthropogenic influences may depend to a large extent on a series of global factors influencing the evolution of large eco-systems (seas and oceans and part of the continents). Here we have in mind the phenomena occurring not only in the Earth's biosphere but also in the upper layers of the atmosphere and in the deep layers of the Earth. These are in the first place the turnover of water and of biologically important elements (C, O, N, P, and certain others) in nature. The occurrence of the corresponding cycles is varied and, apart from the movements of water in the atmosphere and streams of subterranean waters carrying a wide variety of inorganic and organic components, it may involve the circulation of water in the oceans[95,96] and the turnover of the oceanic crust (its formation from melts in the reservoir in the Earth's mantle accompanied by their partial degassing with subsequent subduction of the oceanic lithosphere[97]).

1. Processes in the upper layers of the atmosphere

In this Section we shall discuss the possibility of the existence of fairly intense flows of water, the molecules and cluster of which can entrain also other inorganic and organic components in the upper atmosphere, into the stratosphere and further into the ionosphere and space. The discovery and quantitative analysis of the magnitude of such directed fluxes of substances is essential for the construction of models of the evolution of large eco-systems and for the understanding of the evolution of the entire biosphere as a whole.

The evident influence of the upper layers of the atmosphere on the evolution of biological communities is demonstrated by the ozone layer, which protects biocenoses against the harmful effects of intense UV radiation.[33] The conclusion of international agreements limiting the manufacture and large-scale employment of Freons, which, without reacting with the tropospheric radicals, enter freely the stratosphere, has in fact been associated with the global nature of the danger of the breakdown of the ozone layer on photodissociation of the Freons in the stratosphere.

Many inorganic and organic compounds have been detected in the upper atmosphere at heights of approximately 100 km,[98–100] which indicates the unsuitability of equilibrium barometric ideas for the determination of the density and composition of the atmosphere. At the heights indicated, water may be present in anomalously large amounts, forming silvery clouds, and the sources of this water are by no means always associated with volcanic eruptions. Seasonal changes in the relative concentrations of sodium and potassium in the silvery clouds have been detected, agreeing in the summer with the ratio characteristic of sea water.[99] This shows that sodium and potassium enter the silvery clouds with the wind-driven sea water spray and points to terrestrial rather than cosmic (as a consequence of the interaction of the solar wind and the ionosphere) causes of the appearance of silvery clouds at the heights indicated.

The rate of supply of a wide variety of components from the troposphere to the upper layers of the atmosphere is determined primarily by the turbulent mixing of the atmosphere at least up to heights of approximately 110 km.[101] Evidence for the existence of intense migrations of air masses at heights of 80–90 km (the rate of the wind-induced displacements is approximately 1–2 km h^{-1}) was obtained, in particular, by analysing the form of the silvery clouds and also on the basis of spectroscopic data.[102] A possible source of the turbulence, ensuring the transport of components indicated, is internal gravitational waves propagated from the regions of active meteorological processes occurring in the lower atmosphere (fronts, zones of increased activity) and also from mountainous regions.[101]

The transport of water to the upper atmosphere can be effected by charged water clusters in the electric fields arising between storm clouds in the ionosphere.[98] According to estimates,[98] approximately 1 g of H_2O can be transported with ionic clusters containing 10 H_2O molecules from an area of 1 km^2 per hour with a characteristic overall current of approximately 0.1 A. This corresponds to the water content in a silvery cloud with a volume of approximately 1 km^3 and made up of ice particles approximately 0.12 μm in diameter at a concentration of ~0.1 of a particle per cm^3. Evidently such "upward rain" or "rain on the ionosphere" should eliminate aerosol particles and gaseous components dissolved in water from the atmosphere.

The subsequent transfer of the water molecules and the impurity species, which partly dissociate and ionise, to the upper layers of the ionosphere can occur under the influence of convective plasma streams developing in the ionosphere–magnetosphere system as it drifts through crossed electric and magnetic fields. The electric fields in the boundary regions of the ionosphere arise regardless of the possible fields between powerful storm clouds and the ionosphere.[103,104] Analysis has shown[105] that various types of distribution of the large-scale electric field may arise in the ionosphere–magnetosphere system. A definite type of convective movement of the plasma corresponds to each distribution. The characteristic inhomogeneities existing under these conditions, whose extent in space is approximately $10-10^3$ km,[106] may influence strongly the kinetics of the removal of the components to the upper layers of the ionosphere, including the region of the exosphere (above 500 km) where processes involving the thermal heating of the species as a result of the absorption of UV quanta by oxygen and nitrogen molecules from sunlight take place vigorously. A proportion of the molecules and atoms then acquire thermal velocities exceeding 11.2 km s^{-1}, which is sufficient to drive the species outside the limits of the Earth's atmosphere.

The removal of components of the Earth's atmosphere (predominantly water molecules and the oxygen atoms and ions formed as well as nitrogen atoms and molecules) outside the limits of the Earth's gravitational field occurs also on interaction of the solar wind—the stream of charged particles (predominantly protons,

helium nuclei, and electrons) emitted by the sun—with the external layers of the ionosphere, which form the boundary of the magnetosphere and are turned towards this stream.[103] In the transition layers, formed at the boundary of the region of the strong magnetic field (magnetosphere) and the rapidly moving plasma, strong electric fields arise.[107,108] These fields can induce magnetospheric convection—the acceleration of plasma streams, which promote the removal of neutral and charged components into the region of the direct influence of the solar wind, which "blows off" the atmospheric species into space. The high energy components of the solar wind penetrate the atmosphere down to heights of 40–60 km, so that the processes involving the "blowing off" of species can proceed with different efficiencies as a function of the thickness of the atmosphere—from the mesosphere up to heights exceeding approximately 1000–1500 km, where appreciable concentrations ($\sim 10^2$ cm^{-3}) of oxygen and nitrogen ions have been detected by modern instruments.[109] The possibility of the operation of this mechanism of the removal of atmospheric species into space is indicated by data concerning the effect of the solar wind on cosmic rays. Under conditions where the Earth crosses part of the recurrent high-speed stream of solar wind, part of the stream of cosmic rays "intended" for the Earth is driven off and does not reach the Earth.[110]

The efficiency of the "blowing off" effects increased with increase in the velocity of the particles in the solar wind, provided that their energy is sufficient for the generation of secondary particles and the formation of particle showers, since large overall momenta can then be transmitted to the species (ions, molecules, and clusters) in the atmosphere. It has therefore been of interest to analyse the phenomena occurring on the sun and responsible for the increase in the velocity of the particles of the solar wind. It has come to be assumed that the high-speed streams of the solar wind arise in the coronal holes or in unipolar magnetic regions with an open configuration of the magnetic field.[111] Another possibility for the generation of high-speed streams of the solar wind may be associated with the non-stationary processes in the active regions of the sun or in the vicinity of active formations.[111–113] The acceleration of the protons emitted by the sun is induced, in particular, by the formation at distances of approximately 2000 km from the sun's surface, where the temperature and density decrease sharply, of magnetohydrodynamic Alfven waves,[114] into which the non-linear acoustic waves generated by the layers of the sun's photosphere are transformed.

The generation of streams of the solar wind having anomalously high energies, up to relativistic values, has in fact been attributed to the Alfven waves arising in powerful solar eruptions. The fact that the energies E_p of the protons emitted by the sun can be $E_p \lesssim 3000$ MeV is indicated by the streams of neutrons (these are formed in the atmosphere together with π-mesons) having energies up to 1000 MeV after certain solar eruptions (for example on 21st June, 1980 and on 3rd June, 1982).[115,116]

Since the high speed streams of the solar wind can intensify the "blowing off" of the components of the atmosphere into space, the elucidation of adequate mechanisms of the formation of such streams and of the relation with the visible phenomena and processes on the sun (see also the footnote on p. 1197 below) is important for the analysis of the processes involving the partial "replacement" of the components of the atmosphere and its purification (see below), which influence the evolution of the Earth's biosphere. This is of particularly great current interest in connection with the intensification of the anthropogenic influences on the Earth's ionosphere by powerful electromagnetic radiations, by chemical substances emitted during the flights of ultrasonic aeroplanes, and by the ignition of powerful rockets[117,118] and also in connection with the possibility of stimulating the processes in the ionosphere (for example, on excitation in the latter of plasma-wave discharges[119]).

Naturally, the fluxes and composition of the components carried away from the Earth vary with time and depend on many factors. The discussion in the present Section of the entire set of problems of the "upward mass transfer" beyond the limits of the Earth's gravitational influence appears essential, because it is not clear *a priori* which of the stages of the transport of the components of the atmosphere (primarily water, oxygen, and nitrogen) into space is rate-limiting. It might be thought that each of the stages considered above may under certain conditions prove to be rate-limiting. In the next Section, we shall discuss the range of problems associated with the discovery of the processes occurring in the inner regions of the Earth, which are responsible for the current stable state of the atmosphere despite the processes involving the "cleaning" of the atmosphere by the removal of its components into space, described above.

2. Processes in the inner regions of the Earth

The deep layers of the Earth exert not only a direct influence on the eco-system (during earthquakes or on emission into the atmosphere of the products of volcanic activity) but also an indirect influence, determining the Earth's magnetic field. The influence of the magnetic field on the evolution of eco-systems is exerted when it acts on the functioning of biological objects[24,88,120] and also on the state of aqueous systems as living environments.[24,48,49]

It will be shown below that processes associated with the generation of the Earth's magnetic field can also lead to ecological consequences. According to existing ideas,[121–125] the observed magnetic field is caused by the convective movement, arising in the course of the Earth's rotation, of the conducting medium—the Earth's liquid metal core enclosed in a spherical layer with dimensions $0.19\ R_0 < R < 0.57\ R_0$ between the mantle and the solid inner core (R_0 is the Earth's radius). An obligatory condition for the functioning of this mechanism ("the dynamo-mechanism") is the gyrotropic nature (reflecting non-invariance) of the convective streams in which either right-hand screw or left-hand screw motions should predominate. Mathematically this is expressed by the non-zero value of the average helicality of the streams generated: $\langle \mathbf{v}\,\mathrm{rot}\,\mathbf{v}\rangle \neq 0$, where $\mathbf{v}$ is the local flow rate vector. The Earth's magnetic field has a poloidal (meridional) component with lines of force in the meridional plane and a toroidal (azimuthal) component in which the lines of force run along the latitudes. Under these conditions, only the meridional field has a radial component and extends into the environment. The convective movements in the liquid-metal core, with different angular velocities of the rotation of its different layers, lead to the transformation of the magnetic field indicated, including the interconversions of the components specified above.[121,122] The energy consumed under these conditions on dissipation in the functioning of the dynamo is evolved in the gravitational separation processes in the Earth's liquid core—in the precipitation of heavy substances, in the first place iron, at the lower limit of the liquid core and of light substances, containing the elements S, O, and Si, at its outer limit.

It is important to emphasise that the dynamo-mechanism is merely a mechanism of the intensification of certain seeding magnetic fields, which are generated in the Earth's liquid core. According to Dolginov,[122] the most probable mechanisms of the

generation of such fields are associated with galvanoelectric phenomena, in particular with the "battery" effect. The latter is characteristic of the Lorentzian plasma[92] when the electron concentration and pressure gradients are not parallel. Under the conditions on Earth, the battery field is naturally associated with the large-scale irregularities in the temperature and chemical composition at the interface between the mantle and the liquid core. The changes in the magnitude and sign of the geomagnetic field which occurred in the course of geological epochs (such data are obtained from the analysis of the magnetisation of ancient rocks) are associated, according to Dolginov,[122] with the change in the composition of the interface as a result of the exchange of material between the mantle and the core (cf. Ruzmaikin et al.[124]).

Despite the comprehensive development of the theory of terrestrial magnetism, the question of the nature of the convection in the Earth's core, the nature of the seeding magnetic fields, has still not been unambiguously solved. We shall consider below one of the possible hypotheses[24] concerning the nature of the seeding geomagnetic field, from which follow a series of global consequences related to the evolution of the Earth's eco-systems and to the characteristic features of the formation of a number of useful minerals, the optimum search for and the rational employment of which constitute an important aspect of man's nature-protecting activity.

It has been postulated[24] that in the region of the boundary between the outer part of the Earth's liquid metal core and the lower mantle, where high pressures are combined with shift deformations and the breakdown (regrinding) of rocks, endothermic chemical reactions take place. One of the initial reactants (hydrogen) is dissolved at high concentrations ($\sim 10^{24}$ cm^{-3}) in the Earth's liquid metal core (this hypothesis does not conflict with the possible ideas concerning the formation of our planet).[126]† According to this hypothesis, the Earth's core is a fairly capacious source of hydrogen, which has been active in the course of more than two billion years, i.e. throughout the existence of the hydrosphere. For the densities of the hydrogen dissolved in the Earth's core indicated above, its mass ($\sim 2 \times 10^{26}$ g) exceeds the overall mass of hydrogen in the hydrosphere (1.8×10^{23} g) by three orders of magnitude. This hypothesis is justified by the multiplicity of the consequences arising from it (see below), some of which are apparently susceptible to direct tests. Under the conditions indicated, the hydrogen, which is present in the atomic ionised state in a melt of catalytically active iron-group elements and other heavy elements, can effectively reduce the metal oxides MO_x in the lower mantle with formation of water:

$$MO_x + xH_2 \dashrightarrow M + xH_2O, \qquad (11)$$

and can interact with the metal carbides in the lower mantle, forming methane:

$$M_pC + 2H_2 \dashrightarrow CH_4 + pM. \qquad (12)$$

Water arises also on interaction of hydrogen with the oxygen approaching the core–mantle interface. The products formed as well as the helium and nitrogen emerging from the core are removed to the upper layer of the mantle and then into the Earth's crust.

†Another consequence which may follow from the above model[126] is that helium, nitrogen, and oxygen are dissolved (in smaller amounts than hydrogen) in the Earth's core.

Presumably the interface between the Earth's core and the mantle is not an ideal sphere. It is more likely to be "indented" in a radial direction from the centre and is non-uniform as regards the composition of the rocks at the boundary with the liquid core. In view of the high rates of the catalytic processes indicated, convective mass streams may be initiated in a number of regions of such a non-uniform boundary in the liquid phase of the core. They may be responsible for the transfer of hydrogen to the reaction zones and the temperature gradients generated in endothermic chemical reactions [in the first place on occurrence of reaction (11)] may give rise to certain spatially fixed dissipative structures. Owing to the establishment of non-uniform (with respect to the interface) temperature jumps

$$\Delta T(\mathbf{r})|_{s_i} = T_{s_1}(\mathbf{r}) - T_0 < 0,$$

where $T_{S_i}(\mathbf{r})$ is the local temperature of the lower mantle–liquid core interface (the surface S_i) and $T_0 \equiv T_{S_0}$ is the temperature "at the bottom" (the surface S_0) of the convective zone considered, structures of a mixed type can be formed—Benard[77] and Marangoni[127] structures. Evidently, owing to the non-uniformity (chemical, temperature-dependent) of the surface, asymmetric irregular dissipative structures (humps, eddies) should arise. Such irregularity gives rise to a non-zero average helicality of the streams of the liquid-metal medium generated, which is essential for the generation of the seeding magnetic field.

Owing to the presence of a temperature gradient in the radial direction in such convective structures the temperature in each section parallel to the interface varies within the limits of the cell[77] from a certain maximum quantity at the cell boundary S_u, where the convective stream is directed from the bulk of the core upwards towards the interface, to the minimum value at the boundary S_d, where the stream is directed downwards—into the bulk of the core. Conditions are thereby created for the occurrence of thermodiffusion streams (the Soret effect) of the highly mobile electronic component in the direction from the boundary S_u to the boundary S_d. As a result of this, electric fields $\mathbf{E}_c$, compensating the thermal diffusion electron stream, arise in the region between the above boundaries. These fields must be characterised not only by the components $E_c^{\perp}$ normal to the S_u and S_d surfaces (as a consequence of the Soret effect) but also by the components $E_c^{\parallel}$ parallel to the above surfaces (owing to the variation of the average temperature in the radial direction). Under these conditions, double electrical layers are formed at the boundaries S_u, S_d, S_i, and S_0 and also in the sections S_m through the convective zone where the quantities $T(\mathbf{r})|_{S_m}$ are characterised by local minima or maxima.

It is to be expected that the redistribution of the labile electron density as a consequence of the Soret effect and the generation of the electric fields $\mathbf{E}_c$ lead to additional stabilisation of the dissipative structures. In addition, owing to the appearance of the electric field component $E_c^{\parallel}$, closed circuits L are formed in each dissipative cell, in which eddy currents flow:

$$\oint_L \mathbf{E}_c \, d\mathbf{l} = -\frac{1}{c}\frac{d}{dt}\int_S \mathbf{B} \, d\mathbf{S} \neq 0,$$

where $\mathbf{B}$ is the electromagnetic induction vector, $d\mathbf{l}$ a differential element of the closed circuit L, and S the surface resting on the circuit L.

Evidently in the dissipative cell adjoining the cell under consideration an eddy current flowing in the opposite direction is generated. However, owing to the non-uniformity, mentioned above, of the convective structures formed, in the system investigated the induced resultant magnetic field can be regarded, together with other fields analysed,[122] as a seeding field. The orientation of the circuits L will depend on the geometrical characteristics of the chemical non-uniformities of the interface and on the differential rate of rotation of the liquid-metal phase of the core in the region of the formation of the dissipative structures considered.‡

Evidently the geomagnetic field (when the model considered is adequate) must be associated with the convective mass streams in the Earth's core, of maximum spatial extent, which are generated on reduction of oxides (the commonest compounds in the mantle) accompanied by the formation of water. In a critical analysis of this hypothesis, it is essential to take into account the available data concerning the distribution of water in the Earth's crust and in the hydrosphere during different geological eras and the stochastic changes in the Earth's magnetic field occurring in the given model as a consequence of the decrease in the rate of the chemical reaction (either as a consequence of the exhaustion of the oxides at the core–mantle interface or due to the limitation of the product removal stages). At the same time, data concerning the stochastic nature of the changes in the geomagnetic field apparently give rise to conclusions about the structure of the liquid core–lower mantle interface and about the kinetics of the endothermic reactions occurring in this region and initiating the formation of dissipative structures in the Earth's liquid core. This makes it possible in its turn to predict further changes in the geomagnetic field, which is of undoubted importance for ecological modelling.

A further series of consequences with an ecological and nature-protecting bias follow from the foregoing and refer to problems of the formation of useful minerals. The discovery of the mechanisms of the formation of deposits of ores, petroleum, gas, and coal is useful not only from the standpoint of an effective search for them but also for the rational mining and exploitation of these deposits, which is particularly important since the Earth's resources are already to a large extent exhausted. A theory of the mixed inorganic and organic nature of the formation of petroleum can be established on the basis of the hypothesis that processes (11) and (12) occur.

The methane generated in reaction (12) may participate in the chain of further catalytic incomplete oxidation (with participation of water and oxygen molecules) and hydrogenation processes. These reactions, occurring in the submicropores of the rocks in the Earth's lower mantle at more moderate temperatures than those corresponding to the formation of methane, lead to the synthesis of alkanes (possibly via the formation of CO,[129] alkenes, alkadienes, alkynes, arenes, and acenes,[130–134] which are the simplest components of petroleum.

The subsequent pathway leading to the conversion of the above components into more complex and heavier petroleum fractions involves the transfer of the components via a system of transport channels under the influence of static pressure gradients into regions where their organic (possibly in the presence of fossil residues of organic and bio-organic nature "stored" in these regions) and microbiological transformation takes place under the conditions of diagenesis.

Numerous special studies have been devoted to the problems of the biochemistry and geochemistry of petroleum formation.[135–141] The proposed scheme apparently makes it possible to reconcile the theories of the organic and inorganic origin of petroleum. Firstly, it incorporates naturally organic and microbiological reaction stages,[138–140] including those discovered in the study of petroleum biomarkers.[140] Secondly, the scheme developed here makes it possible to understand the inorganic origin of petroleum and gas in deep deposits.[141] It is regarded as established[142] that the existence of petroleum and gas deposits requires that the deposit be provided with an additional supply of natural gases, in the first place methane, from deeper regions with their partial outflow and scattering in the Earth's troposphere ("ascending mass transfer"), where the hydrocarbons are oxidised to CO_2 in photochemical reactions. The inflow of gaseous hydrocarbons together with hydrogen and helium into bore holes driven into a crystalline foundation has been detected at depths of 2–12 km.[130,143]

Analysis of maps of known petroleum and gas deposits (with discrimination between them as regards type and age) with the aim of their possible inclusion in a single system of "pores" (sites where petroleum and gas have accumulated) and "channels" (transport ways) would be of undoubted heuristic interest from these standpoints. Such systems of pores and channels should begin in the region of the interface between the liquid-metal core and the lower mantle, should pass through the mantle and the Earth's crust, and should terminate in the deposits. The transport pathways may include channels with submicroscopic dimensions and also macrocracks (fluid breaks),[144] through which the continuous hydrcarbon phase is transported. It is evidently necessary to analyse maps on different scales in order to discover the "self-resembling" scale-invariant fractal rules.[145]

Naturally the specification of the proposed scheme in a more concrete form must reflect the genetic relation between the latest shifts of the Earth's crust and the formation of various types of accumulations of petroleum and gas and also the dependence of the phase and chemical compositions of the hydrocarbon deposits on the direction and activity of the latest displacements and on the intensity of the heat flux. Data obtained by deep seismic probing in tectonic studies have shown (this does not conflict with the model) that the Earth's crust is subdivided into blocks of differnt shape and size as a consequence of the formation of vertical and inclined zones with breaks and cracks, many of which can be traced as far as the upper mantle.

Ore formation processes can be considered similarly. They are known to depend largely on the distribution in the Earth's crust of convective fluxes of geothermal waters and on the mineral composition of the rocks through which water is transported to the core-forming zones. When water interacts with the rocks, the composition of the fluid, including the isotope composition of the oxygen in water, evolves. The latter factor provides an effective instrument for the analysis of the ore formation processes. In particular, conclusions have been reached for specific deposits concerning the nature of the structure of the fluid fluxes on the way to the ore formation zones, about the amount of water which has passed through a wide variety of rocks during specific periods of time, about the rate of cooling of rocks, about the features of the

‡ Electric fields of the type indicated can also be generated in the convective region of the sun and in the relatively stable convective structures of the solar atmosphere.[128] These fields not only ensure an additional stability of the structures in the solar plasma but also act as a factor accelerating charged particles (protons, electrons), causing an increase in the energy of the particles of the solar wind (external effect) and non-isothermal nuclear synthesis in the region of the lower boundary of the convective zone (internal effect).

spatial distribution of temperature in the ore formation zones for different times, and about the sequence of the formation of various sections of the deposits.[146–148]

In the general case, the picture of the formation of ore deposits must be supplemented by ideas concerning the genesis of geothermal sources and about the features of the water–rock interaction, which determines, in particular, the rates of filtration, microfiltration, ultrafiltration, and reverse-osmotic penetration of water streams into the Earth's mantle. Subterranean waters are usually considered in terms of a single system of the natural water turnover: evaporation from the surfaces of open water-containing areas—accumulation in the atmosphere—precipitation—stages involving the transport of water incident on soils to subterranean storage areas and further to open water-containing areas, etc. In conformity with Eqn. (11), the water turnover system must be expanded by including in it the sources of water active in the region of the liquid core–lower mantle interface and the systems of transport channels in the Earth's mantle.

As already mentioned, a branched network of pores and channels with different characteristic dimensions, used for the ascending transport of water under the influence of internal pressure gradients, may be formed in the mantle, which is inhomogeneous as regards composition, structure, and the extent of cracks and breaks. Such water is included in the region of the Earth's crust in the normal system of the water turnover.[130,131] The topology of such waterways from the Earth's core can be characterised by the correlation length L_E, which is comparable to the Earth's radius. Conclusions, of heuristic value, about the location of subterranean water streams[149] and the principal breaks through which the hydrosphere is additionally supplied with water follow from the fractal nature of the transport of liquid fluid through the Earth's mantle.

Such analysis, supported by experimental research, may prove useful not only for the rational utilisation and preservation of natural resources already discovered but also for the more effective search for new useful minerals and for the development of general concepts concerning the rational utilisation of natural resources in the future. Indeed, the very processes involved in the search for useful minerals and the mining of deposits already discovered cause harm to nature, damaging local ecological areas. In the initial stages of the utilisation of natural resources, these features exert a lesser influence. The present exploitation of the depths of oceans in order to collect iron–manganese concretions[150,151] as a rich source of copper, nickel, cobalt, and other metals does not constitute a danger to the natural environment. On the other hand, the continuation of the vigorous exploitation of coal and petroleum and gas deposits leads to the breakdown of the natural balances in terms of the solid, liquid, and gaseous components in major subterranean reservoirs, which is riddled with serious consequences, primarily owing to the disturbance of local natural ecological areas.

As regards petroleum and gas as well as fresh water, humanity has approached the stage where it has become necessary to curtail the extraction of these substances to amounts which can be made good under natural conditions. The development of the concept of the "limiting permissible utilisation" (LPU) and the introduction of the corresponding norms as regards the restoration of the given substance in nature has become a matter of urgency. For the solution of such problems, it is necessary to specify adequately the mechanisms of the formation and "ripening" of useful minerals and to approach an understanding of the conditions governing the initiation and acceleration of these processes under natural conditions. One cannot rule out the possibility that it is already necessary to think about "laying down" petroleum and gas deposits for our descendants using for this purpose the deposits which have already been "worked out" but which have retained the entire natural system of "subterranean communications", including the transport systems in the Earth's mantle. It may be that for this purpose it is necessary to introduce into the remaining bore holes certain substances and micro-organisms and to employ other methods involving chemical, biochemical and physical influences.

3. The Earth as a thermodynamically open system

We shall consider yet another important comment. If it is supposed that the formation reactions of water and certain organic chemical compounds from inorganic components are still continuing, then the quasi-stationary level of the World oceans is achieved owing to the existence of a definite flux of water molecules and oxygen atoms and ions from the Earth into space. These molecules entrain other components of the atmosphere, including larger organic molecules (urea, aminoacids, nucleotides, etc.) and clusters (the possible mechanisms of the "blowing off" of such molecules into space were discussed in Section V.1). Evidently the experimental observation of such quasi-stationary fluxes, provided that they exist, would make it possible to refine certain conceptual ideas about the turnover of water and other biologically important elements (N, C, P, etc.) in nature and also the models of the evolution of eco-systems on a global scale [for example, from a study of the purification processes in the atmosphere after major volcanic eruptions, especially since the components of the eruptions can reach the stratosphere (see Section I), in the analysis of the consequences of global radioactive contaminations, in the nuclear winter scenarios,[152] etc.].

It was emphasised above that the directed streams of the molecules of water and other substances into the stratosphere and then into space should serve as an additional (acting together with the turnover of the given substances, processes leading to the degradation and photodegradation of harmful substances, etc.) factor cleaning the atmosphere, because, together with such streams, harmful components can also be carried away outside the limits of the Earth's gravity.

In order to estimate the amounts of water lost by the Earth, we shall assume that throughout the existence of the hydrosphere (2 billion years) the content of hydrogen in the Earth's core diminished by 0.1%, i.e. that the loss of hydrogen per year was approximately 10^{14} g. The average amount of water carried away into space is then about 10^{15} g per year (the flux is $\sim 10^{11}$ H_2O molecules cm^{-2} s^{-1}) for an overall mass of the hydrosphere of approximately 1.6×10^{24} g and of the atmosphere of approximately 0.5×10^{22} g. We may note that the average fluxes of solar wind particles incident on the Earth are $\sim 10^{10}-10^{12}$ particles cm^{-2} s^{-1}. The generation on the sun of ultrafast streams of protons and electrons leads to an increase of the above quantities by 2–3 orders of magnitude with evident consequences for the process involving the "blowing off" of the particles of the atmosphere.§

When the Earth is considered as a thermodynamically open system involved in energy and material exchange with cosmic space, a number of theoretical problems, requiring model justification, arise. In particular, it is necessary to establish the mechanism of the

§ Bearing in mind the ecological problems considered in this article, we may point to the possible analogy between the brief intense external influences purifying the Earth's atmosphere and the cleaning effect of large precipitations of water in St. Petersburg.

generation of the addition momentum ΔM in the Earth–atmosphere system in order to compensate for the difference between the flux of material ΔM_{out} lost from the Earth into space and the flux ΔM_{in} of material (flowing from space to the Earth)—meteor streams and components of the solar wind. There exist also other mechanisms "perturbing" the dynamic behaviour of the Earth–atmosphere system. One of the factors is associated with the position of the Earth in its orbit, since the overall vector of the Earth's orbital velocity and the velocity of the solar system in the Galaxy and the Metagalaxy change in the course of the year. This leads to seasonal variations in the rate of rotation of the Earth about its axis, which is the reason for changes in the elastic stresses within the Earth's crust.[153] One should also note the variable nature of the tidal forces associated with the inconstancy of the moment of the lunar and solar gravitational forces, which leads to oscillations in the Earth's axis (nutation).[153] Fluctuating influences on the Earth's motion are also exerted by processes on the sun, some of which have definite cyclic features.

The dynamic equations describing the Earth–atmosphere system must take into account the entire set of the perturbing external factors indicated and must include terms corresponding to the "sources" and "sinks" of the momentum in order to ensure stable motion of the Earth as a thermodynamically open system. Under these conditions, the entire solar system must be regarded as a complex hierarchy of self-organising subsystems saturated by energy sources and involve a surprisingly large number of collective processes.[154] The stable states of the Earth–atmosphere system occur in the vicinity of local minima in certain generalised functionals with stabilisation of the overall momentum of the Earth and the atmosphere in the vicinity of the mean value. Apparently such local minima characterise the overall stage of the entire solar system as well as the "resonance" stabilisation of the moon, the exotic "reverse" rotation of Venus,[155] and the rings in the satellite systems of the giant planets.[154]

It is important to note that the momentum of the sun (about 2% of the momentum of the entire solar system corresponds to the sun, while the mass of the latter is 99.9% of the total mass) as well as the momentum of each planet in the solar system as a single whole do not remain unaltered during the changes in the relative positions of the sun and the planets.[156] The centre of gravity of the solar system can shift from the central regions of the sun almost by $2R_{\odot}$, where $R_{\odot}$ is the radius of the sun, i.e. outside the limits of the sun. The stability of the states of the Earth and other elements of the solar system indicated above can therefore be partly due to entirely deterministic (in terms of location, in terms of the time of inclusion) internal local rearrangements in each of the celestial bodies, manifested for planets by "planet-quakes", by local rearrangements in the ionosphere ("ionosphere-quakes"), and by volcanic activity, and for the sun of the local processes in its surface region. The latter may include the generation of sunspots, leading to the necessary correction of the intrinsic momentum of the sun and its atmosphere. From this standpoint, numerical calculations of the variations in solar activity (of the relative number of sun spots—the Wolf number or the "indices of solar activity", determined by the flux of the wave type radiation from the sun in the radiowave ranges from metres to centimetres—usually at a wavelength of 10.7 cm[156]) merely as a consequence of a change in the relative positions of the sun and the planets and also the discovery of the sun—planet contribution to the initiation of natural catastrophes on our planet (as a consequence of the effects due to the changes in the momentum of the Earth in the Solar System and the attractive forces from other celestial bodies) may be of definite heuristic value.

It is noteworthy that the changes in the water regime within large regions, in particular the oscillations in the levels of large lakes without outflow (the Caspian and Aral seas and the Balkhash and Chany lakes), associated with natural long-period variations in the rate of rotation of the Earth,[157] as well as the movements of the tectonic plates in the course of the Earth's geological evolution may lead to a spatial rearrangement of the sources and sinks of the momentum i.e. to a change in the location of the regions with the highest seismic and volcanic activities. There is a possibility of a simultaneous "switching on" of atmospheric and intraterrestrial sources and sinks of the momentum, leading to major natural catastrophes, which have been described since ancient times: "... there was a violent earthquake and the sun went black... and the stars of the sky fell onto the Earth... and all the mountains and islands were shaken from their places" (Book of Revelation by John the Evangelist: **6**, 12–6, 14).

It is important to note that external influences leading to catastrophes can also be anthropogenic. One should probably consider major nuclear tests, the ignition of powerful rockets, and sharp changes in the hydrological regions associated with the construction of large dams. Furthermore, unsystematic and extravagant development of the Earth's resources (water, useful minerals) disturbs the complex system of natural hydrothermal and other communications which govern the mass transfer processes (the transport of water and simple inorganic and organic compounds) in the Earth's crust, which is essential for natural processes leading to the formation of new and the long term existence of present deposits of natural resources. The mass redistributions occurring may influence also the geological activity of individual regions and can also initiate natural catastrophes.

In view of the objective necessity for the further utilisation of natural resources and the expansion of the scale of industrial and agricultural products, humanity is forced to develop a strategy for its existence. The prediction of possible situations, including natural catastrophes, on the basis of mathematical models describing the changes in the Earth–atmosphere system under the influence of stochastic external factors becomes important in this connection. In the future, it will actually be possible to refer to a system of measures directed to weaken undesirable natural phenomena and their partial regulation or even complete elimination—by launching special powerful rockets or by nuclear explosions in deep bore holes.

The development of such approaches requires an adequate analysis of the existing and new data concerning the relationships[158] between anthropogenic activities in various regions, supported by experimental justification of the proposed concept—by the study of chemical processes at high temperatures, pressures, and shear deformations, by the study of mass transfer processes in the upper layers of the atmosphere, etc. We may note that direct experimental information about the mass fluxes blown off from the ionosphere into space, characterising the additional purifying capacity of the atmosphere, may be obtained from a comparative analysis of the components of the solar wind incident on the Earth after interaction with the Earth's atmosphere. The mass fluxes carried away from the Earth into space contain definite information about our planet since their composition includes fragments of organic and bioorganic molecules.

It may be thought that all planets with liquid metal cores in all the star systems of the Universe are thermodynamically open (naturally to different extents) systems "breathing" into space.[21,22]

One could imagine also exceptional situations—occurring in explosions of "nova" or "supernova" stars—where instead of "breathing" the corresponding planetary systems are destroyed with ejection of the contents of their atmospheres into space. Admittedly, such a fate does not threaten our planet. The detection in space of regions with an increased concentration of fragments of organic molecules may be an indication of the catastrophes which occurred on other worlds.

Thus one may speak of a dynamic unity of the Earth and the surrounding cosmic space, which means that the enigmas concerning the appearance of living organisms on Earth shift from a purely terrestrial level to a cosmic level. Life, having arisen (or having been created) anywhere, might have embraced those regions of the Universe where the necessary conditions for their development existed. We thus arrive at a more concrete specification of Vernadskii's general ideas[1] concerning the interaction of the inorganic matter of the planet and of the living matter at all the space-time levels of the organisation of the material world, the constant interaction of cosmic organic matter with the living matter on planets, and the wide-scale distribution of living matter throughout the Universe and its cosmic importance.

VI. Conclusion

The efforts of chemical science in connection with problems of ecology have been traditionally directed to current developments in the resource-saving and low-waste technologies and towards an improvement of the efficiency of the system of monitoring of the natural environment. At the same time, the possibilities of chemistry and related sciences in the solution of ecological problems may be expanded. In this section we shall deal with one class of hitherto poorly developed problems whose ecological importance is apparently not fully recognised. This concerns the electromagnetic pollution of the natural environment.[88,159] As a consequence of the experimental theoretical complexities in the problems arising, many of the postulates described below have still not been fully formulated in modern science and should be regarded as controversial.

At the present time, the spectral density of anthropogenic sources of electromagnetic radiation (EMR) within many frequency ranges, primarily in the radio-frequency ranges, exceeds by several orders of magnitude the natural background (generated by the radio emission from the sun, the planets, and other cosmic sources, by phenomena in the Earth's atmosphere, etc.) and by the intrinsic spectral noise in natural radiation receivers (native biological systems, including the human brain and nervous system).

At the same time, many effects on biological systems by the EMR in various frequency ranges, starting from fractions of Hz and up to SHF (wavelength $\lambda \simeq 1 - 10$ cm) and EHF ($\lambda \simeq 0.1 - 1$ cm) ranges. Together with therapeutic effects of EMR in different ranges on man,[88,159] specific (non-thermal) negative effects have been observed after prolonged irradiation, so that limiting permissible levels (LPL) of exposure to EMR have been established. The LPL for irradiation by radiowaves under industrial conditions is 10 μW cm^{-2} in the USSR, 1 mW cm^{-2} in Canada, 10 mW cm^{-2} in the USA and a number of other countries.[159] The existing scatter in the established norms (by up to 3 orders of magnitude in terms of power!) indicate an inadequate level of the current understanding of the specific features of the effect of EMR in different ranges on biological systems—on the human brain and nervous system. On the other hand, the discovery of all the factors influencing the state and functional activity of man, in the first place the functioning of his brain, constitutes a fundamental condition for the existence of civilisation. It is not fortuitous that the United States Senate and Congress have declared the decade starting on 1st January, 1990 as the "decade of the brain".

The human brain, being a non-equilibrium system of the organism, is most capable of "switching over" its state ("forced bifurcation") under the influence of weak external (light, sonic, etc.) signals. The brain is apparently the most highly organised multiparameter dynamic system, each state of which is established as a coherent (concerted) set of ensembles comprising ten and more neurons and characterised by a definite set of metastable levels. The transitions between such generalised states occur via a system of alternatives[77] under the influence of weak signals. The wide variety of states of the brain system is indicated by the virtually "non-deletable" and readily recalled memory, including visual images, manifested by man's creative activity during normal life and in dreams.

Man's light and sound receptor systems, which transmit information to the brain, as well as the olfactory biochemical reception systems, possess a uniquely high sensitivity. It has been shown experimentally that the radio frequency EMR also exerts a direct influence on the sensitive highly non-equilibrium systems of the brain.[159] In biological systems there are no specialised receptor organs for radio signals (in contrast to light signals). One may therefore think that the primary mechanisms of the reception of radio waves are fairly non-specific and are the same for all biosystems.

These influences can be exerted either through a change in the state of the aqueous component of the biosystems, in which the activity of free, non-bound water may be altered under the influence of the radio frequency EMR [49] or through a change in the functional state of the ionic channels in biological membranes as a result of an increase in the degree of hydration of the channels and the consequent loss of selectivity relative to the transfer of ions of different kinds.[24] Further studies should establish with a greater certainty not only the primary mechanisms of the effect of EMR at different frequencies on man but also the systems for further processing in the brain of the information carried by such radiation.

This is of particularly great current interest, since negative influences on man can be exerted not only by anthropogenic sources of EMR but also by major fluctuations in the natural radio frequency EMR background. In particular, the increase in solar activity with increase in the relative number of sun spots and eruptions on the sun, responsible for the increased intensity of the solar wind and streams of plasma clouds away from the sun, leads not only to an increase in the intensity of the intrinsic solar EMR in the radio frequency ranges (type I–V radio waves) but also to the generation of magnetospheric holes and subholes with strong variations in the geomagnetic field on interaction of the streams of solar plasma with the Earth's magnetosphere and ionosphere. A broad spectrum of electromagnetic waves is then excited in the Earth's magnetosphere: "holes" and "swellings" ($\sim 10^5 - 10^2$ Hz); stable and irregular geomagnetic pulsations ($\sim 10^{-2} - 10$ Hz); atmospheric noise ($\sim 1 - 10^2$ Hz); low-frequency radiation ($\sim 10^2 - 10^4$ Hz). This is a consequence of a wide variety of phenomena in magnetospheric holes and subholes: turbulent movements in the magnetospheric plasma, the development of plasma instabilities, the generation of intense electric currents amounting to tens of thousands of amperes in the ionosphere (at heights of approximately 100 km), etc.[109,156] The negative

influences of such magnetic holes on the state of human beings are well known. Although solar activity can be partly associated with the relative positions of the sun and the planets (see Section V), each planet is a source of its characteristic radiation in the ultralong radio frequency range, generated on interaction of the solar wind and the streams of solar plasma with the planet's magnetosphere and atmosphere. Presumably, further progress in the science of the brain, the discovery of the mechanisms of the reception of weak information-containing electromagnetic signals by the organism, will make it possible to understand better all the influences exerted by cosmic space and the environment on man.

We shall make yet another comment. The history of science has shown how difficult it is to predict the true course of scientific progress. It is sufficient to recall the classical statement by Lord Kelvin on the eve of the XXth century, concerning two "small clouds" (the negative results of Michelson's experiments, anomalies in the absorption spectrum of an absolutely black body) which at the time precluded the formulation of physical science in a "final form". The theory of relativity and quantum mechanics were created on this basis. The century coming to its conclusion involved the formulation of its own problems and puzzles. One of the "little clouds" as regards physicists has already been specified: the fact that the measured flux of "solar" neutrinos is smaller almost by a factor of three than the value predicted within the framework of the standard model of the sun. The paradox of the situation consists in the fact that, together with brilliant astrophysical discoveries of the nature of many stellar and quasi-stellar objects separated from the sun by billions of light years, we have the state of affairs where the processes in our Star are still not fully understood!

Here one would wish to mention two other major "clouds" (which arose many centuries before Lord Kelvin's "little clouds"), whose internal essential features have so far been poorly understood, so poorly that many scientists do not consider them seriously. This concerns astrology as the science of relations between the state and evolution of individual living organisms (including man) and eco-systems, on the one hand, and the relative disposition of celestial bodies, on the other, as well as telepathy as the science of processes involving the transfer of information without special signals and technical means (including "thought transfer") at a distance in which the organism makes use of his own memory system and the system for the reproduction of visual images.

We have already discussed above the possible relation between solar activity and the relative positions of the sun and the planets. The fairly well established influence of the state of the sun on the functioning of living systems should be effected primarily through the low-frequency variable magnetic field and different radio frequency ranges generated by the EMR. The problem of how the above radio emissions influence the human psyche and state of health remains, however, unsolved. As regards information signals from bio-objects, including man, if one does not introduce into consideration new postulates (in conformity with Occam's principle), in particular the hypothesis of the existence of "hitherto unknown biofields",[160] one may assume that the transmission and reception of such signals are effective also at radio frequencies, most probably in the centimetre and decimetre ranges.[159] At the present time the thermal radio emission by man (in the ranges indicated and at longer wavelengths — in the decametre, kilometre, etc. ranges), the intensity of which is rigorously related to the temperature of the emitting internal organs, is used effectively for diagnosis at a distance. This also applies to the equilibrium emission by the body in the IR range ($\sim 8-14$ μm).[161] The latter is characterised by a high power (~ 10 mW cm^{-2}) so that the power of the radiation emitted by the entire human body in the IR range exceeds 100 W.[162]

Evidently, for the transmission of information signals by the human brain in radio frequency ranges as well as the establishment of the highest sensitivity for the reception of weak signals, it is necessary that macroscopic ($\sim 1-10$ cm) domain structures, all the neurons of which function in a coherent regime, be formed in the brain. In this case the power of the transmitting signals may exceed by several orders of magnitude the equilibrium thermal background. There are no fundamental prohibitions of the existence of such "telepathic communication" — neither as regards energy characteristics nor as regards the possible highly specific individual sensitivity of natural systems. Naturally, there are major difficulties in the experimental location of the signals transmitted by the brain, which is partly associated with the fairly random character and virtual non-controllability of the most striking manifestations of spontaneous telepathy. There exist also fundamental difficulties in the understanding of the mechanism of the coding of information in the domains of the active medium of the brain capable of being stimulated, the transformation of information into radio wave signals, the reception of the signals in the receiving systems, etc.

In such hypothetical approaches to astrology and telepathy, the problems of these sciences acquire the same essential features and should be solved by discovering the mechanisms of the reception by man of weak information signals in different radio frequency ranges. The question arises whether the "clouds" mentioned above will develop and whether astrology and telepathy will become established as natural scientific disciplines or whether they will still remain for a long time *terra incognita* which will excite the imaginations of impressionable investigators and laymen.

Enigmas in nature have always existed and will exist. Furthermore, the level of the recognised lack of knowledge increases (or at least does not diminish) as reliable knowledge accumulates. Scientific progress is partly effected through this process involving the recognition by man of the depth of his lack of knowledge. However, even regardless of the difficulties concerning astrology and telepathy discussed above, the discovery of information communication, manifested in the reception by living organisms of low-frequency variable magnetic fields and radio frequency EMR, is one of the new and important aspects of ecological science.

This review represents an attempt to analyse the wide variety of problems arising in the formulation of the concept of the survival of humanity combined with the choice of ecological priorities and the aim is to draw the attention of chemists as well as specialists in other fields (ecologists, medical practitioners, biochemists, physicists, and mathematicians) to the possibilitiy of a joint search for and solution of general and what are apparently the most important problems to everyone at the present time — the problems involved in saving the home.

What future awaits us? "Then I saw a new heaven and a new earth; the first heaven and the first earth had disappeared now and there was no longer any sea" — wrote John the Evangelist (Book of Revelation: **21**, 2). What was the new world seen by the Evangelist? After all, the New Testament is threaded by the idea of the multivariability of the future, the understanding of the world as a subject with which humanity has a dialogue and as an open system with an "open future".[163] Not only destructive but also creative, cleansing forces are active in the world (the "white horse", Book of Revelation: **6**, 2, 19, 11) and the scales in the hands of the rider on the "black horse" (Book of Revelation: **6**, 5) can serve as a

symbol of the uncertainty of the ways in which man and humanity as a whole will develop.

This view on the world is adequate, especially now that wide use is made of technologies which can do irreparable harm to the biosphere and when nuclear and chemical weapons have accumulated in amounts sufficient for the complete annihilation of civilisation. The visions of John the Evangelist may prove to represent reality, as already demonstrated by the Chernobyl catastrophe: "... and a huge star fell from the sky, burning like a ball of fire, and it fell on a third of all rivers and streams; this was the star called wormwood and a third of all water turned to bitter wormwood, so that many people died from drinking it." (Book of Revelation: **8**, 10; **8**, 11).

Humanity stands at the crossroads and the face of the "new" Earth will in fact depend on the choice of priorities (ecological, social, ideological etc.) in the development of a survival strategy: either a path will be found and followed to the convergence of world social-political systems, so that the history of humanity does not break off, or civilisation will be destroyed and will be reborn after many thousands or millions of years (possibly "without a sea"?).

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Translated from *Uspekhi Khimii* **60** 2332–2361 (1991) U.D.C. 502.7:504.06:577.1

Certain physicochemical principles of eco-systems and their expression in the form of material inequalities for different levels of initial information

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ABSTRACT. The usefulness of estimates of the contents of various components of ecological systems and subsystems in the form of material inequalities is demonstrated with the aid of the principle of the threshold nature of the action of chemical substances on producers and consumers. The principle of the coupled material-characteristic imbalance is formulated, according to which the unknown part of the mass of the ecological system can be estimated with the aid of inequalities expressing the relations between the masses of the components and their contributions to the overall characteristics of the system as a whole. The possibilities of using material inequalities for different levels of initial information for the monitoring of eco-systems and for the planning of physicochemical nature-protecting measures are demonstrated.

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I. Introduction

Monitoring on the global and regional scale and prediction of the changes in the state of eco-systems and planning of nature-protecting measures necessitates the large-scale and operative estimation of the contents of various components, phases, fractions, and constituents of ecological systems and subsystems and also the determination of the rules governing their compositions.

An ecological system represents a territorially (spatially) isolated integral elementary unit of the biosphere all the components of which are closely related to one another, or a certain assembly of such units.[2]

By an ecological subsystem, we shall understand a part of the eco-system which is imagined to be isolated or which has real physical boundaries and which can contain or not contain producers, consumers, and substrates. Ecological subsystems defined in this way can include waste water before and after purification, liquids contained in closed water supply systems, solid waste stored on military proving grounds and contaminating the lithosphere, various solutions and heterogeneous mixtures undergoing chemical changes in industrial and natural processes, as well as individual living organisms and their components. Under these conditions, one of the features of ecological subsystems is the possibility of their ultimate interaction with the environment and the living organisms present in it. Thus, various substances can enter natural water-containing areas even from a closed water supply system when its hermetic seal fails, while waste aerosols and industrial waters in general lead to daily contamination of the atmosphere and hydrosphere. It is seen from the definition that, in contrast to the eco-system itself, its ecological subsystem can be both homogeneous and heterogeneous, can consist of one component or of a very large number of components, and can be part of nature or an artificially produced mixture.

The principle of the threshold nature of the effect of chemical substances on producers and consumers[1–14] is in the first place the reason why it is useful to estimate in the form of material inequalities the liquid and gaseous waste entering the environment. Secondly, the methods for the large scale monitoring of the states of the atmosphere, the hydrosphere,[15–22] and the lithosphere should not themselves promote additional anthropogenic contamination by chemical substances. Thirdly, when they are applied, one must achieve the most effective utilisation of the initial information collected at considerable material expense. Fourthly, these methods should not entail the destruction or negative changes in biological objects.

The difficulty of collecting detailed information about the state of ecological systems and subsystems and of its subsequent utilisation[23,24] necessitates the establishment of universal characteristics of the compositions of such systems. These characteristics must be suitable for practical use even in the absence of complete data and in the presence of different levels of the initial information.

Thus large scale monitoring and prediction of the state and chemical evolution of ecological systems and subsystems as well as the planning of nature-protecting measures[24-30] require the discovery of the principal rule governing the composition which is applicable to the entire wide variety of information conditions encountered in practice. The specific features of ecological requirements (the principle of the threshold nature of the effect of chemicals contaminating the environment) indicates the suitability of the inequalities in the search for such a rule.

II. Universal rules for the compositions of ecological systems and subsystems in the form of inequalities

The chemical processes in ecological subsystems frequently take place under the conditions of random oscillations in temperature, pressure, the concentrations of reactants, the activity of the catalyst and inhibitors, the magnetic field strength, and other parameters. Furthermore, as already mentioned, there is frequently no exhaustive information about the ecological subsystem. These features necessitate the establishment of new general rules which determine the relations between the amounts of reactants and products in chemical reactions in both homogeneous and heterogeneous ecological subsystems.

Bearing in mind the specific features of ecological subsystems and the principle of the threshold nature of the influence (of various factors), we shall attempt to compare, under the conditions of incomplete initial data, the unknown amount of the system component with a quantity which can be readily calculated theoretically or determined experimentally. We shall explain the idea of this approach by a simple example. Evidently, the overall mass of substances with a molecular weight not less than the specified value cannot be greater than the mass of the entire system. Having divided the left-hand and right-hand parts of the trivial inequality corresponding to this claim by the specified molecular weight and having taken into account the fact that one then obtains on the left-hand side a quantity which exceeds the total number of moles of such substances, we obtain as a result a new relation according to which the total number of moles of substances with a molecular weight not less than the specified value, existing in a certain ecological subsystem (isolated volume), cannot be greater than the ratio of the total mass of the system to the specified molecular weight at any instant during chemical reactions.

Using the definition of the concentration and of the average density, it is easy to demonstrate with the aid of the above rule that the molar concentrations of substances in a certain volume of space where chemical reactions take place cannot be greater at any instant than the ratio of the average density of the entire system at this instant to the molecular weights of the corresponding substances.

The possibility of applying this rule can be illustrated in relation to the industrial synthesis of sulphuric acid by the contact method.[31] This substance exerts a powerful negative effect when it enters the environment. Suppose that an aqueous solution of sulphuric acid with a density of 1841 kg m^{-3} is introduced into the absorption tower. Then, according to the rule established, the concentration of sulphuric acid in the solution entering the tower is $\leqslant$18.79 kmol m^{-3}. If after the reaction with SO_3 and cooling of the liquid phase, the density of the resulting solution is 1838 kg m^{-3}, then, on the basis of the assertion formulated above, we find that the concentration of sulphuric acid in the resulting solution is less than or equal to 18.76 kmol m^{-3}. If the initial sulphuric acid solution contains 98.2% H_2SO_4, then the concentration of sulphuric acid was 18.45 kmol m^{-3}. The final solution with the density indicated at 15 °C can represent 99.3% sulphuric acid and its concentration will be 18.62 kmol m^{-3}. As can be seen from the values obtained, the results are in full agreement with the rule established above.

Thus the general rules postulated above make it possible to estimate at each instant the amounts of both the starting materials and the products present in any isolated volume even for a minimal amount of information available about the chemical reactions and about the influence of numerous random factors and mass-exchange processes.

In order to obtain an expression whereby the weight fractions of the substances in ecological subsystems can be estimated, we write

$$\frac{m_k(t)}{M_\Sigma(t)} \leqslant \sum_{i=k}^{i=l(t)} \frac{n_i(t)\mu_k}{M_\Sigma(t)} \leqslant \mu_k n_{sp}^{\cdot}(t), \qquad (1)$$

where $M_\Sigma(t)$ is the mass of the entire ecological subsystems at time t, $n_i(t)$ and $m_i(t)$ are the number of moles and the mass of the ith substance in the ecological subsystem at time t, μ_k the molecular weight of the kth substance, $l(t)$ the number of substances present in the subsystem at time t, i the summation index such that at a fixed time t the inequalities

$$\mu_1 \leqslant \mu_2 \leqslant \mu_3 \leqslant \ldots \leqslant \mu_{i-1} \leqslant \mu_i \leqslant \mu_{i+1} \leqslant \ldots \leqslant \mu_{l(t)}, \qquad (2)$$

hold, k a fixed value of i, and $n_{sp}^{\cdot}(t) = \left[\sum_{i=1}^{i=l(t)} n_i(t)\right] \Big/ M_\Sigma(t)$, the specific number of moles (the average characteristic of the ecological subsystem) equal to the ratio of the total number of moles of all the substances present in the ecological subsystem to their overall mass.

Eqn. (1) makes it possible to formulate the following theorem:

Theorem 1. *For any chemical reactions in ecological systems and subsystems, the weight fraction of a given substance at any instant cannot exceed the product of the specific number of moles at the given instant and the mole fraction of the given substance.*

Having multiplied the terms of the inequalities (1) by the average density† of the entire ecological subsystems $\bar{\rho}(t)$, we obtain an expression which makes it possible to estimate the concentrations of the components of the ecological subsystem from a minimal amount of data. It permits the formulation of the following rule.

The weight concentration of any reactant cannot be greater than the product of the specific number of moles, the average density of the system at the given instant, and the mole fraction of the substance.

Having used the idea of the material imbalance in relation to the mole fractions of the components of an ecological subsystem, we set up a sequence of inequalities:

$$\frac{n_k(t)}{\sum_{i=1}^{i=l(t)} n_i(t)} \leqslant \sum_{i=1}^{i=k} \frac{n_i(t)\mu_i}{\mu_k \sum_{i=1}^{i=l(t)} n_i(t)} \leqslant [\mu_k n_{sp}^{\cdot}(t)]^{-1}, \qquad (3)$$

where $n_i(t)$ is the number of moles of the ith substance and μ_i is the molecular weight (the weight of one mole) of the ith substance.

† The average density of the ecological subsystem is equal to the ratio of the mass of the entire subsystem to its volume.

Using Eqn. (3), we formulate the second theorem.

Theorem 2. *The mole fraction of a given substance in any reactions in ecological subsystems and subsystems at any instant cannot be greater than the reciprocal of the product of the specific number of moles and the mole fraction of the given substance.*

Since the weight and mole fractions of a substance cannot be greater than unity, their estimates are limited by the values of the products: for the weight fractions $\mu_k n^{\circ}_{sp}(t) \leqslant 1$ and for the mole fractions $\mu_k n^{\circ}_{sp}(t) \geqslant 1$. The expressions for their estimation can therefore be usefully combined into a single universal inequality:

$$\frac{|1-\mu_k n^*_{sp}(t)|+\mu_k n^*_{sp}(t)-1}{2[\mu_k n^*_{sp}(t)-1]} n \frac{n_k(t)}{\sum_{i=1(t)}^{i=t} n_i(t)} + \frac{|1-\mu_k n^*_{sp}(t)|+1-\mu_k n^*_{sp}(t)}{2[1-\mu_k n^*_{sp}(t)]} \frac{m_k(t)}{\sum_{i=1(t)}^{i=t} m_i(t)} \leqslant \leqslant \frac{\mu_k n^*_{sp}(t)[|1-\mu_k n^*_{sp}(t)|+1\mu_k n^*_{sp}(t)]}{2[1-\mu_k n^*_{sp}(t)]} + [\mu_k n_{sp\cdot}(t)]^{-1} \frac{|1-\mu_k n^*_{sp}(t)|+\mu_k n^*_{sp}(t)-1}{2[\mu_k n^*_{sp}(t)-1]}. \quad (4)$$

Consequently the contents of the components in ecological subsystems can be estimated from minimum amounts of physicochemical data when the specific number of moles in the system is known. The new average characteristic introduced here—the specific number of moles—can be fairly readily determined in the case of homogeneous liquid ecological subsystems from the decrease in the freezing point of the solution, or the increase in its boiling point, or osmometrically; for gaseous solutions, this quantity is unambiguously expressed in terms of the pressure, density, and temperature.

A series of practical problems concerning the protection of the environment necessitate the estimation of the content of substances with a molecular weight greater (smaller) than the specified value. For this purpose, using the principle of material imbalance, we shall set up similarly a sequence of inequalities replacing the unknown masses and numbers and moles of the components by larger quantities. As a result, we obtain the third and fourth theorems which are formulated as follows.

Theorem 3. *The sum of the weight fractions of substances with molecular weights smaller than or equal to the specified value at any instant in eco-systems and ecological subsystems cannot be greater than the product of the specific number of moles at this instant and the specified molecular weight.*

Theorem 4. *The sum of the mole fractions of substances with molecular weights greater than or equal to the specified value in ecological systems and subsystems at any instant cannot be greater than the reciprocal of the product of the specified molecular weight and the specific number of moles.*

Thus an objective relationship has been established between the content of the component in the system, the specific number of moles, and the molecular weight. These rules make it possible to differentiate the space of the values of the possible weight and mole fractions of the components constituting the ecological subsystems (Figs. 1 and 2).

Situations are frequently encountered where, apart from the average characteristic of the ecological subsystem (the specific number of moles), data concerning its quantitative composition at a given instant are also known. In order to establish the general rules for the compositions of multicomponent systems applicable for this level of initial data, we shall again make use of inequalities. The method of achieving this aim is expressed in the form of the principle of the coupled material-characteristic imbalance; *the unknown part of the mass of the ecological subsystem can be estimated by comparing the inequalities expressing the relations between the masses of the components and their contributions to the overall characteristic of the entire subsystem.*

We shall write the inequality relating the number of moles of the kth component to the total number of moles in the subsystem:

$$m_k(t)/\mu_k + [M_\Sigma(t) - m_k(t)]/\mu_{max} \leqslant N_\Sigma(t), \quad (5)$$

where μ_{max} is the maximum molecular weight of the component and $N_\Sigma(t)$ the total number of moles of all the substances constituting the system.

We supplement Eqn. (5) by the expression relating the mass of the component to the overall mass of the system through the number of moles of the remaining substances multiplied by the minimum molecular weight, namely

$$m_k(t) + [N_\Sigma(t) - m_k(t)/\mu_k]\,\mu_{min} \leqslant M_\Sigma(t). \quad (6)$$

By dividing inequalities (5) and (6) by the mass of the entire system, we obtain, after algebraic rearrangements, relations which make it possible to estimate in the following manner the contents of the components in ecological systems from the specific number of moles when the qualitative composition is known:

$$\frac{m_k(t)}{M_\Sigma(t)} \leqslant \begin{cases} \mu_k \dfrac{n^*_{sp}(t)\mu_{max} - 1}{\mu_{max} - \mu_k} \\ \text{when} \quad \mu_k n^*_{sp}(t) \leq 1, \\ \mu_k \dfrac{1 - \mu_{min} n^*_{sp}(t)}{\mu_k - \mu_{min}} \\ \text{when} \quad \mu_k n^*_{sp}(t) > 1. \end{cases} \quad (7)$$

The regions where the estimating inequalities, constituting formula (7), are applicable were determined on the basis of the condition $m_k(t)/M_\Sigma(t) \leqslant 1$.

In order to derive relations between the mole fractions of the components and an average physicochemical characteristic of the entire system, we shall take into account the fact that $n_k(t)/N_\Sigma(t) = m_k(t)/[\mu_k n^{\circ}_{sp}(t) M_\Sigma(t)]$. We then obtain from formula (7)

$$\frac{n_k(t)}{N_\Sigma(t)} \leqslant \begin{cases} \dfrac{n^*_{sp}(t)\mu_{max} - 1}{n^*_{sp}(t)(\mu_{max} - \mu_k)} \\ \text{when} \quad \mu_k n^*_{sp}(t) \leq 1, \\ \dfrac{1 - \mu_{min} n^*_{sp}(t)}{n^*_{sp}(t)(\mu_k - \mu_{min})} \\ \text{when} \quad \mu_k n^*_{sp}(t) \leq 1. \end{cases} \quad (8)$$

With the aid of inequalities (4), (7), and (8), it is possible to estimate the weight and mole fractions of the components for two levels of incomplete information.

Calculations based on the universal rules established for the compositions of ecological systems in the presence and absence of qualitative analytical data, carried out with the aid of a computer by

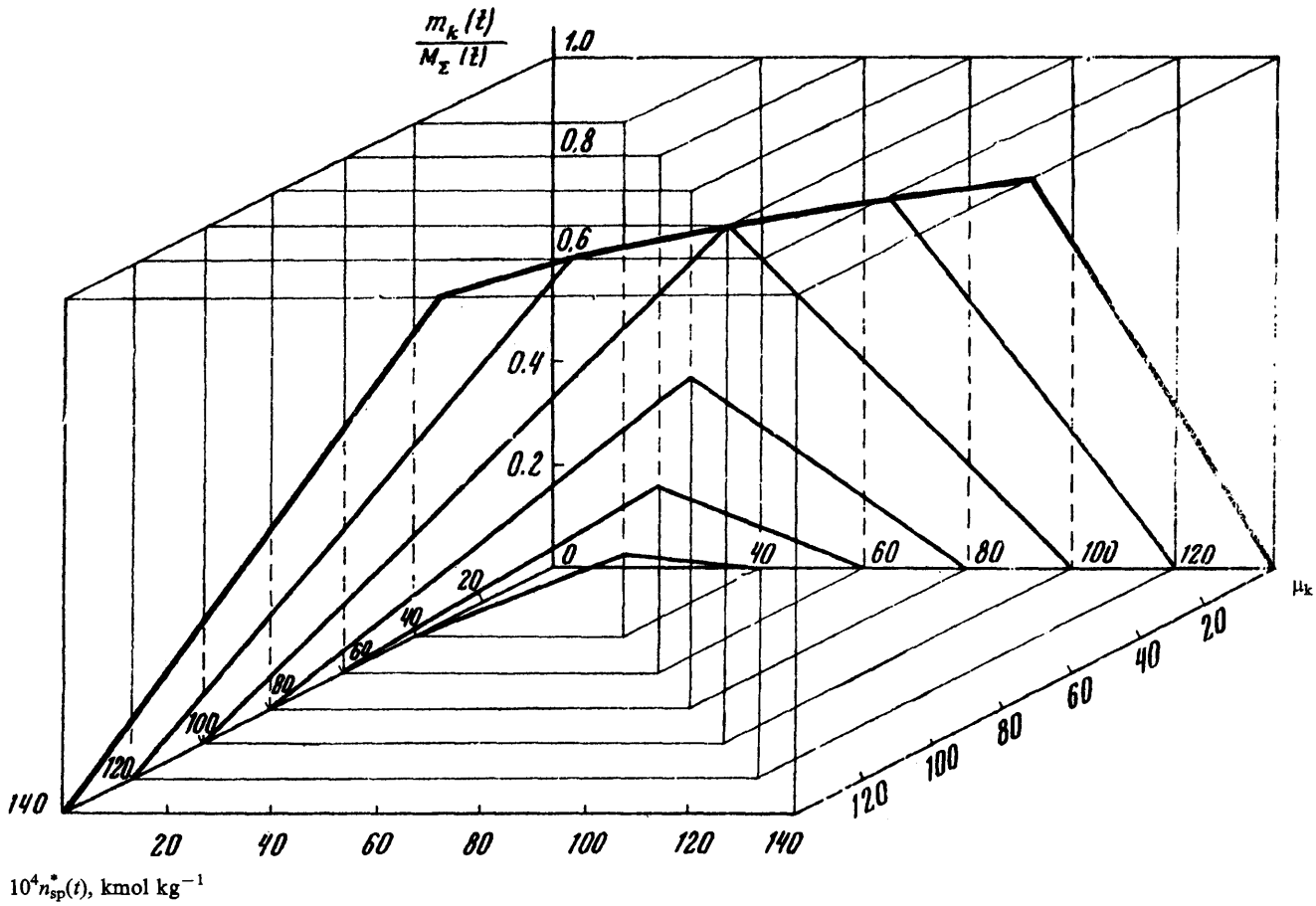


Figure 1. The space of the possible weight fractions of substances constituting eco-systems.

means of a specially developed algorithm and a program written in the BASIC language and based on it, confirmed the possibility of their practical employment. The high degree of generalisation of the above inequalities makes it possible to take into account any chemical, physical (including nuclear) and physicochemical changes in open, closed, and isolated ecological systems and subsystems, taking into account the effects associated with mass-exchange processes. Yet another important feature of these expressions is their low information requirement, i.e. the possibility of their practical application for a small amount of initial data.

Since in certain cases it is simpler for homogeneous and heterogeneous systems to measure experimentally the specific heat and the specific volume than to determine the specific number of moles of the ecological subsystem, we shall find inequalities relating the partial molar quantities and composition for these levels of information.

For this purpose, applying the principle of the coupled material-characteristic imbalance, we set up an inequality for heat capacities using the partial molar heat capacity of the kth component in the following form:

$$C_k^m \frac{m_k(t)}{\mu_k} + [M_\Sigma(t) - m_i(t)] \left(\frac{C^m}{\mu}\right)_{min} \leqslant C_\Sigma(t), \qquad (9)$$

where C_k^m is the partial molar heat capacity of the kth component, $C_\Sigma(t)$ the overall heat capacity of the entire ecological subsystem at time t, and $(C^m/\mu)_{min}$ is the minimum ratio of the partial molar heat capacity to the molecular weight (the minimum partial specific heat).

The inequality coupled with formula (9) is obtained by expressing the mass of the components with the aid of infinitesimal amounts of heat absorbed by them on raising the temperature of the entire ecological subsystem by an infinitesimal amount. Thus,

$$\frac{\mu_k \delta Q_k}{\delta T C_k^m} + \frac{(\delta Q_\Sigma - \delta Q_k)}{\delta T} \left(\frac{C^m}{\mu}\right)^{-1}_{max} \leqslant M_\Sigma(t), \qquad (10)$$

where δQ_Σ is the infinitesimal amount of heat absorbed by the entire ecological subsystem, δQ_k the infinitesimal amount of heat absorbed by the kth component, δT the infinitesimal rise in the temperature of the system on absorption of heat, and $(C^m/\mu)_{max}$ the maximum ratio of the partial molar heat capacity to the molecular weight of the given system (the maximum partial heat capacity).

On dividing inequalities (9) and (10) by the mass of the system and taking into account the fact that

$$\delta Q_\Sigma = M_\Sigma(t) \delta T \overline{C}_{sp}(t) \text{ and}$$

$$\overline{C}_{sp}(t) = C_\Sigma(t)/M_\Sigma(t),$$

we obtained a relation between the specific heat of the entire system

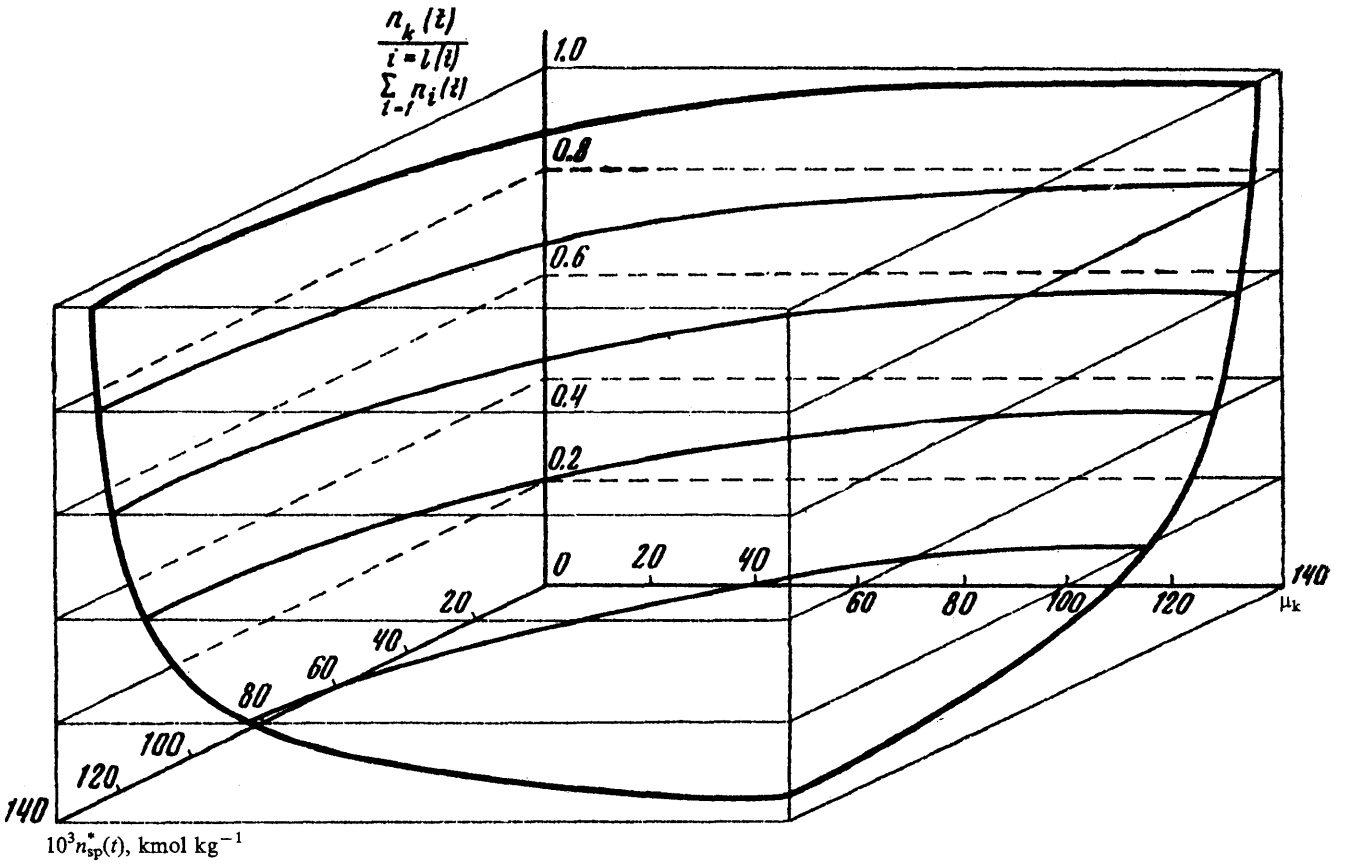


Figure 2. The space of the possible mole fractions of the substances constituting ecological systems. The surface of the maximum possible mole fractions of the substances in the eco-systems is differentiated.

$\bar{C}_{sp}(t)$ and the partial molar heat capacity and the content of the given component:

$$\frac{m_k(t)}{M_x(t)} \leqslant \begin{cases} \dfrac{\bar{C}_{sp}(t) - (C^m/\mu)_{min}}{C^m_k/\mu_k - (C^m/\mu)_{min}} \\ \text{when } \bar{C}_{sp}(t)\mu_k/C^m_k < 1, \\ (C^m/\mu)_{max} - \bar{C}_{sp}(t) \\ (C^m/\mu)_{max} - C^m_k/\mu_k \\ \text{when } \bar{C}_{sp}(t)\mu_k/C^m_k \geq 1. \end{cases} \tag{11}$$

The following rule follows from Eqn. (11):

The weight fraction of any component in a differentiated ecological system (subsystem) at a given instant cannot be greater than the ratio of the product of its molecular weight and the specific heat of the entire system (subsystem) to its partial molar heat capacity.

It can be used when the partial molar heat capacities of the other components constituting the ecological system are unknown. For example, the average specific heat of a human being, constituting a complex ecological subsystem, is 3.59 kJ kg K^{-1}.[32] Consequently, on the basis of this value of the specific heat of the ecological subsystem, one can conclude that the human organism contains not more than 86% of water. This result corresponds to the real situation, since according to Lightfoot,[32] the weight fraction of water in the human organism is 0.75.

We shall make use of the concept of the partial molar volumes of the components in order to obtain new relations. By setting up an inequality with the partial molar volume, we obtain a relation implying that *the weight fraction of any component at a fixed instant cannot be greater than the ratio of its molecular weight to the product of its partial molar volume and the average density of the entire system at this instant.*

For the case where the range of variation of the partial molar volumes is known, we set up two coupled relations for the imbalance of the volume and mass and, on combining them, we obtain, after algebraic rearrangements,

$$\frac{m_k(t)}{M_x(t)} \leqslant \begin{cases} \dfrac{1/\bar{\rho}(t) - (v^m/\mu)_{min}}{v_k{}^m/\mu_k - (v^m/\mu)_{min}} \\ \text{when } \nu^m_k/\mu_k > 1/\bar{\rho}(t), \\ \dfrac{(v^m/\mu)_{max} - 1/\bar{\rho}(t)}{(v^m/\mu)_{max} - v_k{}^m/\mu_k} \\ \text{when } \nu^m_k/\mu_k < 1/\bar{\rho}(t), \end{cases} \tag{12}$$

where $\bar{\rho}(t)$ is the average density of the ecological subsystem at

time t, $(v^m/\mu)_{min}$ and $(v^m/\mu)_{max}$ are the minimum and maximum ratios of the partial molar volume to the molecular weight, and v_k^m is the partial volume of the kth component.

Inequalities which make it possible to express under conditions of incomplete data a relation between the numbers of the components, their specific heats of combustion, and the specific heat of combustion of the entire ecological system can be set up similarly by establishing material inequalities for the imbalances in the masses of the components and in the heat of combustion. It is then possible to demonstrate, in particular, that *the weight fraction of any substance in the ecological subsystem at a given instant cannot be greater than the product of the specific heat of combustion of the system and the ratio of the molecular weight to the molar heat of combustion of the given substance.*

In order to discover the relation between the specific radioactivities of physicochemical systems and their content of radioactive isotopes when incomplete data are available, inequalities were set up expressing the imbalance in the overall radioactivity in terms of the weight fractions of the substances and the masses. It was then shown that the *weight fraction of the radioactive isotopes cannot be greater than the ratio of the specific radioactivity of the physicochemical system at a given instant to the specific radioactivity of the isotopes.*

III. Specific rules for the compositions of homogeneous ecological subsystems

We shall find the general relations for a series of readily determined mean statistical characteristics of homogeneous systems such as refractive index, the radiation attenuation factor, etc., on the one hand, and their contents of the components, on the other.

With the aid of the generalised Debye equation, a relation was found between the refractive index of a homogeneous system n and the content of the kth component:

$$\frac{m_k(t)}{M_\Sigma(t)} \leqslant \begin{cases} \left[r_{max} - \dfrac{n^2-1}{(n^2+2)\bar{\rho}(t)}\right] \Big/ (r_{max}-r_k) \\ \text{when } r_k \leqslant (n^2-1)/[(n^2+2)\bar{\rho}(t)], \\ \left[\dfrac{n^2-1}{(n^2+1)\bar{\rho}(t)} - r_{min}\right] \Big/ (r_k - r_{min}) \\ \text{when } r_k > (n^2-1)/[(n^2+2)\bar{\rho}(t)], \end{cases} \tag{13}$$

where r_k is the specific refraction of the kth component and r_{max} and r_{min} are the maximum and minimum specific refractions of the substances constituting the homogeneous system.

With the aid of the equations set up for the imbalance of the molecular refraction and the number of atoms, it proved possible to estimate the maximum possible number of atoms in the molecules from the relative refractive index under the conditions of incomplete information.

The fact that the fraction of radiation absorbed can be readily measured for homogeneous systems makes it possible to compare it with the contents of substances in multicomponent systems under the conditions of incomplete information. A relation which makes it possible to formulate the following rule can be obtained from the Lambert–Bouguer–Beer Law.

The molar concentration of each component in solution cannot exceed the ratio of the logarithm of the attenuation factor for incident radiation attenuated by a layer of solution of unit thickness to the molar extinction coefficient.

By applying the principle of the material-characteristic imbalance to cases of the absorption of radiation, it is possible to establish the following relation:

$$\frac{m_k(t)}{M_\Sigma(t)} \leqslant \begin{cases} \left[\dfrac{1}{\rho(t)L}\ln\dfrac{I_0}{I} - \varepsilon_{min}^{sp}\right] \Big/ (\varepsilon_k^{sp} - \varepsilon_{min}^{sp}) \\ \text{when } \varepsilon_k^{sp} \geqslant [\bar{\rho}(t)L]^{-1}\ln I_0/I, \\ \left[\varepsilon_{max}^{sp} - \dfrac{1}{\bar{\rho}(t)L}\ln\dfrac{I_0}{I}\right] \Big/ (\varepsilon_{max}^{sp} - \varepsilon_k^{sp}) \\ \text{when } \varepsilon_k^{sp} < [\bar{\rho}(t)L]^{-1}\ln I_0/I, \end{cases} \tag{14}$$

where L is the thickness of the layer through which radiation passes, I_0 and I are the intensities of the incident and transmitted radiation, ε_{max}^{sp} and ε_{min}^{sp} are the maximum and minimum specific extinctions, and ε_k^{sp} is the specific extinction of the kth component.

Setting up similarly the inequality for electrical conductivity, we note that *the number of equivalents in a unit volume of any substance, dissociating into ions in solution, cannot be greater than the ratio of the specific conductance of the homogeneous system to the equivalent conductance of the given substance at infinite dilution.*

For systems containing high-molecular-weight compounds, we find, by setting up material imbalance inequalities, the relation between the viscosity-average, number-average, and weight-average molecular weights, on the one hand, and the distribution of the fractions of the macromolecules, on the other. It has been possible to show that *the weight fraction of macromolecules with a molecular weight greater than or equal to the specified value cannot be greater than the ratio of the viscosity-average molecular weight to the specified value raised to the power equal to the parameter of the Mark–Houwink equation, while the numerical fraction of macromolecules with a molecular weight greater than or equal to the specified value cannot be greater than the ratio of the viscosity-average molecular weight to the specified molecular weight.*

IV. Specific rules for compositions of heterogeneous ecological subsystems

When heterogeneous systems are examined, new tasks, involving the determination of their phase and fractional composition and also of the measure of the fragmentation of phases arise. Therefore, in order to establish the general characteristics of the phase composition of heterogeneous systems, we shall set up relations for the imbalance of the volume and mass, expressing them with the aid of the average density of the entire system and the minimum and maximum densities of its constituent phases. As a result, we obtain a relation between the volume fraction of a particular part of the system and the average density of the heterogeneous system in the following form:

$$\frac{V_k^p(t)}{V_\Sigma(t)} \leqslant \begin{cases} [\bar{\rho}(t) - \rho_{min}]/(\rho_k - \rho_{min}) \\ \text{when } \rho_k > \rho(t), \\ [\rho_{max} - \bar{\rho}(t)]/(\rho_{max} - \rho_k) \\ \text{when } \rho_k \leqslant \bar{\rho}(t), \end{cases} \tag{15}$$

where $V_k^p(t)$ is the volume of the kth phase (fraction), $V_\Sigma(t)$ the volume of the entire heterogeneous system, and ρ_k the density of the kth phase.

Consequently, *the volume fraction of the phase (fraction) of the heterogeneous system cannot be greater than the ratio of the deviations*

of the average density of the entire heterogeneous system and the density of the given phase (fraction) from the minimum or maximum density of the heterogeneous system.

From the inequalities expressing the material-volume imbalance, we obtain

$$\frac{m_k^p(t)}{M_\Sigma(t)} \leqslant \begin{cases} \dfrac{1/\bar{\rho}(t)-1/\rho_{max}}{1/\rho_k-1/\rho_{max}} \\ \text{when } \rho_k < \bar{\rho}(t), \\ \dfrac{1/\rho_{min}-1/\bar{\rho}(t)}{1/\rho_{min}-1/\rho_k} \\ \text{when } \rho_k \geqslant \bar{\rho}(t), \end{cases} \tag{15a}$$

which makes it possible to formulate the following rule:

The weight fraction of the phase (fraction) of an ecological heterogeneous subsystem cannot be greater than the ratio of the deviations of the average specific volume of the entire ecological heterogeneous subsystem and the specific volume of the given phase (fraction) from the minimum or maximum specific volume of the subsystem.

As an example, we shall consider the application of this rule to the determination of the weight fraction of one of the components of DNA from the crab *Cancer borealis*. The average density of this DNA in CsCl solution is $\bar{\rho}(t)$ = 1694 kg m^{-3}, while its maximum density is 1700 kg m^{-3} or the density of the satellite band is 1681 kg m^{-3}. We shall estimate from Eqn. (15a) the weight fraction of the satellite band. Here $m_k^p(t)/M_\Sigma(t) \leqslant 0.313$, which corresponds to the real situation (according to experimental data for centrifugation in a density gradient,[32] the relative amount of the minor component of the DNA of the crab *Cancer borealis* in 0.3). The average density of mouse DNA is 1700 kg m^{-3}, while the maximum density is 1701 kg m^{-3}. Then, according to the rule, the weight fraction of the part with the density of 1690 kg m^{-3} is $\leqslant$0.09 and according to experimental data[33] it is approximately 0.08. Thus the experimental results indicate that the relations established can be applied in practice to heterogeneous ecological subsystems.

In the special case where the maximum and minimum specific volumes of phases constituting the system are unknown, it follows from Eqn. (15a) that *the weight fraction of the phase (fraction) of the ecological heterogeneous subsystem cannot be greater than the ratio of its density to the average density of the entire ecological heterogeneous subsystem.*

We shall use the latter postulate to predict the content of water in an ecological subsystem—an active silt representing a complex heterogeneous system containing micro-organisms and solid disperse particles with the aqueous dispersion medium surrounding them. Comparison of the high-speed estimates of the moisture contents of the active silt with the water contents found as a result of drying (Table 1) shows that in all cases the deviation of the high-speed estimates of the moisture content of the active silt from the exact value hardly exceeds 1.21%. The slightly greater moisture content determined by drying compared with the maximum possible value specified by the high-speed estimates in two cases out of 19 can be explained by errors of the measurement.

Consequently one may assume that the relation established between the weight fraction of the phase (fraction) of the ecological heterogeneous system and the ratio of its density to the average density of the entire system does indeed hold in practice and permits high-speed estimates of the moisture content of the active silt—a specific ecological subsystem used in purification plant for the protection of the environment against substances dissolved in waste water.

Table 1. High-speed estimates of the moisture content of an ecological subsystem (active silt) obtained under the conditions of incomplete information and the moisture contents found by a drying procedure*.

Average density of active silt, kg m^{-3}	Density of water, kg × × m^{-3}	Observed moisture content of the active silt, %	High-speed estimate of the moisture content of the active silt, %	Relative error of the high-speed estimate, %
1000.8	996.3	99.12	$\leqslant$99.52	0.40
1009.2	1002.3	99.13	$\leqslant$99.32	0.19
1002.4	993.8	99.29	$\leqslant$99.14	−0.15
1002.4	994.3	99.24	$\leqslant$99.19	−0.05
1001.24	998.8	99.24	$\leqslant$99.76	0.52
998.72	998.62	99.06	$\leqslant$99.99	0.93
1001.43	998.80	99.15	$\leqslant$99.74	0.59
1000.57	998.23	99.35	$\leqslant$99.77	0.42
1002.27	998.80	98.65	$\leqslant$99.65	1.01
1003.33	998.71	98.35	$\leqslant$99.54	1.21
1000.94	994.76	99.23	$\leqslant$99.38	0.15
998.96	994.70	99.25	$\leqslant$99.57	0.32
997.9	994.62	99.02	$\leqslant$99.67	0.65
999.48	995.78	98.94	$\leqslant$99.63	0.69
1001.72	992.88	99.01	$\leqslant$99.12	0.11
999.48	996.40	99.25	$\leqslant$99.69	0.44
996.93	995.84	99.40	$\leqslant$99.96	0.56
997.38	996.86	99.34	$\leqslant$99.94	0.60
999.11	996.11	99.30	$\leqslant$99.70	0.40

* The experiments were performed under the author's supervision in the Academy of Communal Economy.

We now set up the inequality for the imbalance of specific heats:

$$m_k^p(t)C_{p_k} + [M_\Sigma(t) - m_k^p(t)]C_{p_{min}} \leqslant M_\Sigma(t)\bar{C}_{sp}(t), \tag{16}$$

where $m_k^p(t)$ is the mass of the kth phase, $C_{p_k}^{sp}$ the specific heat of the kth phase, and $C_{p_{min}}^{sp}$ the minimum specific heat of the phases. The mass imbalance can be formulated as follows with the aid of the specific heats:

$$m_k^p(t) + [M_\Sigma(t)\bar{C}_{sp}(t) - m_k^p(t)C_{p_k}^{sp}]/C_{p_{max}} \leqslant M_\Sigma(t). \tag{17}$$

After rearrangements and combination of formulae (16) and (17), we arrive at the following postulate:

The weight fraction of a given phase, in a heterogeneous system, cannot be greater than the ratio of the deviations of the specific heat of the entire heterogeneous system and of the partial specific heat of the given phase from the minimum or maximum specific heats of the phases of the heterogeneous system.

Using the principle of the material-characteristic imbalance, we shall establish the general characteristics of the fragmentation of phases and of the size distribution of particles. By solving this problem with the aid of a sequence of inequalities, we obtain relations equivalent to such assertions.

The weight fraction of a part (fraction) of a heterogeneous system cannot be greater than one third of the product of the specific surface

of the entire system, the density of the disperse phase, and the maximum radius of the particles of the given part; the weight fraction of any part (fraction) of particles of a fragmented phase cannot be greater than the product of the specific number of the particles and the mass of the particle of maximum size in the given part (fraction).

Analysis of the adsorption of a multicomponent mixture can also be carried out under conditions of incomplete information with the aid of the idea of material imbalance. It was found that

$$\Gamma_k(t) \leqslant \begin{cases} (V_\Sigma(0)\bar{\rho}(0) - \bar{\rho}(t)V_\Sigma(t)]/(\mu_k S_{sp} M_\Gamma), \\ \text{provided that the qualitative composition of the mixture of adsorbates is known;} \\ \dfrac{[N_\Sigma(0) - N_\Sigma(t)]\mu_{max} - [V_\Sigma(0)\bar{\rho}(0) - V_\Sigma(t)\bar{\rho}(t)]}{M_\Gamma S_{sp}(\mu_{max} - \mu_k)}, \\ \text{when the qualitative composition of the mixture adsorbate is known if} \\ \mu_k < [V_\Sigma(0)\bar{\rho}(0) - V_\Sigma(t)\bar{\rho}(t)]/[N_\Sigma(0) - N_\Sigma(t)]; \\ \dfrac{\bar{\rho}(0)V_\Sigma(0) - \bar{\rho}(t)V_\Sigma(t) - \mu_{min}[N_\Sigma(0) - N_\Sigma(t)]}{M_\Gamma S_{sp}(\mu_k - \mu_{min})}, \\ \text{when the qualitative composition of the mixture adsorbate is known if} \\ \mu_k \geqslant [V_\Sigma(0)\bar{\rho}(0) - V_\Sigma(t)\bar{\rho}(t)]/[N_\Sigma(0) - N_\Sigma(t)]. \end{cases} \quad (18)$$

Here M_Γ and S_{sp} are the mass and specific surfaces of the adsorbent and $\Gamma_k(t)$ is the degree of adsorption of the kth component from the mixture of adsorbable substances at time t. Thus it is possible to analyse the adsorption process under conditions of a small amount of initial data.

V. Analysis of the deviation from the limiting possible contents of substances and rates of chemical reactions

For a number of problems of the protection of the environment, it is necessary not only to indicate the ranges of the possible contents of substances but also to achieve point predictions of all the quantities and to estimate the possible deviations. Theoretical analysis led to the derivation of formulae demonstrating that, for any prespecified absolute or relative deviation of the content of a component from its maximum possible value, there may exist ecological subsystems such that the real deviation is equal to the specified deviation. This means that the points corresponding to the different ecological subsystems can continuously fill the space of the possible contents of the components determined by the ratio of the average characteristic of the system to the isotypical measure of the properties of the components.

We shall make use of the universal characteristics of the compositions for the point estimates of the contents of the components in ecological subsystems. For a minimum amount of initial data, it is useful to postulate that the point estimate x_{est} of the weight fraction of components with $\mu_l > \mu_k$ is given by

$$x_{est} = 1 - n^*_{sp}(t)\mu_k/2. \quad (19)$$

The relative error of this estimate is

$$\frac{|x_{est} - \sum_{\mu_i > \mu_k} m_i(t)/M_\Sigma(t)|}{\sum_{\mu_i > \mu_k} m_i(t)/M_\Sigma(t)} \leqslant \frac{n^*_{sp}(t)\mu_k}{2[1 - n^*_{sp}(t)\mu_k]}. \quad (20)$$

In the case where qualitative analytical data are also available, the point predictions are refined. It follows from the relations established that in this situation the point estimate of the weight fraction of substances with specific heats greater than or equal to the specified value C^{sp}_k can be obtained with the aid of formula

$$x^c_{est} = 1 - (1/2)[\bar{C}_{sp}(t) - C^{sp}_{min}]/(C^{sp}_k - C^{sp}_{min}), \quad (21)$$

subject to the relative error

$$\frac{|x^c_{est} - \sum_{c_i^{sp} \geq C_k^{sp}} m_i(t)/M_\Sigma(t)|}{\sum_{c_i^{sp} \geq C_k^{sp}} m_i(t)/M_\Sigma(t)} \leqslant \frac{\bar{C}_{sp}(t) - C^{sp}_{min}}{2[C^{sp}_k - \bar{C}_{sp}(t)]}. \quad (22)$$

The non-equilibrium concentrations of reactants and products in the system can also be estimated with the aid of the equilibrium constants for closed homogeneous systems. For this purpose, the equilibrium value of the chemical variable is determined from the solution of the equation containing the equilibrium constant and the initial concentrations of the products and reactants of the chemical reaction.[33] With the aid of this variable, the point predictions of the concentrations of reactants and products and *a priori* estimates of their errors are found.

Table 2. ***A priori*** **estimates of the absolute errors of the point estimates of the rates of chemical reactions for a known ratio of the reactant concentrations.**

Reaction	Order of reaction	Rate constant for reaction	Overall concentration of reactants, kg m^{-3}	Absolute error of the point prediction of the rate of reaction kmol m^{-3} s^{-1}	*A priori* absolute estimate of the error of the prediction of the rate of reaction, kmol m^{-3} s^{-1}
Interaction of triphenylmethyl chloride with methanol	3	4.48×10^{-3} m^3 kmol^{-1} s^{-1}	31,281	$3.407 \cdot 10^{5}$	$\leqslant 3.545 \cdot 10^{-5}$
$NO_2 \rightarrow NO + (^1/_2)O_2$	2	100.6 m^3 kmol^{-1} s^{-1}	$1.84 \cdot 10^{-3}$	$7.9 \cdot 10^{-8}$	$\leqslant 8 \cdot 10^{-8}$
$C_6H_5-C\equiv C-COOH + I_2 \rightarrow C_6H_5-CI= =CI-COOH$	2	1.02×10^{-3} m^3 kmol^{-1} s^{-1}	10,039	$2.965 \cdot 10^{-7}$	$\leqslant 3.465 \cdot 10^{-7}$
Thermal decomposition of dioxane	1.5	5.8×10^{-3} m$^{1.5}$ kmol$^{-0.5}$ s^{-1}	1.45	$1.23 \cdot 10^{-5}$	$\leqslant 1.23 \cdot 10^{-5}$
$CH_2CHBrCOO^- + OH^- \rightarrow Br^- + CH_2CH(OH)COO^-$	2	5.73×10^{-4} m^3 kmol^{-1} s^{-1}	77.786	$6.069 \cdot 10^{-5}$	$\leqslant 6.193 \cdot 10^{-5}$

In order to predict the results of the change in the compositions of ecological systems and subsystems under the conditions of incomplete information, it is essential to analyse the possible deviations of the rates of chemical reactions from their maximum values. As a result of a theoretical study, it has been shown that, by virtue of the limitations to the densities of solutions and to the overall pressure of the mixture of gases, under real conditions the rates of chemical reactions have a relative maximum. It was found that, when account is taken of the first limitation, the rate of the chemical reaction reaches its relative maximum value for molar concentrations of the reactants directly proportional to the ratio of the kinetic orders with respect to these substances to their molecular

weights and, for a limited maximum total pressure of the gas mixture in the reactor, the rate of a chemical gas-phase reaction reaches its maximum value in the case where the partial pressures of the reactants are in the same proportions relative to one another as the kinetic orders with respect to these substances.

The possible ranges of the rates of chemical reactions thus established permitted point predictions of their values and the estimation of the absolute errors of such predictions under conditions of incomplete information. Table 2 presents the results of such predictions. The rate constants for the calculations were taken from Emanuel' and Knorre.[34] In all the cases analysed, such predictions proved justified.

Formulae for the estimation of the concentrations and mass of the products formed as a result of the reactions in ecological subsystems and also inequalities for the *a priori* estimation of their accuracy were derived with the aid of the maximum possible rates of chemical reactions.

In all cases of practical importance, parallel chemical reactions occur when measures are taken for the protection of nature and in respiration, digestion, and other processes where the organisms interact with the components of the environment. Under such conditions, a sequence of the following inequalities can be written for the estimation of the weight fractions of the reactants forming a monotonically non-decreasing sequence of reactivities:

$$\sum_{i=1}^{l_s} m_i(t) \leqslant \sum_{i=1}^{j-1} m_i(0) + [1-\varkappa_j(t)] \sum_{i=j}^{l_s} m_i(0) \leqslant$$

$$\leqslant [1-\varkappa_j(t)] \sum_{i=1}^{l_s} m_i(0) + \varkappa_j(t)\mu_{j-1} \sum_{i=1}^{j-1} m_i(0)\mu_i^{-1} \leqslant$$

$$\leqslant \left\{1-\varkappa_j(t)\left[1-\mu_{j-1}\sum_{i=1}^{l_s} n_i(0) \Big/ \sum_{i=1}^{l_s} m_i(0)\right]\right\} \sum_{i=1}^{l_s} m_i(0), \quad (23)$$

where $\varkappa_j(t)$ is the degree of conversion of the jth substance at time t; $1 \leqslant j \leqslant l_s$; l_s is the number of reactants forming the reactivity sequence.

The following rule follows from Eqn. (23):

The weight fraction of the substances in the mixture, which form a series with monotonically non-decreasing reactivities and which have not entered into parallel chemical reactions, cannot be greater than the sum of the quantity supplementing the degree of conversion of any one substance in the given mixture up to unity and the product of this degree of conversion, the molecular weight of the preceding substance in the reactivity series, and the specific number of moles of the initial mixture of substances forming the given series.

In the case where there is a monotonically non-increasing reactivity, another sequence of inequalities is valid:

$$\sum_{i=1}^{l_s} n_i(t) \leqslant [1-\varkappa_j(t)] \sum_{i=1}^{j} n_i(0) + \sum_{i=j+1}^{l_s} n_i(0) \leqslant$$

$$\leqslant \sum_{i=1}^{l_s} n_i(0)[1-\varkappa_j(t)] + \varkappa_j(t) \sum_{i=j+1}^{l_s} n_i(0) \leqslant$$

$$\leqslant \left\{1-\varkappa_j(t)\left[1-\sum_{i=j+1}^{l_s} n_i(0)\mu_i \Big/ \left(\mu_{j+1}\sum_{i=1}^{l_s} n_i(0)\right)\right]\right\} \sum_{i=1}^{l_s} n_i(0) \leqslant$$

$$\leqslant \left\{1-\varkappa_j(t)\left[1-\sum_{i=1}^{l_s} m_i(0) \Big/ \left(\mu_{j+1}\sum_{i=1}^{l_s} n_i(0)\right)\right]\right\} \sum_{i=1}^{l_s} n_i(0). \quad (24)$$

On the basis of Eqns. (24), we formulate a new rule:

The overall mole fraction of substances which have not entered into parallel chemical reactions by time t and which form a series with monotonically non-increasing reactivities cannot be greater than the sum of the quantity supplementing up to unity the degree of conversion of any of the substances constituting the reactivity series and the ratio of this degree of conversion to the product of the molecular weight of the next substance, after the chosen one, and the specific number of moles of the initial mixture of substances constituting the reactivity series.

We shall make use of the rules established for the occurrence of parallel chemical reactions in order to obtain point estimates of the results of chemical reactions of this type. Here one can write

$$\frac{m_{re}^{est}(t)}{\sum_{i=1}^{l_s} m_i(0)} = 1 - \frac{1}{2}\{1 - x_j(t)[1 - \mu_{j-1}n_{sp}^{s}(0)]\}, \quad (25)$$

where $m_{re}^{est}(t)$ is the point estimate of the overall mass of the substances constituting the reactivity series and entering into chemical reactions and $n_{sp}^{s}(0)$ is the specific number of moles of these substances at $t = 0$.

It follows from Eqns. (23) and (25) that the relative error of such a point estimate must satisfy the inequality

$$\frac{|m_{re}^{est}(t) / \sum_{i=1}^{l_s} m_i(0) - \sum_{i=1}^{l_s}[m_i(0) - m_i(t)] / \sum_{i=1}^{l_s} m_i(0)|}{\sum_{i=1}^{l_s}[m_i(0) - m_i(t)] / \sum_{i=1}^{l_s} m_i(0)} \leqslant$$

$$\leqslant \frac{1 - \kappa_j(t)[1 - \mu_{j-1}n_{sp}^{s}(0)]}{2\{\kappa_j(t)[1 - \mu_{j-1}n_{sp}^{s}(0)]\}}. \quad (26)$$

A point estimate of the mole fraction of the substances which have reacted is obtained similarly using Eqns. (24).

Various mixtures of petroleum products, members of genetic and homologous series, etc., entering the environment and present in various ecological subsystems, belong to the set of substances forming series with monotonically non-increasing or monotonically non-decreasing reactivities in parallel chemical reactions.

Point estimates of the results of parallel chemical reactions in ecological system can be refined, provided that data for μ_{min}^{s} and μ_{max}^{s}—the minimum and maximum molecular weights of the substances constituting sequences with monotonically non-decreasing or monotonically non-increasing reactivities—are available. Since

$$\sum_{i=1}^{j-1} m_i(0) \leqslant \mu_{j-1} \sum_{i=1}^{j-1} n_i(0),$$

it follows that, on the basis of the imbalance of the number of moles in the mixture, we obtain

$$\sum_{i=1}^{j-1} m_i(0)/\mu_{j-1} + \left[\sum_{i=1}^{l_s} m_i(0) - \sum_{i=1}^{j-1} m_i(0)\right] \Big/ \mu_{max}^{s} < n_{sp}^{s}(0) \sum_{i=1}^{l_s} m_i(0).$$

Consequently,

$$\sum_{i=1}^{j-1} m_i(0) \Big/ \sum_{i=1}^{l_s} m_i(0) \leqslant \frac{n_{sp}^{s}(0) - 1/\mu_{max}^{s}}{1/\mu_{j-1} - 1/\mu_{max}^{s}}.$$

On the basis of the latter expression, we find the relation for the case of a monotonically non-decreasing reactivity of a mixture with known values of μ^s_{max} and μ^s_{min}:

$$\sum_{i=1}^{l_s}[m_i(0)-m_i(t)] \Big/ \sum_{i=1}^{l_s} m_i(0) \geqslant \varkappa_j(t)\left[1-\frac{n^s_{sp}(0)-1/\mu^s_{max}}{1/\mu_{j-1}-1/\mu^s_{max}}\right].$$

This makes it possible to obtain the point estimates

$$m^{est}_{re}(t)/\sum_{i=1}^{l_s} m_i(0) = 1-\frac{1}{2}\left\{1-\kappa_j(t)\left[1-\frac{n^s_{sp}(0)-1/\mu^s_{max}}{1/\mu_{j-1}-1/\mu^s_{max}}\right]\right\},$$

and an *a priori* estimate of the modulus of the relative error:

$$\frac{|m^{est}_{re}(t)-\sum_{i=1}^{l_s}[m_i(0)-m_i(t)]|}{\sum_{i=1}^{l_s}[m_i(0)-m_i(t)]} \leqslant \left\{1-\kappa_j(t)\left[1-\frac{n^s_{sp}(0)-1/\mu^s_{max}}{1/\mu_{j-1}-1/\mu^s_{max}}\right]\right\} \Big/$$

$$\Big/ 2\kappa_j(t)\left[1-\frac{n^s_{sp}(0)-1/\mu^s_{max}}{1/\mu_{j-1}-1/\mu^s_{max}}\right].$$

For the case of the monotonically non-increasing reactivity of the mixture, we obtain after similar steps

$$\sum_{i=1}^{l_s}[n_i(0)-n_i(t)]\Big/\sum_{i=1}^{l_s} n_i(0) \geqslant \kappa_j(t)\left(1-\frac{1/n^s_{sp}(0)-\mu_{min}}{\mu_{j+1}-\mu^s_{min}}\right).$$

Consequently the number of moles of the reactive substances constituting a mixture with monotonically non-increasing reactivity can be estimated with the aid of the expression

$$n^{est}_{re}(t)\Big/\sum_{i=1}^{l_s} n_i(0) = 1-\frac{1}{2}\left\{1-\kappa_j(t)\left[1-\frac{1/n^s_{sp}(0)-\mu^s_{min}}{\mu_{j+1}-\mu_{min}}\right]\right\},$$

subject to the guaranteed relative error

$$\frac{|n^{est}_{re}(t)-\sum_{i=1}^{l_s}[n_i(0)-n_i(t)]|}{\sum_{i=1}^{l_s} n_i(0)} \leqslant \left\{1-\kappa_j(t)\left(1-\frac{1/n^s_{sp}(0)-\mu^s_{min}}{\mu_{j+1}-\mu^s_{min}}\right)\right] \Big/$$

$$\Big/ 2\kappa_j(t)\left(1-\frac{1/n^s_{sp}(0)-\mu^s_{min}}{\mu_{j+1}-\mu^s_{min}}\right).$$

VI. Specific features of the estimation of the changes in disperse ecological subsystems when nature-protecting measures are taken

The disperse particles entering the environment, formed as a result of man's industrial activity, exert an appreciable negative influence on consumers and producers. In order to predict the amount of disperse contaminants entering the hydrosphere and the atmosphere together with waste water and gaseous waste, it is necessary to establish the efficiency of the purification of such waste water and gaseous waste as a result of nature-protecting measures. A characteristic of the process involving the removal of disperse particles from an ecological subsystem is the degree of separation (purification) $\varkappa_s$ — a quantity indicating the weight fraction of the disperse phase trapped by means of technical nature-protecting procedures. Another parameter — the relative loss ε — is equal to the weight fraction of the residual disperse phase particles in the liquid or gas after purification. There exists a simple relation between the degree of separation (purification) and the relative loss:

$$\varkappa_s = 1-\varepsilon.$$

If after the completion of the application of nature-protecting measures, no compression or rarefaction of the purified liquid and gaseous media occurred, then the relative loss is equal to the ratio of the output and input weight concentrations of the disperse phase.

Taking into account the specific features of the disperse systems and using a probability (statistical?) treatment of the separation process, we formulate an expression for the degree of separation $\varkappa_s$ in the form

$$\varkappa_s = \int_o^\infty P_{11}(r,t|\mathrm{B})dF_1(r), \tag{27}$$

where $F_1(r)$ is the integral size distribution function of the particles of the disperse phase at the instant when the disperse system is introduced into the separation apparatus and $P_{11}(r,\ t|\mathrm{B})$ is the conventional probability of the separation (of entry into the collector designed for the disperse phase) by time t of a molecule present in particle having a radius r on entry into the apparatus subject to the condition that all the particles and molecules of the disperse medium enter the collectors for the phases undergoing separation.

In the separation of heterogeneous systems in continuous operation apparatus, the particles may become dispersed owing to the presence of velocity gradients in the streams and their impact against the inner surfaces of the apparatus and against one another. The fine particle fragments formed (other characteristics remaining unchanged: density and charge) are in most cases more difficult to separate than the whole particles. If the comminution takes place only at the instant when the particles are introduced into the apparatus, then the efficiency of the separation will be smaller than for gradual dispersion to the same extent. Therefore

$$\varkappa_s > \int_o^\infty P_{11}(r,t|\mathrm{B}\cap\mathrm{Con})dF^{fr}_1(r), \tag{28}$$

where $F^{fr}_1(r)$ is the integral size distribution function of the particles after grinding and $P_{11}(r,\ t|\mathrm{B}\cap\mathrm{Con})$ is the conventional probability of the separation of particles which have retained their initial dimensions subject to the condition that they enter one of the separation zones (one of the collectors).

For further exposition, we introduce the concept of the quasi-size of the separation of order α. We shall define the quantity r_{s_α} as the radius of a particle such that the relation

$$P_{11}(r,\ t|\mathrm{B}\cap\mathrm{Con}) \geqslant 1-\alpha,$$

is valid for $r \geqslant r_{s_\alpha}$. It follows from this definition that in the general case r_{s_α} depends on the current time t. The application of the concept of the quasi-size of the separation makes it possible to take into account the experimentally observed effects involving the loss of individual large particles owing to random influences, eddies, and streams of dispersion media, while finer particles are fully separated.

Using r_{s_α}, we can formulate the following inequality:

$$\int_o^\infty P_{11}(r,t|\mathrm{B}\cap\mathrm{Con})dF^{fr}_1(r) \geqslant (1-\alpha)\int_{r_{s_\alpha}}^\infty dF^{fr}_1(r). \tag{29}$$

Then

$$\varkappa_s \geqslant (1-\alpha)[1-F^{fr}_1(r_{s_\alpha})]. \tag{30}$$

In its turn, we have

$$\int_o^{r_{s_\alpha}} dF_1^{\text{fr}}(r) \leqslant r_{s_\alpha}^n \int_o^{r_{s_\alpha}} r^{-n} dF^{\text{fr}}(r) \leqslant r_{s_\alpha}^n \int_o^{\infty} r^{-n} dF_1^{\text{fr}}(r), \tag{31}$$

whereupon

$$\overline{r_{\text{fr}}^{-n}} = \int_o^{\infty} r^n dF_1^{\text{fr}}(r) \text{ and } \int_o^{r_{s_\alpha}} dF_1^{\text{fr}}(r) = F_1^{\text{fr}}(r_{s_\alpha}). \tag{32}$$

Ultimately, we have

$$F_1^{\text{fr}}(r_{s_\alpha}) \leqslant \overline{r_{\text{fr}}^{-n}} r_{s_\alpha}^n. \tag{33}$$

Consequently,

$$\varkappa_s \geqslant (1-\alpha)(1-\overline{r_{\text{fr}}^{-n}} r_{s_\alpha}^n). \tag{34}$$

The universal relation for the degree of separation thus demonstrated is valid for any form of the size distribution function of particles. This inequality is applicable to both continuous and periodic heterogeneous system separation processes. For its practical employment, it is essential to determine the quantity $\overline{r_{\text{fr}}^{-n}}$ for any positive value of n. For this purpose, we express $\overline{r_{\text{fr}}^{-3}}$ in terms of the particle concentration ν_{fr} after fragmentation. In the case of particles of arbitrary shape, the particle concentration is

$$\nu = \frac{C_o}{\beta_s \rho_1} \int_o^{\infty} \frac{dF_1(r)}{r^3} = \frac{C_o \overline{r^{-3}}}{\beta_s \rho_1}, \tag{35}$$

where β_f is a coefficient equal to the ratio of the volume of the particle to that of the cube having its characteristic dimension (for spherical particles, $\beta_f = 4/3\pi$) and C_0 is the concentration of the particles of the disperse phase.

If the particles of the disperse phase are insoluble in the dispersion medium, then the particle concentration after fragmentation can be found from the formula

$$\nu_{\text{fr}} = \beta_p C_o \overline{r^{-3}}/(\beta_f \rho_1), \tag{36}$$

where β_p is the fragmentation coefficient indicating by what factor the number of particles has increased on dispersion.

It follows from Eqn. (36) that $\nu_{\text{fr}} = \beta_p \nu$. On the other hand,

$$\nu_{\text{fr}} = C_o \overline{r_{\text{fr}}^{-3}}/(\beta_f \rho_1).$$

Hence

$$r_{\text{fr}}^{-3} = \beta_p \beta_f \rho_1 \nu / C_o. \tag{37}$$

We shall refer to the ratio ν/C_0 as the specific number of particles and shall denote it by n_{sp}. We may note that the product $\beta_f \rho_1 | r_{s_\alpha}^3$ is none other than $m_p(r_{s_\alpha})$—the mass of a particle whose radius is equal to the quasi-size of the separation. Then on substituting Eqn. (37) in the inequality (34), we obtain

$$\varkappa_s \geqslant (1-\alpha)[1-\beta_p m_p(r_{s_\alpha})\nu/C_o]. \tag{38}$$

We express $\overline{r^{-1}}$ with the aid of the specific surface. For particles of arbitrary shape,

$$S_{\text{sp}} \geqslant 3\rho_1^{-1} \int_o^{\infty} r^{-1} dF_1(r). \tag{39}$$

This inequality is converted into an equality in the case of spherical particles with an ideally smooth surface. Therefore

$$\overline{r^{-1}} \leqslant S_{\text{sp}} \rho_1 / 3. \tag{40}$$

For $\overline{r_{\text{fr}}^{-1}}$, one can also write

$$\overline{r_{\text{fr}}^{-1}} < S_{\text{sp}}^{\text{fr}} \rho_1/3 \text{ or } \overline{r_{fr}^{-1}} < \beta_s S_{\text{sp}} \rho_1/3,$$

where $S_{\text{sp}}^{\text{fr}}$ is the specific surface after dispersion and β_s is a coefficient showing by what factor the specific surface has increased owing to the fragmentation of the particles. With the aid of the latter inequality, we obtain from Eqn. (34)

$$\varkappa_s \geqslant (1-\alpha)[1-\beta_s S_{\text{sp}} \rho_1 r_{s_\alpha}/3]. \tag{41}$$

When the separation process is effected as a result of the work performed by external forces A, the particles may undergo deformation and fragmentation and an amount of heat Q may be evolved. We denote by $m_1^+(t)$ the mass of the disperse phase entering the apparatus at time t; ΔH_{def} is the change in the internal energy of the heterogeneous system on deformation of the particles. For systems which do not contain highly disperse fractions, one can write for the process under stationary conditions

$$A = \Delta U_{\text{def}} + Q + m_1^+(t)[S_{\text{sp}}^{\text{fr}} - S_{\text{sp}}]\sigma. \tag{42}$$

Hence

$$S_{\text{sp}}^{\text{fr}} = (A - \Delta U_{\text{def}} - Q)/[\sigma m_1^+(t)] + S_{\text{sp}}. \tag{43}$$

Subsequently

$$\beta_s = (A - \Delta U_{\text{def}} - Q)/[\sigma S_{\text{sp}} m_1^+(t)] + 1. \tag{44}$$

Thus the coefficient β_s, taking into account the phenomenon of dispersion during separation, can be found from simple energy relations. It is seen from Eqn. (44) that, other conditions being equal, the coefficient β_s diminishes with increase in the specific surface of the heterogeneous system entering the apparatus, i.e. the intensity of the comminution diminishes with increase in dispersity.

In the absence of dispersion, the coefficient $\beta_p = \beta_s = 1$ and formulae (38) and (41) assume the following form:

$$\varkappa_s \geqslant (1-\alpha)[1-n_{\text{sp}} m_p(r_{s_\alpha})], \tag{45}$$

$$\varkappa_s \geqslant (1-\alpha)(1-S_{\text{sp}} r_{s_\alpha} \rho_1/3). \tag{46}$$

The quantities r_{s_α} can be determined not only theoretically but also experimentally. A suspension (emulsion or aerosol) resistant to aggregation and having a known grain size distribution must be used for the experiment.

When random influences are negligible, for example, when coarsely disperse particles are deposited in the gravitational field, one can assume that all the particles larger than a certain radius r_{s_o}, called the size of the separation, are fully separated. When this condition holds, we find from the inequalities (45) and (46), having put $\alpha = 0$ in the latter,

$$\varkappa_s \geqslant 1 - n_{\text{sp}} m_p(r_{s_o}), \tag{47}$$

$$\varkappa_s \geqslant 1 - S_{\text{sp}} r_{s_o} \rho_1/3. \tag{48}$$

In the analysis of separation processes, the concept of the relative loss (breakthrough) ε is frequently employed. By definition, $\varepsilon = 1 - \varkappa_s$. From the inequalities (47) and (48), we obtain

$$\varepsilon \leqslant n_{\text{sp}} m_p(r_{s_o}), \tag{49}$$

$$\varepsilon \leqslant S_{\text{sp}} \rho_1 r_{s_o}/3. \tag{50}$$

The results of the theoretical study, expressed by the inequalities (45) and (46), can be usefully formulated in the form of the following theorems:

Theorem 5. *The relative loss (the ratio of the output and input weight concentrations) of the disperse phase cannot be greater than the sum of the specified probability and the product of the quantity supplementing to unity the specified probability, the specific number of particles, and the mass of the particle which is not separated with the specified probability.*

Theorem 6. *The relative loss (the ratio of the output and input weight concentrations) of the disperse phase cannot be greater than the sum of the specified probability and one third of the product of the specific surface, the quantity supplementing to unity the specified probability, the density of the disperse phase, and the radius of the particle which is not separated with the specified probability.*

In order to estimate the maximum possible degree of separation, we introduce the concept of the quasi-size of the loss r_{e_α} of order α. The quantity r_{e_α} will be defined as the radius of the particles such that the probability $P_{11}(r, t|\mathrm{B}\cap\mathrm{Con}) \leqslant \alpha$ for $r < r_{e_\alpha}$.

Taking into account the possibility of the fragmentation of particles, we obtain with the aid of r_{e_α}

$$\varkappa_s \leqslant \int_0^\infty P_{11}(r, t \mid \mathrm{B} \cap \mathrm{Con})\, dF_1(r) \leqslant$$
$$\leqslant \alpha \int_0^{r_{e\alpha}} dF_1(r) + \int_{r_{e\alpha}}^\infty P_{11}(r, t \mid \mathrm{B} \cap \mathrm{Con})\, dF_1(r). \qquad (51)$$

Since $P_{11}(r, t|\mathrm{B}\cap\mathrm{Con}) \leqslant 1$, it follows that

$$\int_{r_{e\alpha}}^\infty P_{11}(r, t \mid \mathrm{B} \cap \mathrm{Con})\, dF_1(r) \leqslant \int_{r_{e\alpha}}^\infty dF_1(r). \qquad (52)$$

We therefore have

$$\int_0^\infty P_{11}(r, t|B\cap\mathrm{Con})\, dF_1(r) \leqslant 1 - F_1(r_{e_\alpha}) + \alpha F_1(r_{e_\alpha}). \qquad (53)$$

Since

$$F_1(r_{e_\alpha}) \geqslant 1 - \int_{r_{e\alpha}}^\infty (r/r_{e_\alpha})^n\, dF_1(r) \geqslant 1 - r_{e_\alpha}^{-n} \int_0^\infty r^n\, dF_1(r), \qquad (54)$$

it follows that

$$F_1(r_{e_\alpha}) \geqslant 1 - \overline{r^n}/r_{e_\alpha}^n. \qquad (55)$$

Consequently

$$\varkappa_s \leqslant \alpha + (1-\alpha)\overline{r^n}/r_{e_\alpha}^n. \qquad (56)$$

On the basis of the results obtained, we formulate the following theorem:

Theorem 7. *The degree of separation of a disperse system cannot be greater than the sum of the order of the quasi-size of the loss and the product of the quantity supplementing to unity the order of the quasi-size and the ratio of the initial nth order moment of the random particle radius to the quasi-size of the loss raised to the nth power.*

With the aid of the relations demonstrated, one can also obtain point estimates of the degree of separation of disperse systems with an improved accuracy. Bearing in mind that, when $\alpha = 0$, the relative loss $\varepsilon \leqslant \overline{r^{-n}} r_{s_0}^n$, we can write expressions for the point estimate of the degree of separation:

$$\varkappa_{\mathrm{est.}} = 1 - \overline{r^{-n}} r_{s_0}^n/2, \qquad (57)$$

and for the *a priori* estimate of the modulus of its relative error:

$$\frac{|\varkappa_s - \varkappa_{\mathrm{est.}}|}{\varkappa_s} \leqslant \frac{r_{s_0}^n \overline{r^{-n}}}{2\varkappa_s} \leqslant \frac{r_{s_0}^n \overline{r^{-n}}}{2(1 - r_{s_0}^n \overline{r^{-n}})}, \qquad (58)$$

where $n = 1$, we obtained from the last two relations

$$\varkappa_{\mathrm{est.}} = 1 - S_{\mathrm{sp}} \rho_1 r_{s_0}/6 \text{ and}$$

$$\frac{|\varkappa_s - \varkappa_{\mathrm{est.}}|}{\varkappa_s} \leqslant \frac{S_{\mathrm{sp}} \rho_1 r_{30}}{6 - 2 S_{\mathrm{sp}} \rho_1 r_{s_0}}, \qquad (59)$$

and, when $n = 3$, they assume the following form:

$$\varkappa_{\mathrm{est.}} = 1 - n_{\mathrm{sp}} m_{\mathrm{p}}(r_{s_0})/2 \text{ and}$$

$$\frac{|\varkappa_s - \varkappa_{\mathrm{est.}}|}{\varkappa_s} \leqslant \frac{n_{\mathrm{sp}} m_{\mathrm{p}}(r_{s_0})}{2[1 - n_{\mathrm{sp}} m_{\mathrm{p}}(r_{s_0})]}. \qquad (60)$$

As was in fact to be expected, all the experimental points obtained by different workers[35–38] lie close to the line of the predicted degrees of separation and none fall into the cross-hatched regions of impossible values (Figs. 3 and 4). The closer were the points in Fig. 4 plotted from the experimental values to the abscissa axis, the more accurate was the *a priori* point estimate of the degee of separation of the disperse systems.[38]

VII. The rule for the compositions of simple and complex two-component and multi-component ecological systems and subsystems

Comparison of the rules established above for the compositions of homogeneous and heterogeneous ecological subsystems makes it possible to discover their general features and to proceed to the solution of the problem of the discovery and formulation of the main rule for the compositions of ecological systems and subsystems, generalising the results obtained in the theoretical study.

All the inequalities for the contents of substances, demonstrated for both homogeneous and heterogeneous systems, can be reduced to the following form provided that qualitative analytical data are available:

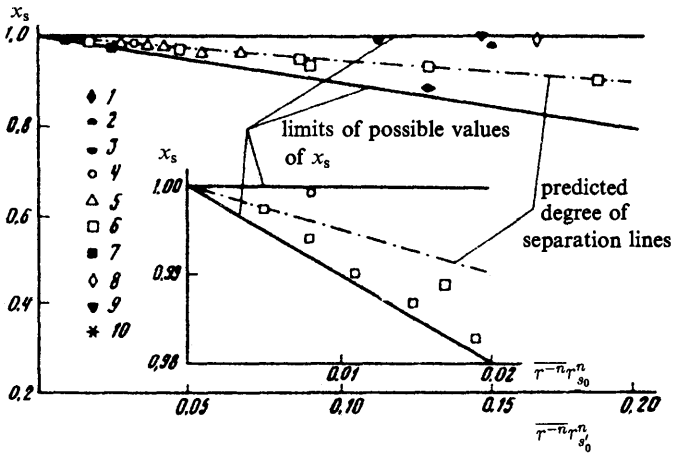
$$\mathfrak{D}_i(t) \leqslant (\overline{\mathrm{S}}(t) - \mathrm{S_b})/(\mathrm{S}_i - \mathrm{S_b}), \qquad (61)$$

where $\mathfrak{D}_i(t)$ is the fraction (weight, mole, or volume fraction) of the component, phase, or part (fraction) of the ecological subsystem, $\overline{\mathrm{S}}(t)$ is an average physicochemical characteristic of the system, $\mathrm{S_b}$ is the boundary value (minimum or maximum) of the isotypical measure of the property of the given substance of the system, and S_i is a measure of the property of the ith component.

The inequality (61) is equivalent to the following formulation of a theorem:

Theorem 8. *The fraction of any component [phase, part (fraction)] of ecological systems and subsystems cannot be greater than the ratio of the deviations of the average characteristic of the entire system (subsystem) as a whole and the isotypical measure of the property of the component, phase, or part (fraction) from their maximum or minimum value.*

Varieties of the expression for the fraction are unambiguously related to the method of averaging the physicochemical characteristic of the ecological system (subsystem). For example, if this is the specific number of moles, then $\mathfrak{D}_i(t)$ will be the weight fraction and if it is the average density $\bar{S}(t)$ then $\mathfrak{D}_i(t)$ will be the volume fraction.



Point	System being separated (purified)	Separation apparatus
1	Aqueous oil emulsion	Ultracentrifuge
2	Tobacco dust	Sleeve filter, No. 2 cloth fabric
3	Tobacco dust	Sleeve filter, No. 5114 nitron fabric
4	Water drops	Cyclone
5	Kaolin suspension	Centrifugal "Plava-E" separator
6	Suspension of poly (vinyl chloride)	Tubular centrifuge
7	Kaolin suspension	Tubular centrifuge
8	Quartz glass suspension	Cup-type centrifuge
9	Suspension of Ammophos sludge	Settling tank
10	Coal powder	Sifting screen

Figure 3. Point estimates of the degree of separation (purification) of disperse systems.

On combining the entire set of relations established, we obtain the following equation:

$$\mathfrak{D}_i(t) = K_i(t)\bar{S}(t)/S_i, \qquad (62)$$

which reflects the principal rule for the compositions of multicomponent ecological subsystems and eco-systems:

The relative amounts (contents) of substances, phases, fractions, parts, and subsystems in any ecological systems (subsystems) can be numerically estimated at any instant by comparison with the ratios of the average (overall) characteristic of the system (subsystem) to the isotypical measures of the properties of the substances, phases, fractions, parts, and subsystems multiplied by coefficients which are always smaller or equal to unity and do not increase by discrete increments together with the uncertainty of the estimate with increase in the level of the reliable initial information.

For the practical employment of the principal rule for the compositions of ecological subsystems and systems, it proved necessary to calculate the coefficients in Eqn. (62). An algorithm was therefore developed for the calculation of these coefficients for different levels of the initial data and a block scheme was set up. For cases of incomplete information, it proved possible to derive formulae permitting the calculation of the coefficients of the principal rule. The possibility of determining the coefficients $K_i(t)$ from thermodynamic and kinetic parameters for higher levels of initial data was demonstrated.

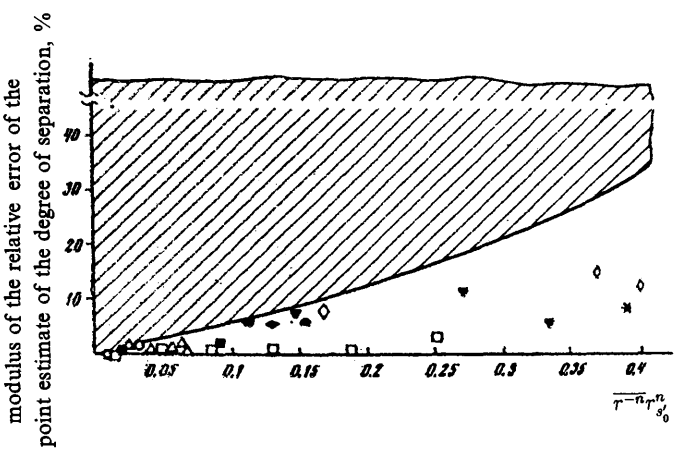


Figure 4. The region of the possible values of the modulus of the relative error of the point estimates of the degree of separation of disperse systems with an improved accuracy. For the designations of the points, see Fig. 3. The cross-hatched region represents the impossible values of the modulus of the relative error (of the points estimates of the degree of separation with an improved degree of accuracy).

On the basis of the principal rule established for the compositions, it was found possible to represent graphically the changes in the compositions of multicomponent ecological systems and subsystems in terms of their variables $\bar{S}(t)$, S_i, and $\mathfrak{D}_i(t)$.

With the aid of the main rule established for the compositions, it has been shown that *the overall (average) characteristic of the entire system (specific heat, specific number of moles, density, specific volume, specific heat of combustion, etc.) is equal* to the product of the isotypical characteristics of the components, their weight fractions, and the reciprocals of the coefficients of the principal rule governing compositions.

The principal rule for the compositions of ecological systems and subsystems can be used not only for the determination of the compositions of the eco-system but also for the solution of certain problems of the protection of the environment, including the organisation of the monitoring and measures ensuring that the limiting permissible concentrations of toxic substances are not exceeded.

Using the author's own experimental data for the specific heats of solution of two- and three-component powders and the specific volume of a specific ecological subsystem (active silt) as well as the literature data,[39,40] the coefficients of the principal rule for the

compositions of eco-systems and ecological subsystems have been found for zero uncertainty in the estimates of the contents of the components. The results of the calculations are presented in Table 3, from which it is seen that, in conformity with the principal rule for the compositions established, all the coefficients are not more than unity.

Table 3. The coefficients of the principal rule for the compositions of ecological systems and subsystems for zero uncertainty in the estimates of the contents of the components.

Ecological subsystem	Components	Average characteristic	Content, weight fraction	$K_i(t)$
Three-component powder	KNO_3,	Specific heat of solution	50.0	0.64
	$CuSO_4 \cdot 5H_2O$,		33.3	0.07
	KCl		16.7	0.17
Two-component powder	KNO_3,	Ditto	33.3	0.94
	$CuSO_4 \cdot 5H_2O$		66.7	0.31
Aqueous solution of methanol	H_2O,	Specific volume of solution	45.8	0.40
	CH_3OH		54.2	0.60
Aqueous HNO_3 solution	H_2O,	Specific heat of solution	80.0	0.95
	HNO_3		20.0	0.05
Gas mixture	$H_2+O_2+H_2O$	Specific number of moles	3.0	0.29
			47.0	0.28
			50.0	0.55
Man	H_2O	Specific heat	75	0.87
Active silt	H_2O	Specific volume	99.12	0.996
	H_2O	Ditto	98.35	0.988

VIII. Measures ensuring that the limiting permissible amounts of liquid and gaseous waste polluting the environment are not exceeded for different levels of initial information

The increasingly acute ecological crisis makes it essential that the following requirement is rigidly adhered to: that the limiting permissible norms as regards gaseous and liquid waste products[2,12] contaminating the hydrosphere and the atmosphere must not be exceeded. The existence of different levels of initial information makes it much more difficult to satisfy this requirement.

According to the definition of the limiting permissible amounts of liquid and gaseous waste, the condition that the limiting permissible concentration of the ith toxic substance in the eco-system is not exceeded is specified by the relation

$$C_i^-(t) \leqslant (\mathrm{LPLW}_i \text{ or } \mathrm{LPGW}_i)/Q(t), \tag{63}$$

where $Q(t)$ is the productivity of the apparatus for the detoxification (purification) of liquid or gaseous waste, $C_i^-(t)$ the concentration of the toxic ith component at the outlet from the detoxification apparatus to the environment, LPLW_i and LPGW_i are the limiting permissible amounts of liquid and gaseous waste, and t is the current time.

For further exposition, we shall make use of the concept of the protection factor (PF_i) for the environment introduced by the present author.[12] By definition, this quantity shows by what factor the weight fraction of the ith toxic component has diminished during the detoxification process as a result of separation and chemical reactions.

The concentration of the ith toxic component at the inlet to the detoxification apparatus can be represented in the following form with the aid of the principal rule for compositions:

$$C_i^+(t) = K_i(t)\bar{\rho}_+(t)\bar{S}_{sp}(t)/S_i^{sp}, \tag{64}$$

where $\bar{\rho}_+(t)$ is the average density at a given instant t of the liquid or gaseous mixture subjected to detoxification.

Using the concept of the protection factor, we shall represent the condition that the limiting permissible concentration is not exceeded in the following way:

$$\frac{K_i(t)\bar{\rho}_-(t+t_r)S_{sp}(t)}{S_i^{sp}PF_i} \leqslant \frac{(\mathrm{LPLW}_i \text{ or } \mathrm{LPGW}_i)}{Q(t+t_r)}, \tag{65}$$

where $\bar{\rho}_-(t + t_r)$ is the average density of the mixture (for example, water or air being purified) entering the environment at time $t + t_r$ after detoxification and t_r is the residence time of the mixture in the detoxification apparatus.

We shall call the ratio $\mathrm{LPLW}_i/[Q(t + t_r)\bar{\rho}_-(t + t_r)]$ the dimensionless limiting permissible amount of liquid waste and $\mathrm{LPGW}_i/[Q(t + t_r)\bar{\rho}_-(t + t_r)]$ the dimensionless limiting permissible amount of gaseous waste. We shall designate them by DLPLW_i and DLPGW_i. The physical significance of the quantities introduced is fairly simple: they indicate the maximum permissible weight fraction of the toxic substance in the liquids and gases entering the environment after detoxification (purification).

Using the concept of DLPLW_i and DLPGW_i, one can write on the basis of Eqn. (65)

$$PF_i \geqslant \frac{K_i(t)\bar{S}_{sp}(t)}{(\mathrm{DLPLW}_i \text{ or } \mathrm{DLPGW}_i)S_i^{sp}}. \tag{66}$$

The last relation proves the following theorem.

Theorem 9. *The protection factor for the environment not less than the product of the reciprocal of the dimensionless limiting permissible amount of liquid (gaseous) waste, the coefficient of the principal rule for compositions, and the ratio of the average specific characteristic of the homogeneous or heterogeneous mixture being detoxified to the isotypical measure of the properties of the toxic component guarantees that the limiting permissible concentration (LPC) is not exceeded.*

Thus, on the basis of the theorem formulated, it is possible to determine the protection factors for the environment which guarantee *a priori* that the limiting permissible concentration is not exceeded for different levels of initial information.

In particular, in the presence of a minimal amount of data, when only the values of $\bar{S}_{sp}(t)$ and S_i^{sp} are known, we have the following expression according to the sequence of inequalities for the detoxification of waste waters and bearing in mind that $K_i(t)$ is always less than or equal to unity:

$$C_i^-(t) \leqslant \frac{K_i(t)\bar{\rho}_-(t+t_r)\bar{S}_{sp}(t)}{S_i^{sp}PF_i} \leqslant \frac{\bar{\rho}_-(t+t_r)\bar{S}_{sp}(t)}{S_i^{sp}PF_i} \leqslant \frac{\mathrm{LPLW}_i}{Q(t+t_r)}. \tag{67}$$

According to the analogous sequence of inequalities for the detoxification of gaseous waste, we obtain a relation for the estimation of the protection factor (in the presence of a minimal amount of information) guaranteeing that the limiting permissible concentration is not exceeded:

$$PF_i \geqslant \frac{\bar{S}_{sp}(t)\bar{\rho}_-(t+t_r)Q(t+t_r)}{(\mathrm{LPLW}_i \text{ or } \mathrm{LPGW}_i)S_i^{sp}}. \tag{68}$$

If S^{sp}_{max} and S^{sp}_{min}, the maximum and minimum specific partial measures of the properties (characteristics) of the components, are known, then it follows from formulae (61) and (62) that the coefficient of the principal rule for compositions $K_i(t)$ can be estimated as follows:

$$K_i(t) \leqslant \begin{cases} \dfrac{\bar{S}_{sp}(t) - S^{sp}_{min}S^{sp}_i}{S^{sp}{}_i - S^{sp}_{min}\bar{S}_{sp}}(t) \\ \text{when } S^{sp}_i \geqslant \bar{S}_{sp}(t), \\ \dfrac{S^{sp}_{max}\bar{S}_{sp}(t)S^{sp}{}_i}{S^{sp}_{max} - S^{sp}{}_i\bar{S}_{sp}(t)} \\ \text{when } S^{sp}{}_i < \bar{S}_{sp}(t). \end{cases} \tag{69}$$

For this level of information, we obtain from formula (69) the relation ensuring unconditionally that the LPC is not exceeded:

$$PF_i \geqslant \begin{cases} \dfrac{\bar{\rho}_-(t+t_r)Q(t+t_r)[\bar{S}_{sp}(t) - S^{sp}_{min}]}{(LPLW_i \text{ or } LPGW_i)(S^{sp}_i - S^{sp}_{min})} & \text{for } S^{sp}_i \geqslant \bar{S}_{sp}(t) \\ \dfrac{\bar{\rho}_-(t+t_r)Q(t+t_r)[S^{sp}_{max} - \bar{S}_{sp}(t)]}{(LPLW_i \text{ or } LPGW_i)(S^{sp}_{max} - S^{sp}_i)} & \text{for } S^{sp}_i > \bar{S}_{sp}(t). \end{cases} \tag{70}$$

Formulae (69) and (70) are special cases of the more general formula (66).

The protection factor can be expressed as a function of temperature, the concentration of added reagents, the residence time, the length of the apparatus, and other technological and design parameters of the detoxification process and apparatus. Therefore, expressing one of such quantities as a function of the reciprocal of the protection factor, it is possible to determine from the inequality (66) the values of the technological or design parameter guaranteeing the satisfaction of the ecological requirement that the limiting permissible amounts of liquid or gaseous waste are not exceeded. For example, if the detoxification of the ith toxic component is described by a first-order chemical reaction equation, then the following expression holds for the protection factor:

$$PF_i = \phi(T) = \exp[At_r \exp(-E_a/RT)], \tag{71}$$

where A is the pre-exponential factor, E_a the activation energy, R the gas constant, T the temperature and $\varphi(T)$ a function of temperature.

Having expressed the temperature T as a function of the reciprocal of the protection factor $\varphi^{rec}(PF_i)$ and then using the inequality (66), we obtain a relation for the determination of the absolute temperatures which must be maintained in the chemical waste water detoxification reaction in order to guarantee that the limiting permissible amount of liquid waste is not exceeded:

$$T \geqslant -E_a/R \ln\left[\frac{1}{At_r}\ln\frac{K_i(t)\bar{S}_{sp}(t)}{DLPLW_iS^{sp}_i}\right]. \tag{72}$$

In another special case, for the detoxification of disperse contaminations with an unknown distribution of grain sizes (by the separation of the disperse particles), using the inequality already established

$$\varepsilon \leqslant \alpha + (1-\alpha)\overline{r^{-n}_{fr}}r^n_{s_\alpha},$$

and theorem 9, we can formulate a sequence of inequalities guaranteeing that the limiting permissible concentration of the disperse phase is not exceeded:

$$\frac{1}{PF_{i_d}} \leqslant \alpha + (1-\alpha)\overline{r^{-n}_{fr}}r^n_{s_\alpha} \leqslant \frac{LPGW_{i_d} \text{ or } LPLW_{i_d}}{Q(t+t_r)C^+_{i_d}(t)} \leqslant$$

$$\leqslant [(DLPGW_{i_d} \text{ or } DLPLW_{i_d})S_{i_d}]/[K_{i_d}(t)\bar{S}_{sp}(t)]. \tag{73}$$

Here the subscript d indicates that the corresponding characteristics refer to the disperse phase. Consequently

$$r_{s_\alpha} \leqslant \sqrt[n]{\left[\frac{[DLPGW_{i_d} \text{ (or } DLPLW_{i_d})]S^{sp}{}_{i_d}}{K_{i_d}(t)\bar{S}_{i_d}(t)} - \alpha\right] \Big/ [(1-\alpha)\overline{r^{-n}_{fr}}]}. \tag{74}$$

Eqn. (74) makes it possible to find the quasi-sizes of the separation which guarantee that the limiting permissible concentration of the disperse phase is not exceeded. After this, it only remains to select the apparatus for the purification of waste water or a dust trapping device with r_{s_α} satisfying this expression.

For known values of the input concentrations (weight and particle concentrations) of the disperse phase and in the absence of effects associated with the fragmentation of particles, the inequality (74) (for $n = 3$) assumes the following form:

$$r_{s_\alpha} \leqslant \sqrt[3]{\left[\frac{LPGW_{i_d} \text{ (or } LPLW_{i_d})}{Q(t+t_d)C^+_{i_d}(t)} - \alpha\right] \Big/ [(1-\alpha)\beta_f\rho_1 n_{sp}]}. \tag{75}$$

Thus the successive employment of the principle of the coupled material-characteristic imbalance has made it possible to obtain a series of inequalities for the estimation of the contents of substances in ecological systems and subsystems for different levels of initial information and to formulate the principal rule for the compositions of such systems. The results obtained can be applied both for high-speed large-scale monitoring and for the design and technical measures to protect the environment, whose aim is to reduce the amounts of different toxic substances entering the hydrosphere, atmosphere, and lithosphere.

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Translated from *Uspekhi Khimii* **60** 2362–2372 (1991) U.D.C. 579.24.242

Membranotropic autoregulatory factors in methane oxidising bacteria

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ABSTRACT. It is possible that the methane oxidising bacteria *M. capsulatus* synthesise in the course of their development and secrete into the culture liquid extracellular metabolites—membranotropic autoregulatory factors d_1 and d_2 the synthesis of which had been observed earlier in other groups of microorganisms. It is shown that the physiological effect of the factor d_2 is due to the influence of the fraction comprising free aliphatic acids and containing mainly palmitic palmitoleic acids. One of the manifestations of the effect of the specific autoregulatory factor d_1 as its concentration increases in the culture medium is the transition of the vegatative cells to a hypometabolic state. The active principle of the factor d_1 is the lactone of 3-deoxypentonic acid. A practical use for the chemical analogues of the autoregulatory factors d_1 and d_2 is suggested.

The bibliogrphy includes 25 references.

The increased ecological requirements as regards the safety of the technologies used in the national economy necessitates the development of new or an improvement of the efficiency of the already available technological solutions subject to the obligatory condition of their ecological cleanliness. One of the most vigorously developing branches of world economic practice is biotechnology, which has acquired the status of one of the priority fields in developed countries. The recognition of the leading role of biotechnology is not fortuitous. The intensification of agriculture and industries satisfying man's immediate needs is associated with the employment of biotechnological processes. Furthermore, the recovery of the environment subjected to anthropogenic influences should not only involve specific solutions based on biotechnological processes but also solutions based on the fundamental knowledge of the reactions and turnover of substances effected with participation of natural biological factors. A special role is attributed in this connection to microorganisms whose activity is associated with conversion cycles of the elements and whose use in numerous industrial processes can provide a basis for the ecologically safe preparation of the required products. The discovery of the characteristics of the vital activity of microorganisms and of the general physiological principles of microbial synthesis and the study of their trophic relations and their resistance and adaptation to environmental factors are therefore of fundamental importance.

Studies of the regulation of the growth and development of methane oxidising bacteria constitute one of the examples emphasising the necessity for extensive study of the characteristics of the vital activity of microorganisms. Methane oxidising bacteria are widely distributed in natural media, they play a major role in the transformations of carbon in nature,[1] and they participate in the formation of hydrogen sulphide in the petroleum stratum waters as a result of the trophic links between methane oxidising bacteria and sulphate reducing bacteria.[2] In national economic practice, methane oxidising bacteria are treated as a promising object for the ecologically clean manufacture of bacterial biomass from natural gas in order to employ it as feed additives, for the isolation of biologically active components from the biomass,[3] for use in mine shafts in order to reduce the concentration of methane in air to diminish the risk of explosion,[4] and as part of the composition of technolgenic biocenoses used in various biological methods for increasing the extraction of petroleum from the given geological stratum.[5] However, one should note that, despite the fairly widescale investigation of the physiology of the bacteria of this group, the characteristics of their development have been little investigated, which creates difficulties in obtaining them for large scale industrial processes. It is known that under unfavourable conditions certain methanotrophic organisms give rise to resting forms: exospores, lipid, cysts, and ripe and unripe cysts of the *Azotobacter* type.[6] For other methanotropic organisms, the resting forms are unknown. The causes of the uncontrolled change in metabolic activity under the conditions of periodic and chemosatic cultivation of methane oxidising bacteria have not been investigated. The instability of the process is frequently observed in the continuous cultivation of *M. capsulatus*, which is accompanied either by a spontaneous increase in the cell population, or a decrease in metabolic activity, or processes involving the lysis of the culture. However, the factors which determine the direction of the processes towards the transition of the cells to a hypometabolic (anabiotic) state or the state of cell autolysis remain unelucidated.

In modern theoretical microbiology, there exists a concept according to which a developing microbial culture represents a self-regulating system, its behaviour being determined both by the action of external factors and by the influence of autoregulatory metabolites, which control the rate and the stages in the develoment of the culture.[7]

In recent years, the elucidation of the role of the autoregulatory metabolites involved in the control of the physiological states of the cells of microorganisms and in the development of their cultures has become a vigorously investigated field. In the most general definition, the autoregulatory factors are understood as physiologically active compounds of different chemical nature, secreted by the microbial population or its components into the surrounding medium, not used for the purposes of constructive and energetic metabolism, and playing in the cell community the role of a signal in relation to the alteration of the quantitative (rate of growth) or qualitative (cytodifferentiation) state of the microbial culture.[8] The principal biological function of the extracellular autoregulatory metabolites is to ensure the occurrence of the intercellular interactions and also the interactions of the microorganisms with the medium, directed towards the active growth of the population and the self-preservation of the species.

The extensive data obtained in the study of low-molecular-weight autoregulatory metabolites, synthesised by organisms at different

levels of development (prokaryotes and eukaryotes and unicellular and multicellular organisms), made it possible to formulate this field of knowledge as a separate science—chemical ecology.

We have discovered[8,9] membranotropic autoregulatory factors participating in the control of the structural state and physiological activity of membranes and hence regulating the metabolic activity of the cell, which is expressed by a change in the intensity of cell proliferation processes and/or the differentiation of the microbial cell. In conformity with the last activity among those listed above, they have been called factor d.[8] It has been shown that microorganisms belonging to various taxonomic groups synthesise in the course of the development of their periodic or non-periodic cultures and secrete into the surrounding (incubation) medium autoregulatory metabolites—factors d_1 and d_2 differing in their chemical nature and physiological activity.[9]

This review presents data concerning the discovery of a specific autoregulatory mechanism of the development of the methane oxidising bacterium *M. capsulatus*, effected with the aid of the membranotropic factors d_1 and d_2, and the study of the chemical nature and biological activity, which is important both for the characterisation of the growth and development of the methane oxidising bacteria in natural populations and for ensuring the stability and improving the productivity of the processes involved in their continuous cultivation.

The following biological tests have been adopted in the isolation and purification of the factors d: (1) the change in the intensity of the respiration of the intact cells and isolated membranes (index of membranotropic activity); (2) the change in the rate of growth of the proliferating culture of the producer (integral index of the metabolic activity of the cells); (3) stimulation of the growth of the resting forms of the producer; (4) induction of the autolysis of the cells and (biological activity of the factor d_2); (5) induction of the transition of the vegetative cells to a hypometabolic or anabiotic state (biological activity of the factor d_1).

The isolation, purification, and identification of the factors d_1 and d_2 are based on the methods of modern lipidology:[10] extraction of the autregulators from the culture liquid by lipophilic solvents, their partitioning in a solvent system as a function of the polarity of the molecules, fractionation on columns and plates with adsorbents using selective eluents and solvent systems, rechromatography for the preparative isolation of chromatographically homogeneous fractions, and gas-chromatographic separation for the determination of the component composition and possible identification.[8,11-13]

The membranotropic autoregulatory factors were isolated from the culture liquid separated from the cells by extraction with 1-butanol (2:1) and the residue, remaining after distilling off the solvent, was separated into two fractions in which the activity of the factor d_1 or the factor d_2 predominated. After the separation on a silica gel column of the "crude" preparation of the factor d_2 (chloroform–alcohol fraction in the chloroform–methanol–water two-phase system in proportions of 2:2:1), the neutral lipids, capable of being eluted with chloroform, exhibited the activity of the factor d_2. On separation of the active fraction by preparative thin-layer chromatography, the activity was observed mainly in the fraction comprising free aliphatic acids (FAA) (Table 1), which was inferred from the ability of the preparation both to inhibit the respiration of the membranes and cells and to induce the autolysis of the latter. The FAA fraction of the factor d_2 as well as the "crude" preparation of this autoregulator stimulated at low concentrations and inhibited at high concentrations the respiration of the producer cells. The degree of inhibition of the cell respiration and of the oxidase activities of the isolated membranes increased with increase in the concentration of the FAA introduced, with decrease in the pH of the incubation medium, and with decrease in the amount of the biological material in the measuring cell. It developed as a function of time and also depended on the physiological age of the culture (Figs. 1 and 2).

Table 1. The change in the rate of the endogenic respiration of the cells under the influence of fractions of the extracellular *M. capsulatus* lipids.

No. of fraction	50 μl ml^{-1} fraction	TLC, R_f*	Rate of consumption of oxygen			OD of cell suspension, % relative to control***
			Control μmol O_2 min^{-1}	expt.** μmol O_2 min^{-1}	expt.** % relative to control	
1	Diglycerides	0.12	0.93	0.86	92.5	88
2	Unidentified	0.16	0.90	1.08	120.0	92
3	Aliphatic acids	0.37	0.96	0.42	43.8	55
4	Unidentified	0.49	0.97	0.81	83.5	97
5	Triglycerides	0.47	0.92	1.03	112.0	88

* The spots on the chromatogram were identified by analogy with mono-, di-, tri-glyceride oleates.

** Data obtained by the polarographic method; the measurements were performed 3 min after introducing the preparation into the measuring cell.

*** OD = optical density of the cell suspension determined 3 h after introducing the preparations of the fractions into the culture.

Gas-chromatographic analysis of the composition of the FAA fraction (of the factor d_2), isolated from the culture liquid in the course of the stable cultivation of *M. capsulatus* in a chemostatic regime, made it possible to determine a wide range of aliphatic acids: with an even and odd number of carbon atoms ranging from C_{12} to C_{18}, saturated acids, and mono-, di-, tri-, and poly-unsaturated acids (Table 2).[14] Palmitic and palmitoleic acids, whose contents reached 36 and 25% respectively, were the main components. Other components present were 6% of stearic acid, 8% of oleic acid, and 6.5% of linoleic acid. Biological tests of the commercial preparations of the individual aliphatic acids, forming part of the composition of the factor d_2 in dominant amounts, established that unsaturated aliphatic acids are responsible for the physiological activity of this autoregulator (Table 3).

Model experiments designed to determine the biological activity of the components of the factor d_2 showed that oleic and palmitoleic acids induce the active lysis of the cells of the culture *M. capsulatus* in the linear growth phase. Thus in the presence of oleic acid, considered as a chemical analogue of the factor d_2, introduced into the cell suspension at a concentration of $(4-70) \times 10^{-2}$ μg ml^{-1}, vigorous lysis of the culture (70%) was observed after only 1 h of incubation, reaching virtually 100% with increase in the incubation time to 4 h (the autolysis of the cell was inferred from the fall in the optical density of the cell suspension and also from the amount of

soluble protein released from the cells into the incubation medium, the level of which amounted to 37% in the given instance). This conclusion agrees with the earlier results of the study of the chemical nature of the factor d_2 in the bacteria *Pseudomonas carboxydoflava* and *Bacillus cereus*.[11]

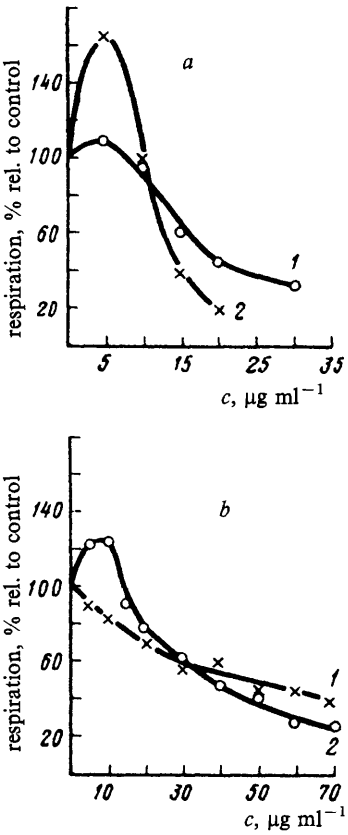


Figure 1. The influence of the factors d_1 (*a*) and d_2 (*b*) of a culture *M. capsulatus* on the endogenic respiration of the producer cells as a function of the concentration *c* of the autoregulator and the physiological state of the cells in the exponential (curve *1*) and linear (curve *2*) growth phases.[13]

The mechanism of the action of FAA (the factor d_2) on cells is based on their ability to be incorporated in membranes without the participation of acyl-transferring proteins.[15] The stimulation of the respiration of the cells of ageing cultures under the influence of low FAA concentrations, which has been demonstrated, can be accounted for by the ability of unsaturated aliphatic acids to increase the liquidity of the membrane lipids, which increases the activity of the electron-transport chain enzymes integrated in the membrane.[16] The stimulation of respiration by saturated aliphatic acids is probably based on their ability to uncouple respiration and oxidative phosphorylation.[17] This effect is more pronounced when the medium is acidified, whereupon the FAA are fully protonated. The introduction of high concentrations of the factor d_2 (20–80 μg ml^{-1}) or of its active principle—unsaturated aliphatic acids, in the given instance oleic and palmitoleic acids (200 nm ml)—into the profilerating bacterial culture leads to a supercritical increase in the liquidity of the membranes, which induces the inhibition of the respiration of the cells and stimulates the autolysis of the cells. This conclusion does not conflict with the available literature data showing that saturated aliphatic acids exert a destabilising influence on membranes.[18]

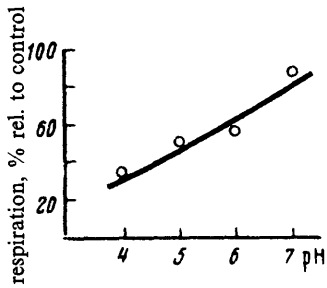


Figure 2. The influence of the factor d_2 of a culture of *M. capsulatus* (20 μg ml^{-1}) on the endogenic respiration of the linear growth phase cells suspended in 0.15 M phosphate-citrate buffer as a function of the pH.

Table 2. The aliphatic acid composition of the extracellular lipids of a *M. capsulatus* culture.[14]

Acids	Content oflipids under chemostatic conditions (D* = =0.21 h^{-1}, *t*=41 °C)%	Content of lipids under lysis conditions, %
12:0	0.63	0.22
13:0	1.07	0.75
14:0	1.45	1.59
14:1	2.32	2.97
15:0	2.70	4.18
15:1	Сл.**	См.***
16:0	36.75	29.21
16:1	24.37	15.71
17:0	0.38	См.***
16:2	3.19	6.86
17:1	0.39	См.***
18:0	6.59	4.54
18:1	8.12	6.73
18:2	6.51	8.87
18:3	1.77	15.51
18:4	3.76	2.82
	$\sum_{unsat}$=50.43	$\sum_{unsat}$=59.47

* D = flow rate, h^{-1}

** The acid was detected in trace amounts (less than 0.01%).

*** The acid was not detected.

It is essential to note that the autolytic degradation of microorganisms induced by the influence of high concentrations of the factor d_2 or its chemical analogue, which has been chosen as the

biological test, represents the response of the cells to the extreme effect of autoregulators. In the course of the development of cultures of microorganisms, the change in the structure and functional activity of membranes under the influence of physiological FAA concentrations ensures that the metabolic processes (katabolic and anabolic), which play an important role throughout the entire life cycle of the microorganisms, remain in balance.

Table 3. The influence of aliphatic acids on the endogenic respiration of the cells of a *M. capsulatus* culture.

Acid concentration nmol ml^{-1}	Cell respiration (% relative to 100% in the control 3 min after the introduction of the acid)			
	palmitic	palmitoleic	stearic	oleic
20	140	150	120	160
200	110	5	115	5
400	85	5	120	5

Thus the biological role of the factor d_2 or microorganisms consists, in the case of the methane oxidising bacteria, in maintaining the liquidity of the cell membrane lipids within the limits ensuring the optimum and necessary lipid–protein interactions through which the functional activity of the membrane is controlled. At the limiting permissible concentration of the factor d_2 in the culture, the latter destabilises the membranes, which induces the development of autolytic processes.

These data can be used to develop procedures for the autolysis of methane oxidising bacterial cells with the aid of the factor d_2 or its chemical analogue in order to obtain the cell protein in a soluble form, which increases significantly the assimilability and digestability of the microbial biomass used as a protein feed additive in protein-balanced feed for agricultural animals and birds.

The results obtained in the determination of the chemical structure and biological activity of the factor d_2 have been used to analyse the data on the stability of the technological process for the preparation of the methanotrophic bacterial biomass under experimental-industrial conditions. In elucidating the causes of the spontaneous autolysis of a chemostatic culture of *M. capsulatus*, we began with the following hypothesis. It may be that under conditions considered the synthesis of the extracellular factor d_2 was increased and hence the balance between the activities of the factors d_1 and d_2 was disturbed in favour of the latter, which stimulated the developing autolysis of the cell. Comparative analysis of the level of the factor d_2 in the versions involving a stably growing chemostatic culture and an autolysing culture showed that in the latter case there was a significant increase both in the activity of the factor d_2 (12.3 units litre^{-1} for the stable culture and 19.6 units litre^{-1} for the autolysing culture) and in the specific content of unsaturated aliphatic acids (Table 1). It is noteworthy that the increase in the sum of unsaturated aliphatic acids in the autolysing culture compared with the stably growing culture is not correlated with the corresponding increase in the activity of the factor d_2. However, the observed fact can be explained by taking into account data showing that the greater destabilising effect of polyunsaturated aliphatic acids on membranes compared with monounsaturated acids. It follows from Table 1 that significant amounts of C_{18} polyunsaturated acids appear in the autolysing culture. Thus the instability of the production of the *M. capsulatus* biomass associated with the autolysis of the cells in the chemostatic culture may be caused by the increase in the level of activity of the factor d_2. On this basis, a possible practical recommendation involves the necessity to achieve balanced levels of the activities of the factors d_1 and d_2, which can be achieved by the artificial introduction of a chemical analogue of the factor d_1.

The question arises what is the autoregulatory factor d_1 of *M. capsulatus*? As shown above, the autoregulatory factors d_1 detected in certain bacteria[9] exhibit a membranotropic activity, a test for which involes a change in the endogenic respiration of cells and in the exogenically stimulated respiration of the membranes. The biological activity of the factors d_1 is manifested by their ability to induce the transition of vegetative cells to the anabiotic state, a test for which involves the formation of refractile resting forms of microorganisms under the influence of the factor d_1.[19]

In the course of the purification of the factor d_1 of a culture of *M. capsulatus*, it was established that the sought type of activity was exhibited by the acetone fraction obtained in the separation of the "crude" preparation of the factor d_1 (aqueous alcohol fraction in the chloroform–methanol–water two-phase system in proportions of 2:2:1) on a silica gel column. Subsequent separation of this fraction by thin layer chromatography in the chloroform–methanol–acetic acid–ethyl ether solvent system (in proportions of 35:5:5:45) revealed that the activity of the factor d_1 was observed in the fraction with R_f = 0.67. After rechromatography, a chromatographically homogeneous preparation was obtained, its individuality being demonstrated by chromatography on Silufol and Merck plates in the initial solvent system and also in the chloroform–acetone–methanol (12:4:1) and the chloroform–methanol (85:15) systems. The chromatographically individual fraction of the factor d_1 had all the properties of the autoregulators of this type described previously. At concentrations of 7–40 μg mol^{-1}, the preparation inhibited the endogenic respiration of the cells and the respiration of the isolated membranes stimulated by NADH and malate or succinate. The degree of inhibition of the respiration depended on the concentration of the factor introduced and the pH of the medium, developing as a function of time (Figs. 3 and 4). The individual isolated fraction of the factor d_1 of a culture of *M. capsulatus* did not exhibit species specificity in relation to both other species of methane oxidising bacteria and bacteria of other genera, but the extent of their effect on the cells was different. The specific biological activity of the factor d_1 of a *M. capsulatus* culture was similar to the activity of the autoregulators of this type in previously investigated bacteria.[8,9] In doses of 20–80 μg ml^{-1}, the factor d_1 induced the formation of refractile anabiotic forms of *M. capsulatus*. It follows from the adopted definition of the resting forms of microorganisms, that specialised cells, whose formation is a natural event in the cycle of the development of microbial cultures, may be included among them.[20] On the basis of the foregoing, conditions were selected for the cultivation of *M. capsulatus*, where provision was made for the possible increase in the synthesis of the factor d_1 in the culture, as a consequence of which the cycle of its development terminated with the formation of refractile forms similar to those obtained when the bacterial cells were acted upon by the pure preparation of the factor d_1. The refractile forms of *M. capsulatus*, both obtained on treatment with the factor d_1 and formed in the

natural cycle of the development of these bacteria, exhibited all the characteristics of the resting forms of the microorganisms: the absence of an experimentally determined metabolic activity, an increased refraction of light by the organisms as a consequence of the dehydration of the cell protoplast, prolonged survival, and the characteristic features of their ultrastructural organisation which are different from those of vegetative cells.

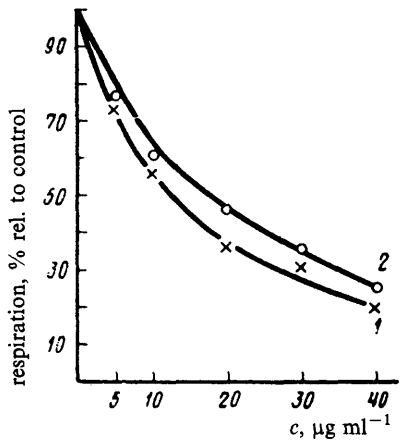


Figure 3. The suppression of the NADH-oxidase (curve *1* and malate oxidase (curve *2*) activities of the isolated membranes of *Micrococcus lysodeikticus* by the factor d_2/[13]

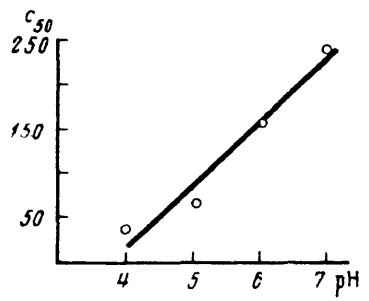


Figure 4. The influence of the pH of the incubation medium (0.2 M phosphate-citrate buffer) on the inhibition by the factor d_1 of the endogenic respiration of the *M. capsulatus* cells; c_{50} = amount of the factor d_1 (μg ml^{-1}) causing 50% inhibition of the respiration of the cells.

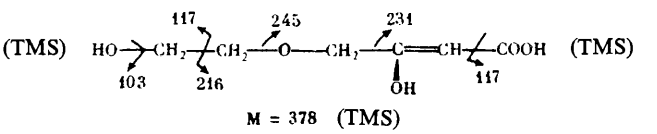
Thus the anabiotic cells, whose formation is induced by the activity of the factor d_1, can be classified as cyst-like anabiotic forms designed to preserve the bacterial species under conditions unfavourable for growth.

The authors suggest that the resting forms described for certain methane oxidising bacteria are apparently formed with participation of their factors d_1 and the differences, mentioned by Gal'chenko et al.[6] and Whittenburg and Dalton,[21] between the structures of their envelopes and their refractile properties are caused by the conditions which determine the activity of the above autoregulator and its concentration. The complete analogy in the manifestation of the biological activity of the factor d_1 of the *M. capsulatus* bacteria and the previously described factor d_1 of the *P. carboxydoflava* and *B. cereus* bacteria suggests also the identity of the mechanisms of their action on the structural organisation of the membranes.[22,23] The mechanism of the action of the factor d_1 on the lipid bilayer of the membrane is apparently based on the formation of a network of intermolecular hydrogen bonds between the functional groups of the autoregulator molecule and the lipid molecules, which leads to the immobilisation of the lipid matrix. A consequence of the structural reorganisation of the membrane (polycrystallisation) is a change in the functional activity of the enzymes integrated in it (in particular inhibition of the enzymes of the electron-transport chain), a change in the permeability of the membrane to univalent ions, and the associated dehydration of the cell (the increase in refractility). Thus the factors d_1 are capable of modifying the structure of the lipid phase of the membrane, increasing its microviscosity, in contrast to the action of the factors d_2, which increase the liquidity of the membrane.

Finally, one should note yet again that the regulatory function of the factors d_1 and d_2 of microorganisms depends not only on their concentration in the developing culture but also on the external cultivation conditions, in particular on the pH and ionic composition of the growth medium. In this connection, they can be regarded as mediators of the transmission of the external signal to the cell.

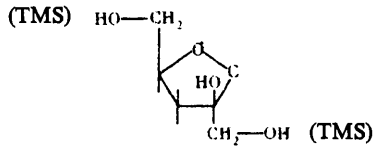
Having described the biological activity of the factor d_1 of a *M. capsulatus* culture, we shall turn to the problem of the identification of its chemical structure. The determination of the structure of the factors d_1 was based on the results of spectroscopic and mass-spectrometric analyses and proton magnetic resonance spectra. It had been shown previously[12] that, as regards their chemical nature, the factors d_1 of the *P. carboxydoflava* and *B. cereus* bacteria are alkoxybenzenes, which are present in the bacterial cultures in the form of a mixture of isomers or homologues differing in the positions of the hydroxy-groups in the ring and the configuration of the alkyl group.

It has been demonstrated by chromatograph-linked mass-spectrometric analysis under the conditions indicated by Svetlichnyi et al.[11] that two substances enter into the composition of the active principle of the factor d_1 of a *M. capsulatus* culture. These substances cannot be identified by computer from the Wiley and NBS libraries. However, their retention times are in the region of linear C_{10} aliphatic acids, C_6 polyfunctional acids, and deoxypentoses. Mass-fragmentation analysis revealed that the spectra of both compounds contain common ions characteristic of carboxylic acids (the ions 117, 129, 135, and 145) and a hydroxy-group (alcohol group) (the ion 103). This shows that the above substances are related—isomers or molecules with small structural differences. The structures of the test molecules are the same as far as the ion 261. On the basis of a computer search catalogue, the following structure of the molecules, which explains the mass-spectrometric data for these compounds, can be put forward according to the details of the fragmentation of the molecules (under the influence of electron impact at 70 eV):



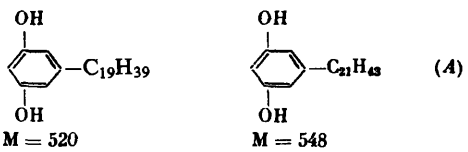
M = 378 (TMS)

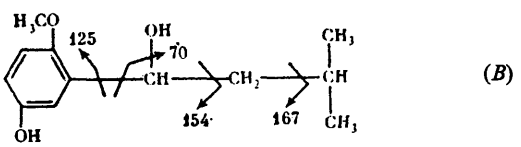
The closest version suggested by the computer in the identification process indicates that these substances are lactones of pentonic acids.[24] They give rise to many of the ions present in the alcoholic derivatives of the test substances, namely 103, 117, 129, 131, 133, 147, 217, 245, and 235. The lactone of 3-deoxypentonic acid (M = 378, trimethylsilyl derivative) is closest to the test substances:



M = 378 (TMS)

The chemical structure of the factors d_1 isolated from the *P. carboxydoflava (A)*, and *B. cereus (B)* cultures is as follows:[12]





M = 210

Thus investigations have shown that the chemical nature of the factor d_1 of a *M. capsulatus* culture, inducing the formation of anabiotic forms of the producer, differs from that established previously for the factor d_1 of the *P. carboxydoflava* and *B. cereus* bacteria. The very fact of the observation of differences between the chemical structures of compounds exhibiting the same type of biological activity is very interesting. Studies on the final identification of the chemical structure of the factor d_1 of a *M. capsulatus* culture as well as the determination of the nature of the factors d_1 of other microorganisms appears to be extremely significant. Firstly, these data can provide an idea about what general structure or functional groups are responsible for the biological activity associated with membrane polycrystallisation processes, the changes in the functional activity of the membranes, and the dehydration of cells in the course of the development of the anabiotic state. Secondly, the expansion of knowledge about the structures of compounds exhibiting the type of activities investigated is essential for the selection of cheap and readily available chemical analogues for their practical application in the development of technologies associated with the employment of stabilised cells in order to produce bacterial preparations for different purposes.

In conclusion, one must emphasise yet again that the data described constitute only a special example of the large field of biological knowledge concerning the nature and action of low-molecular-weight metabolites, whose function is to control the changes in the qualitative state of the organism, the physiological activity of the cells, and their interaction with one another and with the surrounding medium. One should note the necessity for the study of the biological activity of autoregulators strictly in relation to changes in the external conditions in the surrounding medium, in the given instance the conditions in the cultivation of microorganisms. The combination in one system of our ideas about the role of external and endogenic (autoregulatory) factors in cell proliferation processes (the growth of the culture) and cytodifferentiation will promote the acquisition of fundamental knowledge about the features of the vital activity of microorganisms in their environment. In addition progress in studies on the mechanisms of the regulation of the growth and development of microorganisms may serve as a basis for a theory of controlled cultivation and may help in the solution of specific biotechnological problems.

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Translated from *Uspekhi Khimii* **60** 2373–2411 (1991) U.D.C. 546.215

The role of hydrogen peroxide in natural aquatic media

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ABSTRACT. Chemical and biochemical processes defining the H_2O_2 cycle in natural waters and in biological subjects are examined. Assessments are given of the inflow of H_2O_2 into surface waters from the atmosphere, data are collated on the H_2O_2 content of sea and fresh water. Photochemical, catalytic and biochemical processes make the main contribution to H_2O_2 formation. The interaction between intracellular redox processes of aquatic microorganisms and the redox state of aquatic media is discussed. Biotic and abiotic processes for the decomposition of H_2O_2 in natural waters and the role of free radicals connected with the H_2O_2 cycle in the self-purification of natural aquatic media are examined. Data are presented which indicate the important role of H_2O_2 in the formation of the biological wealth of natural waters.

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I. Introduction

Truisms of the type "water is life" and "without oxygen the living world cannot exist" are well-known. Water is contained not only in the hydrosphere but is also one of the essential components of the atmosphere and is present in the lithosphere in large quantities and in the free state. In its turn molecular oxygen exists not only in the form of an atmospheric gas but is also partially dissolved in water and is contained in ground gases. The effects of water and oxygen on living processes are different. Organic life without water is impossible in principle, and strictly it originated on the Earth without oxygen.

It is known that oxygen is formed in photosynthesis by a 4-electron oxidation of water. In its turn oxygen is converted back into water by a 4-electron reduction. However in nature single-event 4-electron processes are only effected in specific biological and catalytic systems.[1,2] As a rule various intermediates are formed as a result of the oxidation of water or the reduction of O_2, among which is hydrogen peroxide, the stable intermediate product of 2-electron conversions of oxygen and water.

Even on the basis of such general considerations it may be proposed that hydrogen peroxide must accompany the oxidation–reduction conversions of oxygen and water. Even more, it is fairly difficult to purify water from traces of H_2O_2 without using special measures. The overall question is, in which processes and in what amounts is it formed and decomposed, and what is the "purpose" of hydrogen peroxide in the life processes of aerobic organisms and in the environment? The present review is devoted to the examination of these questions and their application to the problem of setting the quality of natural waters.

II. Methods for detecting hydrogen peroxide

The content of hydrogen peroxide in the environment is not large, so special, highly sensitive methods are required for its detection. Such methods have been developed only comparatively recently due to the recently awakened interest in studying the role of H_2O_2 in the environment. Methods of titrating H_2O_2 using the iodometric procedure[3] have a lower limit of sensitivity at the 10^{-5} M level. Sinel'nikov[4] has successfully reduced the level of sensitivity of the iodometric titration to 10^{-6} M, however the method is extremely laborious and is not widely used. Electrochemical methods of analysis of H_2O_2 are also not widely used at present, although the highly sensitive chromatographic method of analysis for the content of H_2O_2 in aqueous media is based on the use of an electrochemical transducer. Spectral methods, such as chemiluminescent, fluorometric and photometric methods, are the most widespread.

1. Chemiluminescent methods

Chemiluminescent methods have the greatest sensitivity. The oxidation reaction of luminol and other substances with hydrogen peroxide is used in these essentially kinetic methods for generating electronically excited species emitting quanta of light. The intensity of the chemiluminescence is proportional to the H_2O_2 concentration in the sample being analysed. The methods using luminol are the most widespread.[5] Luminol is very soluble only in a medium of pH $\gtrsim$ 10 so reaction is effected in an alkaline medium in the majority of chemiluminescent methods using it. Cobalt salts, haematin, potassium ferricyanide, etc. are used as catalysts of H_2O_2 decomposition in alkaline medium.

Various dissolved organic and inorganic compounds are present in natural aquatic objects. Some of them participate in the catalysis of H_2O_2 decomposition in alkaline medium (in which the analysis is carried out), others react with reactive intermediate particles or affect the properties of the catalyst used and the reaction kinetics. Because of this the chemiluminescent procedure does not always give correct results. It is necessary to construct calibration graphs of 'added

hydrogen peroxide *vs.* signal observed' for each new sample investigated. In addition, control analyses of water samples where hydrogen peroxide would be completely decomposed are necessary for background information. Catalase is usually used as the additive to decompose H_2O_2.

The enzyme peroxidase also serves as catalyst of the chemiluminescent emission of luminol when it is oxidised with hydrogen peroxide.[6] This reaction is effected in neutral or weakly alkaline media with an optimum in the region of pH 8–8.5. Impurities in natural waters may prove to have a marked inhibiting action because of the low solubility of luminol in neutral media.

Comparatively recently several sensitive chemiluminescent procedures for determining hydrogen peroxide in solution have been developed which are based on the luminescence of peroxyoxalates, which are the oxidation products of oxalate esters with hydrogen peroxide.[7–9]

Fluorimetric and photometric methods of determining H_2O_2, based on the peroxidase oxidation of specific substrates, are widespread. In the absence of kinetic chemiluminescent methods, the fluorescence and photometric methods may be regarded as stoichiometric. The decrease in the initial reagent or the concentration of final product of the peroxidase reaction are recorded. It is necessary to be confident that the stoichiometry of the reaction of H_2O_2 with the substrate is retained over a fairly wide range of conditions of carrying out the analysis.

The selective peroxidase oxidation of hydrogen donors with hydrogen peroxide and other organic peroxides has been known for a long time. Substrates include phenols, aromatic amines, triarylmethanes and certain heterocyclic compounds.

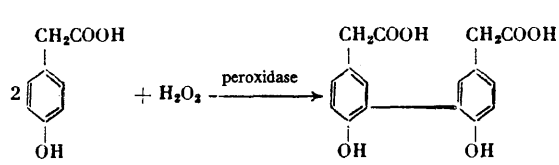
2. Fluorimetric methods

Fluorimetric methods of determining trace amounts of H_2O_2 have been carried out in two ways.

The first comprises oxidation of an H donor substrate, possessing marked fluorescent properties, with hydrogen peroxide into a non-fluorescent product. In this case the concentration of H_2O_2 is measured by the decrease in fluorescence intensity. Scopoletin (a fluorescent phenol) has been used as a donor for horse radish peroxidase when determining the H_2O_2 content of cell cultures.[10–12]

Zika and collaborators,[13–15] Kieber and Helz[3] and Holm and collaborators[16] have modified this procedure to be suitable for the analysis of the H_2O_2 content of natural waters. The procedure enables continuous automated measurements to be carried out.

In the second variant *p*-hydroxyphenylacetic acid is used as substrate for the peroxidase reaction. Oxidation of this substrate leads to the formation of a product possessing fluorescent properties.[9,17–26]



Fluorescence analysis is suitable only for relatively pure water since fresh and coastal sea waters contain a large quantity of interfering organic components.[27] An advantage of the method is the possibility of extended storage of the fluorescent product in the water sample being analysed.

3. Photometric methods

The photometric methods of determining H_2O_2 are the most widespread.[28,29]

In 1970 Motolla and collaborators[30] were the first to use the peroxidase oxidation of the leuco form of the dyestuff Crystal Violet to develop a highly sensitive analytical method for determining hydrogen peroxide.

This method was later used for the analysis of natural samples.[31] The procedure proposed[31] was inadequate due to the non-linear character of the dependence of the absorption of the oxidised form on H_2O_2 concentration in the sample and the extended (about an hour) time to carry out the analysis at a comparatively low sensitivity (10^{-5} M).

Optimisation of that method[30,31] has been carried out[25] by varying reagent concentrations, the order of mixing and the conditions of conducting the analysis. Overall the optimisation successfully increased significantly the sensitivity (10^{-7} M), reduced the time to carry out the analysis (3 min), reduced the consumption of reagents and secured linearity for the calibration graph. It became clear, in particular, that the growth rate and level of dyestuff coloration achieved (Malachite Green, Crystal Violet) depended on the relative content of peroxidase and humic compounds in the water. This is seemingly linked with the formation of a complex of the peroxidase with humic compounds and the participation of the reactive residues of the humic compounds in the reaction with the peroxidase–peroxide complex.

Under optimum conditions, using leuco-Crystal Violet (LCV) in the analysis of water samples for H_2O_2 content, 5 mg litre^{-1} leuco base and 20 mg litre^{-1} horse radish peroxidase were taken. Reaction was carried out in pH 4.5 acetate buffer (0.05 M). When carrying out serial measurements it is possible to prepare a "developing" solution containing a 10 times more concentrated mixture of leuco base and peroxidase in acetate buffer. In this way the analysis reduces to adding 1 ml mixture to 9 ml water sample to be analysed.

The advantages of the photometric methods of analysing samples of natural waters for H_2O_2 content are the simple design of the apparatus, the possibility of visual control (of Crystal Violet), the possibility of extended storage of "developed" test samples (F-substituted Malachite Green[32]) and the possibility of increasing the sensitivity of the method by the use of liquid chromatography.[23]

Among the disadvantages of the method are the need to conduct the reaction in weakly acidic media and the possible consequent appearance of unexpected factors affecting the results of analysis and the effect of turbidity of the water samples being analysed on the results of the photometric measurements (the need to filter or centrifuge test samples with a high content of suspended particles). In addition the need to construct calibration graphs for determining the apparent extinction coefficient of the dyestuff and the usually low solubility in water of the leuco base of the dyestuff lead to competition of the peroxidase–peroxide complex from H donors contained in the water sample being analysed.

Recently *N,N*-diethyl-*p*-phenylenediamine has been proposed as a peroxidase substrate. It possesses favourable analytical properties and a high solubility in water.[33]

As has been shown[31,34,35] when analysing natural waters using leuco Crystal Violet, the characteristic blue colour is determined by the presence in the water test sample of H_2O_2 exclusively and not organic peroxides. Nevertheless it is necessary to carry out experiments with catalase added to the water being analysed in order to allow for the possible contribution of organic peroxides to the observed colour and to determine the background absorption.

The emergence of coloured forms of leuco bases in the water samples may arise not only from the peroxidase reaction but also from the possible content of other oxidising agents in the medium. In order to verify such a possibility it is necessary to carry out a "cold" experiment without addition of peroxidase to the sample being analysed.

The photometric method of analysing low concentrations of H_2O_2 may be used in the kinetic mode. This is determined by the formation of a coloured compound (I) on reaction of H_2O_2 with peroxidase. In the presence of H_2O_2 and a suitable substrate the stationary concentration of compound (I) is determined by the rate of its formation (proportional to the H_2O_2 concentration in the medium) and its apparent transformation constant (proportional to substrate concentration). By measuring the concentration of compound (I) and knowing the rate constant for the reaction of H_2O_2 with peroxidase, it is possible to calculate the concentration of hydrogen peroxide in the medium.

Table 1. Content of H_2O_2 in natural waters.

Water sample	Place of sampling	$[H_2O_2]$, 10^7 M	Reference
Snow	Japan	20–40	[36]
Rain	Japan	100–250	[36]
	USA, California	3–40	[37]
	USA, Florida	9–75	[13]
	USA, North Carolina	0.01–1.5	[38]
	USA, North Carolina	1.5–45	[39]
	Gulf of Mexico	114–820	[40]
	Western Atlantic	84–206	[40]
	USA, Florida	284±38	[40]
	USA, California	9–880	[41]
	USA	3–720	[20]
Sea water	Gulf of Mexico	0.14–1.7	[12]
	Gulf of Mexico	1.7–2.9	[42]
	Gulf of Mexico	1.2–1.4	[43]
	Gulf of Mexico, at the coast	1.0–2.4	[44]
	Gulf of Mexico, far from the coast	0.9–1.4	[44]
	Biscayne Bay (Florida coast)	0.8–2.1	[45]
	Bahamas Bank	0.5–1.9	[45]
Estuaries	Pacific Ocean, Peruvian coast	0.08–0.7	[46]
	Chesapeake Bay	0.03–17	[47]
Fresh water	Volga, USSR	13–32	[4]
	Reservoirs, USSR	7–13	[48–50]
	USA, S.E.	0.9–3.2	[14]
Ground waters	USA	0	[14]

III. Distribution of hydrogen peroxide in the environment

Up to the middle sixties the attention of investigators was mainly drawn to hydrogen peroxide because of its practical use and as a convenient model reagent for studying mechanisms of catalytic oxidation–reduction processes. Even in the forties it was known that H_2O_2 was contained in rainfall in fairly large concentrations. Much work has appeared recently devoted to the detection of H_2O_2 in various natural waters. The results of some of these investigations are collected in Table 1.

1. Hydrogen peroxide in the atmosphere

The presence of H_2O_2 in the atmosphere was known even in the XIX century. The main mass of hydrogen peroxide is roughly in the thirteen kilometre layer of the troposphere. Hydrogen peroxide is present in the atmosphere in the gaseous state and in solution in drops of atmospheric moisture such as clouds, rain, mist and haze.

The ratio of the quantities of H_2O_2 in these forms is determined by three factors. Clouds occupy ~0.1 portion of the volume of the troposphere,[51] the coefficient of filling a cloud volume with drops of moisture is $\sim 10^{-6}$,[51] and the Henry constant, characterising the distribution of H_2O_2 between the aqueous and gaseous phases, is 1.2×10^5 mole litre^{-1} atm^{-1}.

$$[H_2O_2]_{(dis)} = K_H P_{H_2O_2}$$

It follows from these characteristics that

$$M_{H_2O_2(g)}/M_{H_2O_2(dis)} \simeq 1/(0.1 \times 10^{-6})(1.2 \times 10^5),$$

i.e. the main mass of H_2O_2 is in the gaseous phase.

The total quantity of atmospheric H_2O_2 in our estimation based on the vertical profile of H_2O_2 distribution in the troposphere is ~2 megaton.

The formation of H_2O_2 in the atmosphere is photochemical in nature.[52]

$$O_3 + h\nu \rightarrow O_2 + O('D), \text{ at } \lambda < 310 \text{ nm};$$

$$O(^1D) + H_2O \rightarrow 2OH, \; k_2 = 2.2 \times 10^{-10} \text{ cm}^3.\text{sec}^{-1}$$

Both species $O(^1D)$ and OH react with methane.

$$O(^1D) + CH_4 \rightarrow OH + CH_3, \; k_3 = 1.4 \times 10^{-10} \text{ cm}^3.\text{sec}^{-1},$$

$$OH + CH_4 \rightarrow H_2O + CH_3, \; k_4 = 2.3 \times 10^{-12} \exp(-1700/T) \text{ cm}^3.\text{sec}^{-1}.$$

In the subsequent chain of conversions the first stable oxidation products of methane, viz. CH_2O, H_2O, O_3 and H_2O_2, are formed.[52]

$$CH_3O + O_2 \rightarrow CH_2O + HO_2, \; k_5 = 3.9 \times 10^{-14} \exp(-900/T) \text{ cm}^3.\text{sec}^{-1},$$

$$HO_2 + HO_2 \rightarrow H_2O_2 + O_2, \; k_6 = 2.3 \times 10^{-13} \exp(-600/T) \text{ cm}^3.\text{sec}^{-1},$$

$$HO_2 + HO_2 \xrightarrow{M} H_2O_2 + O_2, \; k_7 = 1.7 \times 10^{-33} \exp(-1000/T) \text{cm}^6.\text{sec}^{-1},$$

where M is any particle in the medium (N_2, O_2, H_2O etc.) participating in the termolecular reaction to draw off the excess energy.

The oxidation of other hydrocarbons in the atmosphere leads to the formation of H_2O_2 by side reactions. Since methane is the main organic compound in the atmosphere the photoinitiated oxidation of methane may be considered to be the main source of H_2O_2.

The consumption of gaseous hydrogen peroxide in the atmosphere occurs by three routes.[52]

$$OH + H_2O_2 \rightarrow H_2O + HO_2, \; k_8 = 1.9 \times 10^{-12} \exp(-160/T) \text{ cm}^3.\text{sec}^{-1},$$

$$H_2O_2 + h\nu \rightarrow 2\dot{O}H, \; \lambda \leqslant 400 \text{ nm},$$

$$H_2O_{2(g)} \rightarrow H_2O_{2(dis)}.$$

Within the framework of a one-dimensional model of the atmosphere the following equation holds true for each height.

$$[H_2O_2] = \frac{k_7[H^{\cdot}O_2]^2}{k_3[OH] + a_9 I_\lambda + \varkappa_{10}},$$

where a_9 is the capture cross section for a photon with a defined λ,

I_λ is the intensity of solar radiation of wavelength λ at height H, $\varkappa_{10}$ is the apparent rate constant of "rain out" hydrogen peroxide by its absorption into atmospheric moisture and removal from the atmosphere with rain.

The significance of the terms in the denominator can be determined as a function of height. The last of the components has the greatest significance for tropospheric conditions, i.e. $[H_2O_2]_g$ is high in the troposphere if $[HO_2^{\cdot}]$ or $[\dot{O}H]$, which is linked linearly with $[HO_2^{\cdot}]$, are large and the content of atmospheric moisture is low. Since the formation of OH occurs at a rate proportional to $[O_3]$, $[H_2O]$ and the intensity of UV irradiation, then the greater these factors are the greater will be $[H_2O_2]$. $[H_2O_2]$ will be greatest in a well-illuminated and humid atmosphere with minimum aerosol content. The presence of aerosols of natural or anthropogenic origin may lead to a reduction of $[\dot{O}H]$ and correspondingly of $[H\dot{O}_2]$.[53] As is evident from the equation a 3–5 fold reduction of $[HO_2^{\cdot}]$ occasions a 10–25 fold reduction of $[H_2O_2]$.

The overall quantity of hydrogen peroxide passing from the atmosphere with precipitation to the surface of the oceans and land in a year may not exceed the quantity of $O(^1D)$ atoms generated in that time. However a global calculation of that sort is fairly complex. It is possible to estimate the maximum quantity of H_2O_2 falling onto the Earth from the atmosphere by proceeding from an average figure for precipitation of ~1000 mm in a year and the concentration of H_2O_2 in the precipitation. The latter figure varies within wide limits, from zero to 10^{-4} M[55] (see also Table 1). Taking a value of $[H_2O_2]$ ~10^{-5} M as being characteristic, we find ~200 g H_2O_2 falls each year on each square metre of land and ocean surface. To this figure must be added the hydrogen peroxide dissolved in natural waters and moisture of the soil. To make any global estimate of the quantity of H_2O_2 passing into water in this way is impossible since this quantity will be determined by the mixing layer renewing the contact surface of water and air. The problem of the dynamics of gases dissolving in water has been specially considered.[56] The time for H_2O_2 to reach the equilibrium concentration $[H_2O_2]_{dis}$ in drops of atmospheric moisture is several seconds.[56] Taking a value of $K_H = 1.2 \times 10^5$ mole litre^{-1} atm^{-1}, we obtain $[H_2O_2]_{dis} \sim 10^{-4}$ M. However this value characterises $[H_2O_2]$ in a thin surface layer. Diffusion transfer even in a metre thick water layer would require ~10^7 sec at a diffusion coefficient of ~10^{-5} cm^2 sec^{-1}. A more effective mechanism for the transfer of H_2O_2 from the surface is wind and wave mixing of the surface layers of the water. In order to assess the maximum quantity of H_2O_2 which may pass into natural waters by solution from the atmosphere it is possible to use the expression

$$\frac{dN}{dt} = \frac{\bar{v}n}{4} S\alpha,$$

where $\bar{v}$ is the root mean square velocity of gaseous particles, n their concentration, S the contact surface of gas with liquid and α the coefficient of accommodation.

Putting the values $t = 3.15 \times 10^7$ sec (1 yr), $S = 10^4$ cm^2 (1 m^2), $n = 2.2 \times 10^{10}$ cm^{-3},[51] $\bar{v} = 4.2 \times 10^4$ cm sec^{-1} and $\alpha = 0.18$[57] into the integrated form of this equation, we obtain $N = 1.23 \times 10^{24}$ ~2 mole, i.e. 70 g m^{-2}, a number comparable with the estimate given above for the quantity of H_2O_2 passing into natural waters with rainfall. One must not overlook the hypermaximal character of the given estimate made using the maximum concentration of H_2O_2 in the gas being absorbed by a constantly renewed water surface. Seemingly it is reasonable to speak of two channels, close in scale, for the inflow of H_2O_2 from the atmosphere, viz. with rainfall and by dissolving gaseous H_2O_2. It is interesting to note that if decomposition and other chemical conversions of hydrogen peroxide do not occur in natural waters then $[H_2O_2]$ of ~10^{-4} M, i.e. of the order of a saturating H_2O_2 concentration, would have accumulated in a stirred surface layer of thickness 20 m in a year.

Both fluxes of hydrogen peroxide from the atmosphere into natural waters, as already mentioned above, are highly sensitive to anthropogenic contamination of the atmosphere by aerosols and are reduced ten-fold by serious contamination. This is linked with the chemical origin of H_2O_2, viz. its formation on recombination of $HO_2^{\cdot}$ radicals. The reduction in the quantity of H_2O_2 in precipitation may be even greater due to autocatalytic oxidation of sulphite ions by hydrogen peroxide taking place in the droplets of clouds.

$$H^+ + HSO_3^- + H_2O_2 \rightarrow 2H^+ + SO_4^{2-} + H_2O.$$

Analysis of the various processes for oxidising HSO_3^- with oxygen or ozone and the catalysis of these processes by ions of iron and manganese showed that the oxidation of HSO_3^- with hydrogen peroxide is more significant.[58,59] It was noted previously,[60] that as $[SO_2]_g$ increased then $[H_2O_2]$ in raindrops was reduced. In other investigations an inverse proportional relationship was noted between the concentrations of sulphate ions and of hydrogen peroxide in rain water.[61,62] There are also other data obtained in aerochemical investigations of the chemical composition of cloud droplets,[63] in which such a correlation was not detected.

The problem of relating the compositions of raindrops and cloud droplets is not simple. There are differences in their lifespans (~1 h for clouds and ~100 sec for rain) and dimensions, the radius of a cloud droplet is 10 μm and of a raindrop is 300–1000 μm. A change in the composition of a falling raindrop compared to cloud occurs through absorption of various gaseous constituents and capture of aerosol particles. However in the lifespan of a raindrop the equilibrium concentrations of absorbed substances are reached only in the thin surface layers of a drop due to the low rate of diffusion. We are unaware of a quantitative solution to the problem of relating the composition of a raindrop to the composition of a cloud allowing for the absorption of gases in the atmosphere near the ground. There is considerable interest in the investigation of the H_2O_2 content in fossil ice in Greenland and Antarctica.[8] It turned out that in the Northern Hemisphere H_2O_2 was detected in significant concentrations in ice, the age of which was estimated at tens of thousands of years. This observation is the basis for the statement that hydrogen peroxide is an inherent component of atmospheric precipitation, a natural "companion" of O_2 and H_2O.

It also follows from these data,[8] that in the ice of Antarctica, in contrast to the Arctic, the H_2O_2 content falls rapidly with the age of the ice. It is not excluded that this is linked with a fall of H_2O_2 under the influence of solar UV radiation. The results of measuring H_2O_2 in the fossil ice of Antarctica indicates indirectly the natural occurrence of an "ozone hole" over Antarctica in times past. Attention has primarily been paid to these "holes" only since the early eighties.[64,65] The changes in UV radiation in the troposphere affect the photodissociation reaction which leads to a change in the equilibrium concentrations of the atmospheric oxidising agents, viz. O_3, $\dot{O}H$, $HO_2^{\cdot}$, H_2O_2.[66]

Measurements of the H_2O_2 content of snow revealed the correlation that the greater the atmospheric contamination by smoke the lower was the H_2O_2 concentration in melted snow.[67] This observation is in agreement with the hypothesis given above that an increase in aerosol contamination is associated with a reduction in the stationary concentration of $\dot{O}H$ and of $HO_2^{\cdot}$ and a large

reduction in H_2O_2 concentration in the gaseous phase. When the atmosphere is contaminated by both aerosols and sulphur dioxide it is possible that the oxidation of HSO_3^- remains incomplete in drops due to the decrease of $[H_2O_2]_g$ and correspondingly of $[H_2O_2]_{dis}$. In this event rainfall may contain unreacted oxidation substrates, such as sulphite ion and formaldehyde. This leads to the fact that in many areas substances which react efficiently with H_2O_2 are discovered in the water instead of H_2O_2. Nevertheless it can be proposed that the flux of oxidation equivalents in the form of hydrogen peroxide dissolved in water is reduced depending on the industrial development of a region. Moreover, it is possible for predominantly reduction equivalents (metal ions in the reduced form, sulphite ions, other reduced forms of sulphur) to reach the Earth's surface. This problem has not been studied adequately.

2. Hydrogen peroxide in the sea

The content of H_2O_2 in natural waters was determined for the first time in 1966 by Van Baalen and Marler[12] in the Gulf of Mexico. These investigations stimulated authors to study the ecological role of blue-green algae. The H_2O_2 content of the sea proved to be $\sim 10^{-7}$ M. It was suggested that atmospheric precipitation, metabolites of aquatic organisms and photochemical processes are the sources of H_2O_2.

After a long interruption the study of the H_2O_2 content of the sea was continued in the eighties by Zika and collaborators.[45,68] It was shown that the H_2O_2 content of the water of the Gulf of Mexico fell from $(1.2-1.4) \times 10^{-7}$ M in the surface layer to 5×10^{-9} M at a depth of 100 m.[43,69]

A detailed study of the distribution of hydrogen peroxide in the waters of the Gulf of Mexico was undertaken in 1985.[44] In oligotrophic regions weakly saturated with organic substances the H_2O_2 content in the water varied within the limits $(1.2-1.6) \times 10^{-7}$ M, while at a depth of 40 m, in a layer of convective mixing, the H_2O_2 concentration remained approximately constant, and below this it was reduced. In the coastal zone insignificant diurnal changes of H_2O_2 concentration were observed, viz. from 1.7×10^{-7} M at 8 am to 1.9×10^{-7} at 2 pm in May and from 1.9×10^{-7} M at 6 am to 2.9×10^{-7} M at 6 pm in August. Below the 20 m layer of efficient mixing the concentration was reduced to 0.3×10^{-7} M and did not undergo diurnal variations.

A tenfold and greater increase in concentration in layers at depths up to 50 m and over was shown after rain.[40]

An investigation of the H_2O_2 content in the ocean along the coast of Peru has been described.[46] A correlation was recorded between the H_2O_2 content of the water and biological activity and photochemical reactions.

The possible role of microorganisms in the formation of H_2O_2 in sea water has been established.[70] The ability to produce H_2O_2 not only by the action of sunlight but also in the dark was discovered in certain forms of algae. Not all algae possess this property. The sea diatom *Thalassiosira weissflogii* does not produce H_2O_2 in the dark or in the light.

The distribution of H_2O_2 in estuarine water has been studied.[47] The investigation was carried out in November. A diurnal variation was detected in the H_2O_2 content of water, the maximum hydrogen peroxide concentration of 9×10^{-7} M being reached at 6 pm. Seasonal variations were detected in the H_2O_2 content of the water from 0.35×10^{-7} M in February to 1.3×10^{-6} M in July.

The H_2O_2 content of water in the northwest portion of the Black Sea has been measured.[71] The H_2O_2 concentration did not exceed 1.5×10^{-7} M. Substances with a reducing nature, reacting efficiently with H_2O_2, were recorded in certain samples in place of H_2O_2.

The distribution of H_2O_2 concentration in the water of the White Sea has been studied using chemiluminescent methods.[72] Colleagues of the Pacific Ocean Oceanological Institute of the Far Eastern Division of the USSR Academy of Sciences have carried out investigations in many regions of the world's oceans.[73] The H_2O_2 concentration in these investigations varied within the limits 20 to 470 nM.

Methods for modelling mathematically the H_2O_2 distribution in sea water in time and space have been discussed.[74]

3. Hydrogen peroxide in inland fresh water

The first measurements of the H_2O_2 content of inland natural waters were made by V E Sinel'nikov using chemiluminescent and iodometric methods.[4,48,49,75–77] The investigations were mainly carried out on the Volga over several years at the end of the sixties and the beginning of the seventies. The H_2O_2 content in Volga water varied within the limits of 3×10^{-7} to 3×10^{-6} M. As a result it was concluded that 10^{-6} M was a typical value for the H_2O_2 content of uncontaminated sections of the water.[48]

According to these investigations microorganisms, particularly algae, play a major role in the formation of H_2O_2 in natural waters.[78] A significant increase (up to 10^{-5} M[79]) in H_2O_2 concentration was detected in the zone of contamination of reservoirs by domestic effluent, containing readily oxidisable organic compounds. The content of organic peroxides accompanying H_2O_2 was measured by iodometric titration using catalase to destroy hydrogen peroxide. Their concentration did not exceed 10% of the H_2O_2 concentration.

Later, in the early eighties, a study was undertaken of hydrogen peroxide in fresh natural waters.[31,34] Samples of water which were used for farm irrigation, samples of river water, drainage from fields and unpurified sewage were taken. They were irradiated under laboratory conditions with an artificial light source simulating sunlight. The concentration of H_2O_2 formed was $(2-7) \times 10^{-6}$ M for the majority of samples studied, while in water samples taken from biologically clean ponds it was 3×10^{-5} M.

A diurnal variation was detected in the H_2O_2 content of the surface water layer of a pond on a sunny day of 2.9×10^{-7}, 8.8×10^{-7} and 1.5×10^{-8} M at 8 am, 1 pm and midnight respectively.[8]

Many measurements of the H_2O_2 content of various water samples were carried out in this country in the eighties. The main results of these measurements have been collated.[80–83] Investigations were carried out using chemiluminescent and peroxidase photometric methods.

In the same regions of the Volga where Sinel'nikov had carried out measurements 10–15 years previously, an intensification of the diurnal variation and the initiation of seasonal variations were detected[82] in the H_2O_2 content of the water. In May the H_2O_2 concentration in Volga water near Volgograd varied between 10^{-6} and 3×10^{-6} M. Towards the middle of June the H_2O_2 content of the water began to undergo sudden diurnal changes. In sunny weather the maximum H_2O_2 content occurred at 4 pm and the minimum in the early morning hours. In overcast weather hydrogen peroxide was, in general, not detected. Shortly afterwards a period arrived when H_2O_2 generally disappeared from Volga water. On the contrary, titration of natural water with small additions of hydrogen peroxide enabled the detection of the presence in it of compounds of a reducing nature which reacted efficiently with H_2O_2. The authors thereby recognised a change in the state of the medium from normal

oxidising, when H_2O_2 was present in the water, to quasi-reducing, when a reducing agent was recorded in place of H_2O_2 and was titrated by adding H_2O_2. This change of the "sign" of the redox state of the medium was apparently produced for the first time in the mid-seventies and led to the catastrophic change in the ecosystem of the Volga (see Section VIII, No. 2).[80]

The results of measuring the H_2O_2 content of the waters of the Volga,[82] the Dnieper[84] and other waters of this country show that the seasonal change of the dynamic redox state of aquatic media has in recent years become the rule and not the exception.

IV. Processes forming hydrogen peroxide in natural waters

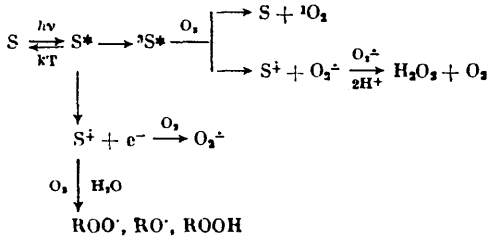
The fact that part of the H_2O_2 concentration in water undergoes diurnal changes correlating with solar activity suggests that hydrogen peroxide is formed predominantly by photochemical reactions. At the same time the formation of H_2O_2 in aquatic media is linked with the activity of algae and bacteria. The general considerations expressed at the beginning of the review also indicate the possible role in the formation of hydrogen peroxide of catalytic oxidation processes of readily oxidisable compounds with oxygen. We will discuss the most probable channels of introduction into aquatic media in more detail.

1. Photochemical processes in natural waters leading to the formation of H_2O_2

The photochemistry of natural waters is one of the most successfully developed areas of studying chemical processes occurring in the environment.[85,88]

Electronically excited species are formed by the action of solar radiation ($\lambda \geqslant 300$ nm) in water as primary products. These include S*, $^1O_2$ (S are organic compounds, photosensitisers, dissolved in water),[89–92] free OH radicals,[87,93–97] $O_2^{\cdot-}$,[14,34,98–101] peroxy radicals ROO·[93,102] and solvated electrons.[92,103–106] The reaction of the reactive intermediates with one another and with compounds dissolved in water may lead to the formation of H_2O_2 in an aerobic medium.[15]

The general scheme for the photochemical conversions of organic substances (S) in natural waters as a result of direct photolysis may be represented as follows.[107,108]

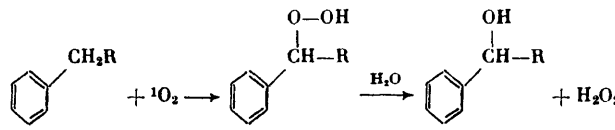


Organic substances dissolved in natural waters are mainly humic compounds. The efficiency of forming H_2O_2 in aquatic solutions containing humic and fulvic acids, and also various amino acids, has been studied and it was discovered that the rate of forming H_2O_2 was greater in humic than in fulvic acids.[31,34] Tryptophan was the most productive of the amino acids, absorbing light in the longest wave region of the UV spectrum.

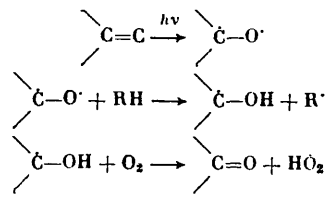
Test samples of surface and ground water with various contents of humic compounds have been irradiated with sunlight[14] and it was discovered that the rate of H_2O_2 formation correlated with the concentration of compounds absorbing light in the near UV region.[15]

The presence of $O_2^{\cdot-}$ in natural waters has been confirmed by adding superoxide-dismutase and also acceptors of $O_2^{\cdot-}$ such as dichlorophenolindophenol, cytochrome C and nitrotetrazolium blue.[14,34,98,99,109]

It was shown that $O_2^{\cdot-}$, as a precursor of H_2O_2, is also formed on photolysis of tryptophan.[34,110,111] Flavins also differ from other compounds of biological origin by having a high efficiency of H_2O_2 formation.[112] The generation of H_2O_2 is accelerated in the presence of electron donors. A high rate of hydrogen peroxide formation through the intermediate formation of $O_2^{\cdot-}$ radicals was observed in photochemical conversions of pyruvate, glyoxalate and other keto-acids especially in the presence of H donors. The accelerating effect of electron donors (H atom) on the rate of formation of H_2O_2 may be linked with their participation in reaction with $^1O_2$ [113] with the formation of $O_2^{\cdot-}$ radicals or with oxidising agents S^+ with subsequent oxidation of the resulting radical–donor by molecular oxygen. Hydrogen peroxide may be formed as the product of the reaction of $^1O_2$ with certain organic compounds avoiding the step of forming $O_2^{\cdot-}$ radicals.[114]



Carbonyl compounds readily take part in a photochemical reaction of a different type. In particular, humic acids form reactive biradicals in the excited state.[115,116]



Many of the resulting radicals undergo various conversions in an aerobic medium in the presence of variable valency metal ions, often with the intermediate formation of H_2O_2 (see Section VII).

Both organic and inorganic compounds may undergo photochemical conversion in natural waters and as a result various reactive intermediates are formed. In an aerobic medium this may lead to the initiation of radical processes of oxidation of the organic compounds dissolved in the water with the accompanying formation of H_2O_2.

Free radicals, chiefly $\dot{O}H$, are the primary products of photochemical conversions of inorganic compounds as a rule.[117–119]

$$NO_3^- \xrightarrow{h\nu,\,H^+} NO_2 + \dot{O}H,$$

$$NO_2^- \xrightarrow{h\nu,\,H^+} NO + \dot{O}H.$$

In addition $O_2^{\cdot-}$ radicals may be formed on photolysis of certain oxides of a semiconductor type.[42,120,121]

$$TiO_2^{2+} \xrightarrow{h\nu} TiO_2^+ + e^- \xrightarrow{O_2} O_2^{\cdot-}$$

Transition metal complexes are subject to photochemical conversion, being decomposed by the action of light with the formation of a metal ion in the reduced form. These processes occur

with the highest efficiency in the case of iron complexes, which absorb light in the near UV region.[122,127]

$$FeOH^{2+} \rightarrow Fe^{2+} + \dot{O}H,$$
$$FeHO_2^{2+} \rightarrow Fe^{2+} + H\dot{O}_2,$$
$$FeC_2O_4^{+} \rightarrow Fe^{2+} + CO_2^{\pm} + CO_2 \text{ etc.}$$

Some copper complexes are reduced in sea water by sunlight.[69]

$$CuX^{+} \rightarrow Cu^{+} + X,$$

where X^- is an anionic ligand.

Manganese[128,129] and chromium[130,131] ions also participate in photochemical conversions.

The role of metal ions in H_2O_2 formation in aquatic media will be discussed in more detail below.

2. The formation of H_2O_2 by redox catalytic processes

Most reactions in natural systems are effected with the participation of dissolved oxygen and variable valency metal ions.

It has been shown that copper ions participate in H_2O_2 formation in sea water.[132] Hydrogen peroxide at a concentration of 10^{-7} M affects the Cu^+/Cu^{2+} ratio and the autoxidation of chloride complexes of Cu^+ and Cu^{2+} leads to the formation of H_2O_2. This process has been studied in detail.[133,134] The mechanism of the process includes the intermediate formation of copper-oxygen complexes.[135]

$$Cu^+ + O_2 \rightleftharpoons (CuO_2)^+ \rightleftharpoons Cu^{2+} + O_2^{\cdot-},$$
$$O_2^{\cdot-} + Cu^+ \xrightarrow{2H^+} Cu^{2+} + H_2O_2,$$
$$CuO_2^+ + Cu^+ \xrightarrow{2H^+} 2Cu^{2+} + H_2O_2.$$

In addition to autoxidation reactions of transition metal ions, oxidation reactions of various readily oxidisable organic compounds, catalysed by metal ions, may contribute to H_2O_2 formation.

Ascorbic acid[136] and dihydroxyfumaric acid[67] are typical examples of reducing compounds which form stoichiometric quantities of H_2O_2 on oxidation by oxygen of the air. These redox ligands (DH^-) react with metal ions, with copper ions in particular, with the formation of the reduced form which participates in the activation of O_2.[138]

$$\left.\begin{aligned} &Cu^{2+} + DH^- \rightleftharpoons CuDH^+ \underset{-H^+}{\dashrightarrow} Cu^+ + D^{\cdot},\\ &CuDH^+ + Cu^{2+} \underset{-H^+}{\longrightarrow} 2Cu^+ + D, \end{aligned}\right\} \text{reduction of metal}$$

$$\left.\begin{aligned} &Cu^+ + O_2 \rightleftharpoons CuO_2 \dashrightarrow Cu^{2+} + O_2^{\cdot-},\\ &CuO_2^+ + DH^- \underset{-H^+}{\longrightarrow} Cu^+ + D + H_2O_2. \end{aligned}\right\} \text{activation of } O_2$$

A radical mechanism forming H_2O_2 is also possible by the catalytic oxidation of reducing agents which are efficient electron donors (H atom).[137,138]

$$O_2^{\cdot-} + DH^- \rightarrow HO_2^- + D^{\cdot-},$$
$$D^{\cdot-} + Cu^{2+} \rightarrow Cu^+ + D.$$

Chain processes are in essence similar reactions, the termination of which occurs by destruction of the chain propagators ($O_2^{\cdot-}$, Cu^+, D^-) on heterogeneous impurities or by recombination with one another.

The catalytic oxidation rate of ascorbic acid and related reducing agents with oxygen is far higher than with hydrogen peroxide, which also leads to the accumulation of H_2O_2 in the medium.

3. The role of microorganisms in the formation of hydrogen peroxide

Van Baalen and Marler[12] and Sinel'nikov[78] were the first to reach the conclusion that the role of algae in the process of forming H_2O_2 is important. Even earlier Mehler[139–141] had demonstrated in classical studies the ability of chloroplasts to produce H_2O_2 under the action of light. It was later shown that, in the process of forming H_2O_2, oxygen may oxidise reduction equivalents in the electron transport chain of photosynthesis.[142–146]

The photochemical formation of H_2O_2 was demonstrated for the first time in 1973 by Patterson and Meyers on irradiating the blue-green alga *Anacystis nidulans* with light of wavelength 620–675 nm.[147]

By adding 3-(3,4-dichorophenyl)-1,1-dimethylurea (DCMU) to block Photosystem II, it was shown that the photosynthetic apparatus was the source of reduction equivalents for the formation of H_2O_2 when reducing O_2. The rate of forming H_2O_2 grew on adding to the medium either inhibitors of the Calvin cycle (PCMB, iodoacetamide) or an inhibitor of phosphorylation (carbonyl cyanide *m*-chlorophenylhydrazone) and also under conditions of CO_2 deficiency. Components of the Calvin cycle suppress H_2O_2 formation.

The conclusion was reached[147] that reduction equivalents, for which O_2 and CO_2 compete, are produced in algae cells by the action of light. It was proposed that the centre of H_2O_2 formation was localised in the final reducing step of Photosystem I.

In addition to *Anacystis nidulans* a large number of fresh water[148] and marine[70] algae were discovered to be capable of producing H_2O_2 in the external medium in the process of photosynthesis. No correlation was noted between the morphological features or the accepted nomenclature differentiation of the algae and their ability to produce H_2O_2. The kinetic characteristics of the process of forming H_2O_2 for the various algae species differed markedly.

It was also discovered[70,148] that certain types of algae are able to produce H_2O_2 not only by the action of light but also in the dark. This shows that the H_2O_2 formation by algae may not be linked solely with photosynthesis.

Palenik and collaborators[149,150] have shown the role of intracellular L-aminoacid oxidases (deaminases) in the formation of H_2O_2 by the reaction:

$$R{-}CHNH_3COO + H_2O + O_2 \rightarrow R{-}CHOCOO^- + NH_4^+ + H_2O_2.$$
(L-aminoacid) (α-ketoacid)

The ammonium ion liberated in the reaction is captured by algae cells (*Pleurochrysis carterae*) and used as a source of nitrogen.

Other surface deaminases are known which participate in the transformation of nitrogen in seawater. These include amino-oxidases, which oxidise primary amines (ethanolamine, putrescine) in the presence of phytoplankton and the polyaminooxidase of the diatom *Thalassiosira weissflogii*, which uses spermine and spermidine as substrates with the formation of H_2O_2 as a side product.[151]

The activity of the surface deaminases is usually large when the growth of phytoplankton is limited by nitrogen. For this reason these processes are usually effected in regions with a low content of inorganic forms of nitrogen (for example in the open ocean).

The quantitative contribution of processes involving deaminases has not been established. The formation of H_2O_2 in abiotic processes occurs at a greater rate than in biotic processes in surface water while at depth the biotic contribution becomes dominant.[15] Palenik and collaborators[149] have established that the

rate of H_2O_2 formation by *Pleurochrysis carterae* reaches $(1-2) \times 10^{-9}$ mole litre^{-1} h^{-1}. Since aminoacid oxidases are widely distributed among microalgae and other deaminase reactions may lead to the formation of H_2O_2, the biological production of H_2O_2 in the dark may be significant in several cases.

It has been shown[152,153] that non-photosynthetic photochemical processes for H_2O_2 formation are also effected efficiently in algae cells by the action of the UV component of sunlight, as a result of the photolysis of water-soluble intracellular components. A portion of the resulting hydrogen peroxide is decomposed by intracellular enzymes (catalase, peroxidase, see below) but a portion of it is eliminated into the external medium. The rate of photoproduction of H_2O_2 and its stationary concentration in the medium depends on both the species of algae and on the age of the culture.[109] The precursor of H_2O_2 in algae cells is the $O_2^{\cdot-}$ radical.

It has been shown[154] that H_2O_2 is formed on autoxidation of ferredoxin. On the other hand the formation of H_2O_2 was detected in membrane preparations from blue-green algae *Anabena* with the ferredoxins washed away.[146]

V. The role of hydrogen peroxide in the formation of a single "cell–medium" redox system

The hydrogen peroxide cycle in natural waters is closely linked with the exchange of oxidation–reduction equivalents between the aquatic organisms and the surrounding medium. It is possible to draw conclusions on the principles of such a redox exchange both within the limits of a cell and between a cell and the external medium which have a bearing on the general principles of the functioning of the living cell.[155]

1. Intracellular redox processes involving H_2O_2

The redox state of the intracellular medium is determined by the interconnected distribution of the oxidised and reduced forms of variable valency metal ions entering the active centres of oxidation–reduction enzymes and labile redox metabolites, such as NADP/NADPH, cytochrome C (Fe^{3+}/Fe^{2+}), ATP/ADP + P (P is phosphate), etc. The oxidation state of cytochrome C determines the respiration rate of a cell and accordingly the rate of phosphorylation processes. Phosphate plays a regulatory role in maintaining the intracellular redox state, its exchange with the external medium is regulated by the cell.

The interaction of intracellular redox systems implies the exchange of oxidation–reduction equivalents between the cell structures. In other words, a system exists for the regulation of the intracellular redox state on which the occurrence of such complex biochemical processes as cell respiration, protein synthesis and the secretion of hormones and neurotransmitters depend.

Hydrogen peroxide together with O_2 play a special role in the redox processes in the cell.

The intracellular content of H_2O_2 in algae cells is determined not only by photochemical processes but also by other oxygen-dependent processes in the cell. Among them a central place is occupied by biological oxidation processes involving O_2, viz. the oxidase (oxygen acts as an electron acceptor), oxygenase (oxygen acts as a donor of an O atom) and the peracid oxidation of lipids occurring with the participation of O_2 and free radicals. The enzymes known to form H_2O_2 in metabolic processes involving O_2 are glycolate oxidase, α-gulonolactone oxidase, aldehyde oxidase, xanthine oxidase, D-aminoacid oxidase, monoamine oxidase, galactose oxidase, prostaglandin synthetase, dihydroorotate dehydrogenase and certain others.

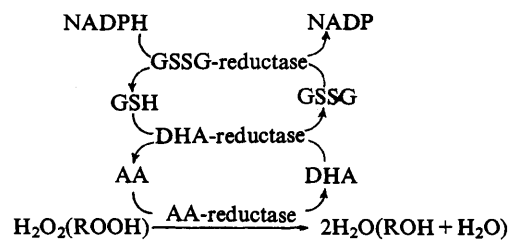
Hydrogen peroxide is formed in the living cell in the mitochondria, microsomes and in peroxysomes.[156–158] The formation of H_2O_2 also occurs on oxidation of NADPH in the endoplasmic reticulum. It was shown[159] that up to 15% of the total oxygen required by a cell for life is converted into H_2O_2.

The H_2O_2 content of different cells under dark conditions varies within wide limits, from 10^{-9} to 10^{-6} M.[159,160] In the case of algae the stationary H_2O_2 concentration reached in the medium on illumination with sunlight varies, depending on the species of algae and their functional state, within the limits 3×10^{-6} to 3×10^{-5} M.[109] It is probable that such high H_2O_2 concentrations are also reached in algae cells. Many algae express H_2O_2 to the external medium which indicates that processes using peroxide oxidation equivalents are weakly developed in them.

The enzymes superoxide dismutase, catalase and peroxidase serve as physiological regulators of the intracellular hydrogen peroxide content.[161,162] In a comparative study of the catalase activity of various species of blue-green and green algae, it was discovered that the blue-green were far less active.[163] In addition the catalase of blue-green algae proved to be more sensitive to the action of solar UV irradiation than did that of green algae.[164]

The deficiency of catalase activity in many algae is compensated by glutathione- and ascorbate-dependent peroxidases.[164] A high glutathione reductase activity and high concentration of glutathione (3×10^{-3} M) were discovered in the blue-green algae *Nostoc muscorum*[165] which is characterised by a high rate of H_2O_2 formation both in the dark and in the light.[148] This alga does not contain glutathione peroxidase,[166] but displays high dehydroascorbate reductase and ascorbate oxidase activity.

An overall scheme has been suggested for regulating H_2O_2 content in the cells of blue-green algae.[166]



where GSH (GSSG) and AA (DHA) are the reduced (oxidised) forms of glutathione and ascorbic acid respectively.

According to such a mechanism relatively large quantities of the H_2O_2, which passes into a cell at a rate up to 30% of the photosynthetic transport of electrons, may be destroyed.

In mammalian cells glutathione has a leading role in maintaining the stationary H_2O_2 concentration. This compound is the main stock of mobile sulphydryl groups and the dependence of the rate of the glutathione peroxidase reaction on hydrogen peroxide concentration complies with an equation of zero order.[167] Up to 70% glutathione peroxidase is found in the cytosol and 30% in the mitochondria. A feature of glutathione peroxidase is the ability to use fatty acid hydroperoxides as oxidising agents. This plays a decisive role in the regulation of peroxide oxidation of lipids. A supply of reduction equivalents in the form of NADPH is necessary for glutathione peroxidase to function.

Various amines and phenols are typical substrates for the peroxidase reaction.[168] The mechanism of action of peroxidase has

been discussed in detail.[134] A peroxidase function is possessed not only by the peroxidases themselves but also by other haem-containing proteins, particularly cytochrome P-450.[169] Chloroperoxidase occupies a special place among the peroxidases as it catalyses the decomposition of H_2O_2 as well as substrate oxidation.[170]

In its turn catalase also possesses peroxidase activity in relation to certain substrates.[171] Thus catalase participates in the peroxidase oxidation of ethanol,[162] causing the development of an unbalance in the redox state of the cell.[172]

The kinetic feature of catalase, in contrast to the peroxidases, is its absence of substrate saturation. When exogenous hydrogen peroxide passes into the cell, on average 40–60% of its metabolism is linked with catalase and the remaining peroxide participates in peroxidase oxidation processes.[173]

In addition to direct H_2O_2 formation in enzymic processes a large portion of the intracellular hydrogen peroxide is formed by the disproportionation of O_2^-.[153] According to one estimate,[160] the stationary concentration of O_2^- in liver mitochondrial membranes is 10^{-11} M. The O_2^- radicals formed in the cell participate both in dismutation reactions, catalysed by superoxide dismutase, and in the initiation of free radical processes.[174,175] In spite of the fact that the O_2^- radical is a natural metabolite of the cell, it is toxic in excess.[174,176]

Hydrogen peroxide may display a toxic effect at concentrations significantly exceeding the physiological.[177,178] At high concentrations hydrogen peroxide inactivates the transformation of DNA[179] and also induces chromosomal aberrations in ascites tumour cells.[180] Other physiological changes by the action of H_2O_2 are known.[178]

On the other hand the physiological concentration of H_2O_2 is not only non-toxic but is also necessary for normal cell activity.[155] It has been shown[172,181–183] that hydrogen peroxide participates in the regulation of cellular respiration. It was also shown that by itself H_2O_2 does not induce the peroxide oxidation of lipids,[184] it does not destroy mitochondria[185] but it is used by plant cells to induce intracellular reduction processes.[186]

It is known that a normal (stationary) level of peroxide oxidation of lipids is inherent for the cell membrane.[169] This is necessary for the regulation of the various cell functions and for the whole organism such as the setting of the metabolic state of the respiratory chain, changes of membrane permeability, etc. It is also known that lipoperoxides are obligatory intermediates in hormone biosynthesis (prostaglandin, progesterone), and participate in the hydroxylation of the cholesterol group of steroids.[175]

Under hyperbaric conditions a simultaneous increase occurs in the concentration of H_2O_2 and of free radicals in the cell which leads to a reduction in the NADPH/$NADP^+$ ratio. In its turn this causes a reduction in the content of reduced glutathione in the cell and correspondingly to the activation of peroxide oxidation of lipids. The reaction of O_2^- with H_2O_2, catalysed by metal complexes, may participate in the initiation of peroxide oxidation of lipids.[187,188] It was shown[184] that this reaction is also responsible for the inactivation of algae cells under the action of solar UV radiation.

This same reaction seemingly serves as a basis for the phenomenon of "photooxidising death", the sudden cessation of the "bloom" of blue-green algae in a deficiency of CO_2.[189,190] Under these conditions both hydrogen peroxide and its precursor, the O_2^- radical, are formed in the cell. The cells become sensitive to the action of light not only in the absence of CO_2 but also by the action of DCMM, the inhibitor of Photosystem II.[190] "Photooxidative death" is accompanied by decolourisation of the photosynthetic pigments, but this process is not linked with cell death.

The source of CO_2 in the "bloom" process of blue-green algae is not so much atmospheric carbon dioxide gas as the activity of bacteria. The more extended and stable bloom of eutrophated reservoirs in particular is linked with this circumstance.[191] The high sensitivity of blue-green algae to photooxidative inactivation explains why algae of this type are better able to function under conditions of oxygen deficiency, in a quasi-reducing medium and under weak illumination.

2. Exchange of oxidation–reduction equivalents between a cell and the external medium

Isolation of a cell from the extracellular medium is essential to preserve the continuity of the intracellular redox state. The presence of exchange with an extracellular redox system increases the possibility of a cell changing the direction of the intracellular redox processes but the danger of an adverse action of the external medium on the internal redox state of the cell is contained.

Many intracellular metabolic processes are linked with the transmembrane transfer of oxidation–reduction equivalents from the cell to the external medium and *vice versa*.

Hydrogen peroxide, together with O_2, serves as a carrier of oxidation equivalents in nature. Consequently the problem of H_2O_2 transport within the limits of the cell and through the cell membrane is important. It has been shown[155] that the mitochondrial membrane is weakly permeable to H_2O_2 while other biological membranes are fairly readily permeable. So from hyperoxic conditions, where large quantities of H_2O_2 are formed,[192] 10–40% hydrogen peroxide penetrates the cytosol and may then pass from the cytosol to the external medium[157] The high permeability of cell membranes for H_2O_2 also follows from the data on the kinetics of the formation and destruction of hydrogen peroxide in cultures of algae.[84,153]

Many intracellular metabolic processes are linked with the transmembrane transfer of reduction equivalents from the cell into the external medium. The obvious role of such exchange is displayed in the vital activity of microorganisms. Thus the initial stage of the multiplication of many bacteria is linked with the formation of a reducing medium.[193] If a substance having a reducing nature is introduced into the culture medium then the induction period in the multiplication of bacterial cells disappears but on introducing an oxidising agent it is increased.[193] In the growth process of bacterial cultures the redox potential of the medium is reduced and anaerobic strains are characterised by large shifts of potential in comparison with aerobic.

It has been shown[194] that ferricyanide is reduced in yeast cultures. Addition of citrate, a component of the Krebs cycle, accelerates this process, although citrate itself does not react with ferricyanide. This experiment shows that reduction equivalents formed in the Krebs cycle are partially eliminated into the external medium. The flux of reduction equivalents is determined by the intracellular redox system and is increased on inhibiting the processes transferring them to O_2.

Transfer of reduction equivalents to the external medium serves as one of the main processes securing the optimum redox state of the cell. An essential role in transmembrane transfer of reduction equivalents is assigned to the ascorbate/dehydroascorbate redox system.[155]

The available data show that a close interconnection exists between the metabolic activity of microorganisms and the redox state of the surrounding aqueous medium. The existence of a single

redox system for the intra- and extracellular media is in agreement with the ideas of Skadovskii,[195] who considered a reservoir to be a biological individual, and also with the hypothesis of Academician Vernadskii that natural water is a bioinert body.[196] In fact a natural aquatic medium like a monoculture of microalgae, must be considered as a specific organism possessing an insignificant integration of cells. In this "organism" extrametabolites of hydrobionts may play the role of "media hormones" regulating the composition of cenoses.[197] A decisive role in setting the qualitative state of an aquatic medium under natural conditions belongs to the smallest forms of hydrobionts, since, as emphasised,[195] the margin between physicochemical and biological processes is eroded as the dispersity of the hydroecosystem is increased.

Possible mechanisms for the participation of microorganisms in the redox systems within reservoirs include the following five main types of reaction:[151]

1) the excretion of a compound of a reducing nature into the external medium,

2) transmembrane electron transfer to an extracellular electron acceptor,

3) catalysis of extracellular redox reactions by an enzyme localised on the external surface of the cell,

4) catalysis of redox reactions by an extracellular enzyme bound to the cell surface with the participation of a reducing agent excreted by the cell,

5) catalysis by the cell surface of non-enzymic redox reactions with the participation of extracellular redox factors.

The expression of soluble organic compounds into the external medium is a characteristic of growing cells. According to one estimate[198,199] 5–10% of the total carbon of phytoplankton is expressed into the medium and serves as a source of reduction equivalents for carrying out chemical and biological reactions. Many of the excretions participate in complex-forming reactions with metals[200–202] and thereby affect their redox catalytic activity. Thus, certain aquatic microorganisms are capable of producing siderophores binding iron ions.[203] Other bacteria using sulphate as a source of electrons eliminate sulphides which participate in the reduction of metals.[204]

Electrons formed in the cell in photoreactions (or in respiratory processes) may be transferred to the outside of the cell surface and used in the reduction of various cellular substrates. These electron-transfer processes are effected by trans-plasma membrane reductase, which transports electrons from the intracellular donor (NADH, NADPH) to an extracellular electron acceptor. Such membrane-impermeable oxidising agents as ferricyanide, cytochrome C and copper complexes are reduced directly on the cell surface.

Microorganisms may also catalyse extracellular redox reactions (and hydrolysis reactions) through ectoenzymes immobilised on their outer surfaces. A whole class of surface enzymes exists, such as deaminases, typical of phytoplankton which catalyse the elimination of NH_4^+ on oxidation of nitrogen-containing organic compounds[151] with simultaneous reduction of O_2 to H_2O_2 (see Section IV).

In contrast to the intracellular enzymes functioning in strictly controlled conditions (ionic strength, pH, content of Ca^{2+}, Mg^{2+}, etc.) the ectoenzymes are closely dependent on the state of the external medium. In particular metal ions contained in the aqueous medium may lead to inactivation of ectoenzymes. For example, alkaline phosphatase in a phytoplankton culture or in full-scale samples are inhibited by copper(II) ions even at very low concentrations in the medium.[205] The high sensitivity of the ectoenzymes to the presence of metals may determine the ecotoxic properties of the latter, differing from their toxicity towards metabolic processes such as photosynthesis or respiration, which are integrated with a large number of biochemical reactions.

The reduction of extracellular substrates may also occur directly on the reduced parts of the cell surface without the participation of enzymes. Such reactions may proceed both in the dark and in the light. The reactions are non-enzymic and require regeneration of the reducing agent. The reduction of ions of copper and iron by microalgae cells may serve as an example of such reactions.[151]

Many forms of microalgae, including diatoms,[150] pyrophytes[206] and blue-green algae[207] reduce intracellular electron acceptors. Using *Thalassiosira weissflogii* as an example it was shown[208,209] that three types of reducing agents participate in these processes:

1) reducing agents eliminated by cells and not regenerated in the absence of microalgae,

2) reduced parts of the cell surface which may be inactivated by pretreatment of the algae with oxidising agents,

3) surface reductases, the activity of which does not depend on illumination.

There are compounds dissolved in the culture medium of *T. weissflogii* after filtration of the algae which reduce complexes of copper(II)[208] and iron(III).[209] The chemical nature of the reducing compounds is unknown. It has been suggested that they may be polysaccharides forming part of the cell wall (polygalacturonic acid) or a sulphydryl-containing protein or amino acid.[208]

Two types of reduction centre are encountered on the surface of cell membranes. In the alga *T. weissflogii* such centres are not regenerated, but are oxidised on preliminary treatment with copper(II) ions and such treatment does not affect the ability of cells to reduce metal complexes by the enzymic route. The surface redox reactions of cells are catalysed by reactive groups in the case of *Dunaliella tertiolecta*.[208]

The reduction of copper(II) occurs only in light (>425 nm) and the copper(I) ions formed are oxidised by molecular oxygen. Regeneration of the reduced groups on the cell surface is effected by extracellular photochemical processes. Intact cells of *T. weissflogii* reduce membrane-permeable copper(II) and iron(III) complexes with a potential in the range from −10 to +100 mV both in the light and in darkness by enzymic processes involving transmembrane reductases.[151] Plasma membrane redox activity is linked with the consumption of nitrate by the algae,[210] such that the rate of formation of reduction equivalents by the cell reaches 10% of the rate of reduction of nitrate.[15]

Transmembrane reductases are also present in other microalgae and macrophytes and probably in water bacteria. The evidence for this is the oxidation and reduction by cells of various membrane-permeable compounds. Plasma membrane redox systems also participate in the reduction of variable valency metal ions in cells of higher plants and mammals.[211]

Plant cells are able to reduce iron(III) chelates, including Fe EDTA.[212] This occurs in two ways. The first is by the action of ectoenzymes bound to the cell surface, forming NADH under the action of malate dehydrogenase and using the NADH in the reduction of iron(III) chelates by ferri-NADH oxidoreductase.[213] The second route is the formation of a superoxide radical in the plasma membrane redox system, this radical then participates in the reduction of Fe(III).[214] The extracellular reduction of iron is closely linked with its consumption by phytoplankton cells.[215–217] The subsequent oxidation by hydrogen peroxide of metal ions reduced by ectoenzyme action serves as an important link in the cycling of variable valency metal ions in aquatic media.

A numerical assessment has been made of the rate of formation of Cu(I) in coastal sea waters by the action of cellular water-soluble reducing agents.[69] This rate was 2 nmole litre^{-1} d^{-1} which proved to be 10 times greater than the rate expected for plasma membrane reductase of algal cells at a population of 10^7 per litre water. The conclusion was drawn that it was necessary to allow for the contribution of bacterioplankton and also of abiotic processes for a complete estimate of the reduction rate of copper.[151]

Confirmation has been obtained in the case of manganese of the participation of ectoenzymes both in its oxidation and in reduction. The manganese cycle in the illuminated zone of natural waters includes a redox transition between dissolved Mn(II) and particulate Mn(IV).[218–223] The oxidation of Mn(II) is effected by the photosynthetic activity of fresh water algae.[219] The resulting Mn(IV) forms part of the composition of extracellular carbonic anhydrase which catalyses the conversion of bicarbonate to CO_2. In oxygenated[220] and anaerobic[219] sea water the oxidation of Mn(II) by aquatic microorganisms is effected by a different mechanism. The measured rate of Mn(II) oxidation is 100 times greater than the rate of uptake of manganese by phytoplankton[220] and far greater than the rate of abiotic oxidation of Mn(II) in a sterile medium.

Two processes make the main contribution towards maintaining manganese in the reduced state in water close to the surface. These are the photoreduction of manganic oxide[222] and the reductive dissolution of MnO_x by hydrogen peroxide[224] produced particularly by phytoplankton aminooxidase.

Hydrogen peroxide is also implicated in the intra-algal iron cycle, participating in both the oxidation of Fe(II)[225,226] and in the reduction of Fe(III) in the light. Biota may promote these reactions through the activity of their own extracellular enzymes.

VI. Processes decomposing hydrogen peroxide in natural waters

The formation of H_2O_2 in natural waters by photochemical and catalytic processes is accompanied by processes decomposing it. Judging by the diurnal dynamics of the H_2O_2 content of aquatic media the processes forming and decomposing H_2O_2 are balanced and one may speak of the stationary (or quasi-stationary) concentration of hydrogen peroxide. This concentration depends not only on the rate of H_2O_2 formation but also on the kinetic characteristics of the decomposition process.

The decomposition of H_2O_2 in natural waters has been discussed many times.[31,80,82,152,227–230] The half-conversion time of H_2O_2 in eutrophic waters is about 1 h.[31] It has been shown[229] that in oligotrophic waters in the dark the half-conversion time for decomposition of hydrogen peroxide is 130 h and 10 h in fresh water. These data show that, as in the process of formation, abiotic and biotic processes may participate in the decomposition of H_2O_2.

1. Abiotic processes for the decomposition of H_2O_2 in natural aquatic media

The whole data accumulated on the catalysis of H_2O_2 decomposition by transition metal ions may be used to describe the abiotic processes of H_2O_2 breakdown in natural media.[134,231] Natural waters are characterised by a low metal ion concentration, neutral pH value, indefinite composition and low ligand concentration. Several monographs and reviews have been devoted to the study of the forms in which metal ions exist in natural waters.[200,201,232,233]

It may be concluded on the basis of the data available that of the metal ions, which are potential catalysts of H_2O_2 decomposition, only copper ions and chelate complexes of iron are found in a homogeneous state in natural aquatic media.[234]

The relative contribution of the various metal ions to H_2O_2 decomposition has been studied.[235] It was shown that the catalytic breakdown of hydrogen peroxide in neutral aqueous solution is effected mainly by microcolloidal iron hydroxide and by copper ions. In the first case the process is effected by a nonradical mechanism and in the second through the formation of free radicals.[132,236]

$$CuOH^+ + HO_2^- \rightarrow Cu^+ + O_2^{\cdot-}.$$

The reaction of Cu^+ and H_2O_2 has been studied in detail.[133] The primary product of this reaction is the CuO^+ species which may be considered as a hydrolysed Cu^{3+} ion.[1] In the absence of extraneous reactive substrates this species oxidises water (and is decomposed) with the formation of an OH radical.[133,237]

$$Cu^+ + H_2O_2 \xrightarrow[-H_2O]{} \begin{array}{c}(OH^-)CuO^+\\ \uparrow\downarrow -H^+\\ CuO^+\\ \uparrow\downarrow H^+\\ CuOH^{2+}\end{array} \xrightarrow[H_2O]{} CuOH^+ + \dot{O}H$$

In a similar manner the OH radical appears in the reaction of Fe^{2+} and H_2O_2 in neutral medium as a result of the conversion of a first-formed particle of the type of $FeH_2O_2^{2+}$ or FeO^{2+}.[1]

In the presence of an H donor species such as CuO^+ and FeO^{2+} react with the donor by a two-electron mechanism.[237]

$$CuO^+ + DH_2 \xrightarrow[-H_2O]{} Cu^+ + D.$$

In this case hydrogen peroxide is consumed in the catalytic oxidation of the donor without the formation of intermediate free radicals.

The H donors themselves (redox ligands) may participate in the formation of free radicals[239] by virtue of the specific property of partial charge-transfer of the complexes.[1,238]

$$Cu^{2+} + DH^- \rightarrow CuDH^+,$$
$$CuDH^+ + H_2O_2 \xrightarrow[-H_2O]{} Cu^{2+} + D^{\cdot} + \dot{O}H.$$

It must be emphasised that the metal ion in this reaction remains in the oxidised state. The introduction of redox ligands into an aqueous medium containing H_2O_2 and copper ions may initiate the formation of OH radicals in it, which play an important role in processes of self-purification of natural waters.[240] On the other hand the introduction of H_2O_2 into a medium containing the H donor DH_2 may lead to the oxidation of this reducing agent without the formation of free radicals.

$$Cu^+DH_2 + H_2O_2 \xrightarrow[-2H_2O]{} Cu^+ + D.$$

Strictly speaking these two extreme cases also illustrate the difference in principle between the two redox situations which may occur in natural waters, viz. an oxidative and a quasi-reductive state of the aquatic medium (see below). In the first case reducing agents initiate the breakdown of H_2O_2 into free radicals, in the second hydrogen peroxide is consumed in the oxidation of a reducing agent introduced into the medium.

In addition to catalytic breakdown, the decomposition of H_2O_2 into free radicals by solar radiation is important under natural conditions.[96,241,242]

2. The role of microalgae in H_2O_2 decomposition

The separation of the biotic and abiotic contributions to the kinetics of H_2O_2 decomposition[230] observed in natural waters is extremely arbitrary since natural water is in principle a catalytic oxidation–reduction system of an open type. As a result of the activity of microorganisms there is a constant exchange in it of oxidation–reduction equivalents between the biota and the aquatic medium. It is possible to interrupt this flux by filtration of water samples through a fairly fine porous filter (usually 0.22 μm). However, stopping the flux changes the observed kinetic picture in an appreciable manner. Consequently more adequate information may be obtained by combining full-scale investigations on H_2O_2 decomposition in natural waters[80,82] with the investigation of model systems in cultures of algae and bacteria.

A detailed study of the kinetics of H_2O_2 decomposition by microalgae has been carried out.[152,153] The main conclusion of the investigations was the existence of two basic types of biotic processes of H_2O_2 decomposition which differed in the dependence of reaction rate on the initial hydrogen peroxide concentration.

For young cultures of algae the reaction is first order with respect to H_2O_2 concentration and its rate (w_1) is proportional to the biomass of the microorganisms (chlorophyll concentration).[152] In the case of natural algocenoses and old cultures there is in addition a contribution from a reaction of zero order with respect to H_2O_2 concentration,[84,153] the rate of which (w_0) is also proportional to the biomass of algae. The relative contributions of the first and zero order reactions depends on the initial hydrogen peroxide concentration (the greater its concentration, the greater the contribution of the first order reaction) and also on the state of algocenosis or of the alga culture.

Investigations carried out with whole and powdered algae and adding inhibitors of various reactions showed[84] that the first order reaction is caused by the action of catalase, while peroxidase processes make the main contribution to the zero order reaction. The catalase reactions are localised in the cell membrane fractions and the peroxidase in the water soluble fraction (not separated on centrifugation for 5 min at 10000 rpm).

Kinetic saturation of the peroxidase reaction at relatively low H_2O_2 concentrations is linked with the limited rate of intake (w_r) of peroxidase substrates (H donors). Experiments with an added dehydrogenase inhibitor (*m*-cresol) showed[84] that substrates of the peroxidase reaction pass into the medium as a result of the action of dehydrogenases.

It was shown[82] that reducing agents, H donors, react efficiently with H_2O_2 and are not only formed in algae cells but are also eliminated from them to the external medium. The rate of formation of reducing compounds (w_r) is proportional to the algal biomass and depends on the ecological situation in algocenosis. Blue-green algae are the most efficient producers of reducing agents.

The rate of decomposition of hydrogen peroxide in natural waters (w_d) is determined by the rate of formation of reducing compounds and the rate of their catalytic decomposition (w_1).

$$w_d = w_0 + w_1 = w_r + \varkappa_1 [H_2O_2],$$

where $\varkappa_1$ is the observed first order rate constant.

In a quasi-stationary state the rate of decomposition of H_2O_2 coincides with its rate of formation (w_f).

$$w_d = w_f = w_r + \varkappa_1 [H_2O_2].$$

From which it is obvious that

$$[H_2O_2] \simeq (w_f - w_r)/\varkappa_1.$$

In other words, the content of hydrogen peroxide in a natural aquatic medium is determined by the difference in the rates of flux within the reservoir of H_2O_2 and reducing agents which react with O_2 far less efficiently than with H_2O_2. The two redox states of the aquatic medium, which differ in principle, are distinguished by the ratio of these rates (see above).

As was indicated, a change in the redox state of the medium accompanies the bloom of blue-green algae and is caused by their ability to produce reducing compounds in the external medium which react efficiently with H_2O_2.

VII. Radical processes for self-purification linked with the hydrogen peroxide cycle

As is seen from the data given in Sections IV and VI the processes of forming and breaking down H_2O_2 in natural waters are accompanied by the formation of free radicals in the medium. Of the other processes leading to free radicals mention must be made of the possible role of radiochemical processes, collapse phenomena (effects of cavitation of gaseous microbubbles in deep tanks[243,244]), acoustic phenomena,[245,246] uptake of reactive atmospheric gases[94,247–249] and biological processes.[250]

Radiochemical processes are only effected after radiation contamination of a locality,[249] since the natural radiation background is small. The contribution of collapse and acoustic phenomena to the formation of free radicals has not been studied quantitatively. The uptake by water of atmospheric ozone may make a significant contribution.[249,251]

In the absence of contamination, O_3 dissolved in water breaks down by a radical chain mechanism with the participation of $\dot{O}H$, and $O_2^{\dot{-}}$ radicals in chain propagation reactions.[248,252–254] Ozone reacts with reducing agents (H donors), when present in the water, with subsequent breakdown into radicals.[248]

$$O_3 + DH^- \rightarrow HO_3 + D^{\dot{-}},$$
$$HO_3 \rightarrow \dot{O}H + O_2.$$

Quantitative assessment of the contribution of the various routes to the formation of free radicals is difficult.[96] For practical purposes it is important to have an estimate of the stationary concentration of free radicals. It is possible to obtain this assessment both by direct measurements and by calculation, determining independently the rate of formation of radicals and the observed rate constant of their destruction in the medium in question.

1. Free radicals in natural waters

The methods of detecting free radicals in natural waters are based on the use of various types of radical "trapping". Depending on concentration, the "trap" may intercept either all the radicals formed in the medium or only a small proportion of them. In the first case the rate of formation of radicals in the system is determined from the rate of supply of the trap or the rate of accumulation of its reaction product with the radical. In the second case, knowing the

rate constant for the reaction of the trap with a given radical, it is possible to assess the stationary concentration in the medium.

Mill and collaborators[93] applied the trap method to the assessment of the free radical content of natural waters for the first time. They used toluene to intercept ȮH radicals and pyridine to intercept RO_2 radicals.

The dye *p*-nitrosodimethylaniline (PNDMA), which is widely used for the same purpose in radiation chemistry, was used as a trap.[81] This dye is gradually decolourised in samples of natural waters, chemical–biological processes making a decisive contribution. The rate is sharply reduced in filtered samples.

The trapping method has been significantly improved in recent years. The use of stable nitroxyl radicals for trapping gives the best results.[255–262] The stable product formed with this or with any radical may be identified chromatographically and the nature of the initial radical is thereby clearly established. Using such traps data have been obtained on the stationary concentrations and formation rates of free radicals and of other reactive intermediates in various natural waters (Tables 2 and 3).

Table 2. Typical values for the concentrations of reactive intermediates in natural surface waters.[107,261,262]

Reactive species	Rate of formation, mole litre^{-1} sec^{-1}	Decay rate constant, sec^{-1}	Concentration in surface layer, M (depth 1 m)	Note
*S	$(3–300)\cdot10^{-9}$	$5\cdot10^{5}$	$(1–5)\cdot10^{-13}$	
$^1O_2$	$(3–300)\cdot10^{-9}$	$2.5\cdot10^{5}$	$10^{-14}–10^{-13}$	sea environment
	–	–	$10^{-14}–10^{-12}$	fresh waters
	–	–	$8\cdot10^{-14}(5\cdot10^{-14})$	fresh waters [263]
ROO	$10^{-11}–10^{-10}$	0.1–1(?)	$10^{-11}–10^{-10}$	
ȮH	–	10^{7}	$2\cdot10^{-19}$	sea environment
	$10^{-11}–10^{-10}$	$(0.2–2)\cdot10^{5}$	$(2–6)\cdot10^{-16}$	fresh waters
	–	–	$2\cdot10^{-18}(4\cdot10^{-17})$	fresh waters [263]
e_{aq}^-	$(5–10)\cdot10^{-11}$	$(0.5–1.5)\cdot10^{7}$	$(1–2)\cdot10^{-17}$	
	–	–	$1.2\cdot10^{-17}(5.2\cdot10^{-18})$	[263]
$O_2^{\cdot-}$	$10^{-11}–10^{-7}$(?)	10^{-3}(?)	$10^{-9}–10^{-8}$(?)	
	0.14–0.79 * nM kg^{-1} min^{-1}	–	–	sea environment [262]

Note. Numerals in square brackets denote references.

measured by the rate of decolourisation of PNDMA in distilled water. The proportion of radicals participating in the reaction with inhibitors of radicals contained in a water test sample is determined by the rate of decolourisation of PNDMA in natural water. Since the values of k_i for the overwhelming majority of traps lie in the range 10^8 to 10^{10} M^{-1} sec^{-1},[264] it may be assumed that $k_i \sim 10^9$ M^{-1} sec^{-1} and, depending on the size of the $\Sigma k_i[S_i]$ parameters, the observed concentration in aqueous medium of the trap for ȮH radicals (S_e) is assessed from:

$$S_e = \Sigma[S_i] \approx 10^{-9}.(\Sigma k_i[S_i]).$$

Table 3. Measured and estimated stationary concentrations and production rates (w) of ȮH radicals under the action of sunlight in samples of sea and fresh water.[96]

Sample	[OH], 10^{18} M	$w_i\times10^{12}$ mole litre^{-1} sec^{-1} (nM h^{-1})	Contribution from various radical sources, % (source concentration, μM)			
			NO_3^-	NO_2^-	H_2O_2	DOC*
Open ocean surface water (Sargasso Sea)	1.1±0.1	2.8±0.2 (10.1)	1 (0.05)	–	4 (0.05)	95 (200)
Gulf stream surface water	1.2	3.1 (11.2)	–	–	–	–
Deep water samples (Sargasso Sea, 700 m)	6.3±0.3	15.9±0.7 (57.2)	19 (10)	1 (0.01)	3 (0.1)	77 (70)
Deep Gulf Stream water samples (700 m)	5.8	14.7 (52.9)	–	–	–	–
Subtropical coastal waters (Biscayne Bay, Florida, high tide)	9.7±1.2	24.4±3.0 (87.8)	2 (2.0)	–	2 (0.2)	96 (300)
Ditto (low tide)	13.7±1.7	34.5±4.3 (124.2)	–	–	–	–
Coastal waters of temperate latitudes (Vineyard Sound, Massachusetts)	10.6	26.5 (95.4)	–	–	–	–
Equatorial upwelled water	7.4	18.6 (67.0)	3 (5)	25 (0.2)	3 (0.1)	65 (200)
Coastal upwelled water	26.3	66.1 (238)	7 (15)	35 (1)	6 (0.1)	52 (300)
Fresh water enriched with DOC	840	420±58 ($1.5\cdot10^3$)	–	–	–	–

*DOC, dissolved organic compounds.

2. Kinetic methods of assessing the stationary concentration of radicals and their role in the self-purification of natural aquatic media

As has been indicated it is necessary to know the rate of formation and the observed rate constant for disappearance in order to assess the stationary concentration of free radicals.

The last of these parameters is determined fairly simply for ȮH radicals using PNDMA. A method has been developed[81,240] for measuring the "inhibiting ability" parameter in an aqueous medium, viz. $\Sigma k_i[S_i]$ sec^{-1} where S_i is the trap for ȮH radicals contained in the water, k_i the rate constant for the reaction of ȮH with the trap S_i. The essence of the method is that ȮH are formed by the photolytic decomposition of H_2O_2 and the rate of formation is

If H_2O_2 is added to natural waters and the change in S_e is followed as H_2O_2 is decomposed, then it is possible to estimate the fraction of H_2O_2 decomposing into radicals.

$$\alpha = \Delta S_e/\Delta[H_2O_2].$$

According to one estimate[265] this fraction varies for different natural waters from 0.1 to 0.5 and is 0.3 on average. Thus about 30% hydrogen peroxide is decomposed into ȮH radicals in natural waters.

The process of forming H_2O_2 also proceeds through the intermediate formation of radicals. As was shown in Section IV, $O_2^{\cdot-}$

radicals serve as precursors of H_2O_2. The disproportionation of two $O_2^{\cdot-}$ radicals in neutral medium occurs with low efficiency,[266] and at low formation rates the catalytic processes involving copper ions are more probable.

$$O_2^{\cdot-} + Cu^{2+} \rightleftharpoons CuO_2^{+} \rightleftharpoons Cu^{+} + O_2,$$
$$O_2^{\cdot-} + Cu^{+} \rightleftharpoons CuO_2^{+} \xrightleftharpoons{2H^+} Cu^{2+} + H_2O_2.$$

The magnitudes of the rate constants for the reactions of $O_2^{\cdot-}$ with Cu^{2+} and Cu^{+} are close[267] so that the ratio of the rates of these reactions is determined by the redox ratio $[Cu^{2+}]/[Cu^{+}]$. In an oxidising medium the reaction of Cu^{+} with H_2O_2 leads to a reduction in the H_2O_2 yield due to the reaction of $O_2^{\cdot-}$ with Cu^{+}. This is reflected in the observation that in the presence of the enzyme superoxide dismutase (SOD) the rate of H_2O_2 formation in natural waters is usually increased.[98,99] If the rate of H_2O_2 formation is half the formation rate of $O_2^{\cdot-}$ radicals in the presence of SOD then in its absence a portion of the $O_2^{\cdot-}$ radicals participate in the reduction of H_2O_2 to OH radicals.

$$O_2^{\cdot-} + H_2O_2 \xrightarrow[H^+]{Cu^{2+}/Cu^{+}} O_2 + \dot{O}H$$

Correspondingly, it is possible to assess the extent of transformation of initially formed $O_2^{\cdot-}$ radicals into OH from the difference in the rates of the photochemical formation of H_2O_2 in the presence and absence of SOD. This fraction varies depending on the chemical composition of the aquatic medium, but is usually about 50%.

In the quasi-stationary approach the rates of formation and breakdown of H_2O_2 are therefore equal to one another and in these processes the rate of OH radical formation is an appreciable fraction of the hydrogen peroxide formation or decomposition. For a rough assessment of the rate of formation of OH it is possible to take the rate of the photochemical formation of H_2O_2 in the aquatic medium:

$$w_i \approx w_f.$$

Knowing w_f and the parameter $\Sigma k_i[S_i]$, it is possible to assess the stationary OH concentration and the apparent rate constant for the radical oxidation of any contaminating substance P (k_p):

$$[OH] = w_i/\Sigma k_i[S_i],$$
$$k_p = k_{(OH+P)}[OH] = k_{(OH+P)}w_i/\Sigma k_i[S_i],$$

where $k_{(OH+P)}$ is the bimolecular rate constant for the reaction of OH with P.

Various peroxidase self-purification processes are efficiently brought about in the presence of H_2O_2 in aquatic media in addition to the radical reactions.[152] Thus 3,4-dichloroaniline undergoes practically no conversion in a state of natural algocenosis in the dark in the absence of added H_2O_2 and is rapidly consumed if hydrogen peroxide is added to the algae.[265] In a similar manner various amines, which are peroxidase substrates, are oxidised on storing with algal cultures.[152]

The rate of the H_2O_2 cycle within reservoirs thereby reflects the efficiency of radical (and peroxidase) processes of self-purification of aquatic media. This enables assessment of the potential for chemico-biological self-purification of aquatic media, which is essential for assessing the acceptable loading of organic contaminants in natural reservoirs both in combination with and in relation to individual compounds.[71] The quantity of hydrogen peroxide formed (and decomposed) in natural waters gives an idea of the quantity of dissolved organic compounds which may be oxidised in extracellular chemico-biological processes (the chemico-biological self-purification potential). Under actual conditions a portion of the H_2O_2 is formed without the formation of reactive intermediates and the breakdown of H_2O_2 may be effected by a catalase mechanism, also without the formation of intermediates.

VIII. The hydrogen peroxide cycle within reservoirs and the biological wealth of aquatic media

On a global scale the fluxes of oxidation and reduction equivalents in the biosphere are balanced in the processes of photosynthesis and respiration. In addition to this global redox system there also exists in natural waters quasi-stationary redox subsystems comprising hydrogen peroxide and reduction equivalents of biotic origin. In view of the diversity and complexity of the mechanisms of H_2O_2 reactions with indigenous reducing agents under natural conditions, useful information for describing them adequately may be obtained from a study of model catalytic redox systems.

1. Modelling redox processes involving hydrogen peroxide within reservoirs

Ascorbic acid, hydroquinone and glutathione stand out among the most widely distributed reducing agents in nature as peroxidase substrates.[155] The redox catalytic reactions involving ascorbate ion have been studied in most detail.[268] As was indicated above, ascorbic acid is oxidised more efficiently by oxygen than by hydrogen peroxide. Another feature of ascorbic acid is the initiation of coupled processes of radical oxidation of various compounds difficult to oxidise.[239] A third feature is that ascorbic acid is an efficient H donor, for example in relation to organic radicals,[137] preventing the oxidation of organic substances. At the same time ascorbic acid radicals, stabilised by a system of double bonds, are kinetically extremely inert.[138]

Hydroquinone is a precursor of aquatic humus. In spite of its wide practical use in various investigations the mechanism of the redox catalytic reactions of hydroquinone are still unclear. A detailed kinetic investigation has been carried out of the catalytic oxidation of hydroquinone by hydrogen peroxide in the presence of copper ions.[269] It was found that in addition to non-radical processes hydroquinone participates in coupled radical oxidations of compounds difficult to oxidise. Hydroquinone thereby serves as the most suitable reducing agent to put into the medium in the presence of H_2O_2 to model the radical self-purification process induced by reducing compounds of biogenic origin.

Thiol compounds form part of proteins, humic compounds and metabolic products of water organisms, particularly micro-algae.[270,272] However the mechanism of the catalytic redox reactions involving thiols, and glutathione in particular, has been insufficiently studied. This gap has been partially closed.[269] It was shown that glutathione possesses extremely important features.

First of all glutathione readily reduces copper ions and forms stable (covalent) mono and less stable bis complexes with Cu^{+}.

$$2Cu^{2+} + 2GSH \xrightarrow[-2H^+]{} 2Cu^{+} + GSSG,$$
$$Cu^{+} + GSH \rightleftharpoons CuGSH^{+},$$
$$CuGSH^{+} + GSH \rightleftharpoons Cu(GSH)_2^{+}.$$

The complexes $CuGSH^+$ and $Cu(GSH)_2^+$ reversibly add O_2 (see Ref. 273) but are not decomposed to electron transfer products. The reduction of O_2 is effected directly to water by reaction of the oxygenated complex with a second glutathione copper complex, avoiding the formation of intermediate hydrogen peroxide.

$$Cu(GSH)_2^+ + O_2 \rightleftharpoons (GSH)_2CuO_2^+,$$

$$(GSH)_2CuO_2^+ + Cu(GSH)_2^+ \xrightarrow[-2H_2O]{} 2Cu^+ + 2GSSG.$$

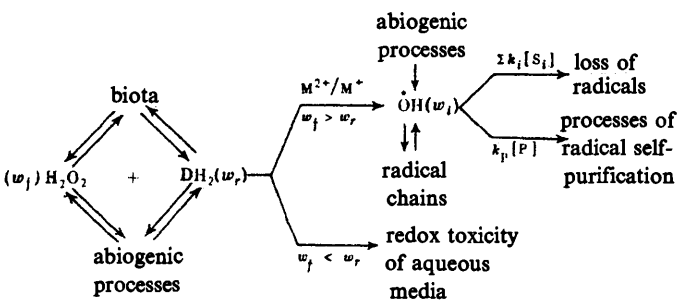
Evidently the oxidation of glutathione will proceed extremely slowly at low natural concentrations of copper.

The glutathione Cu^+ complexes react far more efficiently with hydrogen peroxide.

$$Cu(GSH)_2^+ + H_2O_2 \xrightarrow[-2H_2O]{} Cu^+ + GSSG.$$

Glutathione and seemingly other thiol compounds bind copper ions in the form of unreactive, biologically inaccessible complexes. Glutathione may thereby work as a reducing agent, modelling the onset of toxicity and the inhibition of self-purification processes of natural aquatic media by reducing toxicants.

Generalised results of full-scale and laboratory investigations[274] have enabled us to propose a dynamic chemico-biological redox model for natural aquatic media.



The gist of the model is as follows. In a natural aquatic medium biotic and abiotic processes are in constant operation forming oxidation and reduction equivalents, which react with one another. The results of these interactions are determined by the ratio of the fluxes within reservoirs of reactive oxidation equivalents, hydrogen peroxide (w_f) and the reducing compounds (DH_2) reacting efficiently with them (w_r). If the flux of oxidation equivalents predominates ($w_f > w_r$), an oxidative state is set up in the medium. Reducing agents entering the medium are either oxidised by hydrogen peroxide or initiate conjugated radical processes of self-purification of the aquatic medium from the contaminating compounds (P). If the flux of reducing agents exceeds the H_2O_2 flux ($w_r > w_f$) then a quasi-reductive redox state is set up in the aquatic medium (on increasing the flux the reducing agents will be gradually oxidised by oxygen dissolved in the water). Under these conditions various toxic effects arise in the water.[82]

2. Hydrogen peroxide and the biological wealth of an aquatic medium

The participation of H_2O_2 in the self-purification of an aquatic medium is closely linked with maintaining its biological wealth. However there is another aspect to biological wealth connected with the hydrogen peroxide cycle within reservoirs. One speaks of the redox-toxicity factor of a medium which arises when quasi-reductive conditions become established in an aquatic medium.[80,82]

It has been shown[275] that the presence of H_2O_2 is necessary in an aquatic medium for the development of fish in the early stages. This is linked with the possible participation of peroxy oxidation equivalents in bringing about metabolic redox processes. In fact a certain optimum H_2O_2 content exists in a natural aquatic medium, at which the chemico-biological redox processes within the reservoir are balanced. Unbalance of these processes may lead to two specific situations.

As was indicated in Section VII, in an aquatic medium the H_2O_2 cycle is closely linked with the free radical cycle. At the same time (see Section V) the H_2O_2 cycle is closely linked with the microelement cycle (particularly manganese ions). On increasing the free radical processes the oxidation of Mn(II) may be accompanied by the formation of metastable microcolloidal particles with mixed valency Mn(III,IV)[276,277] possessing strongly expressed oxidative properties. This is linked with the fact that the Mn(IV) ion, although having a high oxidation potential, is extremely inert in reactions of ligand substitution by virtue of the particular features of its electronic structure (d^3). Correspondingly the reduction of Mn(IV) by reducing compounds is brought about comparatively slowly. The Mn(III) ion (d^4), on the other hand, has a labile coordination sphere and is an efficient oxidising agent, possessing a high oxidation potential. The Mn(III) ion in microcolloidal particles of mixed valency is reduced to the Mn(II) ion which readily disproportionates with a neighbouring Mn(IV) ion with the formation of two more Mn(III) ions, i.e. particles with even more marked oxidative properties. The formation of such particles is particularly characteristic of aquatic media subjected to radiation contamination.

The hyperoxidising state of the medium, when metastable microcolloidal particles of bound or adsorbed Mn(III,IV) are present in the water, proves to be toxic for fish, a disease of the gills is observed. The factors controlling the emergence of the hyperoxidising state of the medium have not yet been clarified. Another, more completely studied phenomenon linked with the unbalancing of oxidation-reduction processes is the formation of a quasi-reducing state of an aquatic medium (see Section VI). Under these conditions a whole range of negative factors arise.

There is seemingly a reduction in the ability of the medium towards self-purification which leads to the accumulation of a whole series of toxic agents in the water.

Since the emergence of quasi-reducing conditions is usually accompanied by vigorous development of blue-green algae in the water, the majority of negative consequences are linked with precisely this factor. Blue-green algae occupy a special position in the ecosystem of modern reservoirs. In summer months they frequently become the dominant species in the phytoplankton.

The combination of an ability to photosynthesise, to consume organic compounds from the external medium[278] and to fix atmospheric nitrogen[279] causes the high adaptability of these microorganisms. In comparison with green algae and diatoms, blue-green algae effect photosynthesis at far lower light intensities and in the dark respiration consumes far less energy. The inhibitory effects of elimination and breakdown products of blue-green algae have great importance for other representatives of the algoflora.[280] Blue-green algae are most suited to living in reducing conditions. In the bottom layers of water they may vigorously assimilate sulphur in its sulphydryl form.[281]

The massive development of blue-green algae leads to many negative consequences. At bloom in a reservoir the pH of the medium increases, sometimes to values of 10–12. This creates

pathogenic microflora and of stimulants of intestinal illnesses, including cholera bacillus.[281] The situation is very dangerous when, in their life cycle, many forms of blue-green algae eliminate into the aquatic medium compounds which possess a strong toxic action.[280,282–285] Cases of mass destruction of animals and diving birds linked with the bloom of blue-green algae have been recorded in many regions of the Earth since the middle of this century.[286]

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The combination of literature data and our investigations indicates the important role of hydrogen peroxide in the aquatic component of the environment. Seemingly the evolution of aerobic life in the ocean also proceeds with the participation of H_2O_2 as the basic form of activated oxygen.[287] The oxidising character of the medium is also a condition for the rich functioning of the water ecosystem.

Under the influence of anthropogenic factors the content of H_2O_2 in natural aquatic media may be increased or decreased. An increased concentration of H_2O_2 into the overshoot zone is recorded on dropping unpurified domestic effluent into a reservoir. A sudden reduction of hydrogen peroxide concentration is possible on dropping biologically purified effluent into the reservoir due to reaction with reducing compounds introduced with the effluent.

The content of H_2O_2 in the air and in atmospheric moisture may be reduced (with SO_2 overshoot) or increased (with overshoot of organic substances) in a similar way. When the air is contaminated with sulphur oxides, sulphuric acid and incompletely oxidised sulphite will enter the soil ecosystem in place of oxidation equivalents such as H_2O_2. Such a substitution has an unfavourable action on the functioning of the soil ecosystem.[288]

In addition to its effect on the oxidation-reduction state of aquatic media, hydrogen peroxide makes an appreciable contribution to the formation of free radicals and participates in the self-purification of waters from difficultly oxidisable organic compounds. Free radicals may also have a significant effect on the biological richness of aquatic media, participating in the oxidation of compounds involved in biochemical cycles, in the initiation of peroxide oxidation of lipids, etc. Seemingly in natural waters, as in the cell, there is a physiological optimum both in H_2O_2 content and in the stationary concentrations of active intermediates.

The effect of anthropogenic factors on the H_2O_2 content of natural waters may be compensated by artificial addition of oxidation equivalents (H_2O_2, soluble peroxy compounds) to water or to the soil ecosystem (in irrigated farming). By varying the H_2O_2 content it is possible to regulate the biological richness of aquatic media, to suppress the development of undesirable microorganisms, blue-green algae in particular, and to intensify self-purification processes. The practical application of such measures to large bodies of water and areas requires large quantities of H_2O_2. Consequently a promising direction for investigation is the design of heterogeneous systems (with combined photo-sensitisers) generating H_2O_2 efficiently under the action of sunlight. The manufacture of small scale electrochemical generators of H_2O_2 based on the cathodic reduction of O_2 would also be promising.

An absolute requirement is the putting into practice of prophylactic measures to prevent the introduction of reducing compounds into reservoirs together with effluent which has passed biological purification. Water-submersible sources of UV irradiation may be used for this purpose. Under the action of hard UV radiation H_2O_2 is formed in waste water, radical chain oxidation processes are initiated, pathogenic microflora perish, aromatic compounds are hydroxylated, organochlorine compounds are dechlorinated and the overall content of dissolved organic compounds is reduced.

Regrettably the solution of many ecological problems encounters a shortage of H_2O_2. In practice H_2O_2 is not used in the purification of waste water, in spite of the fact that there is a multitude of patents to that effect and hydrogen peroxide is applied widely worldwide in the purification of domestic and industrial waste water.[289]

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Translated from *Uspekhi Khimii* **60** 2412–2421 (1991) U.D.C. 542.61

Supercritical extraction and prospects for the creation of new waste-free products

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ABSTRACT. The principal ideals underlying a new separation procedure—supercritical extraction—are described and its advantages and disadvantages are considered. The properties of supercritical gases such as solvent power and selectivity are discussed. The possibilities of supercritical extraction in the solution of applied problems in the protection of the environment are demonstrated: purification of waste waters, regeneration of sorbents, detoxification of toxicants.

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I. Introduction

The tasks faced by modern chemical engineering in connection with the problems concerning the protection of the environment can be performed only on the basis of the ecological optimisation of the existing and the creation of new low-energy low-waste chemical processes. One of the promising aspects of the creation of such processes, which has been attracting increasing attention by investigators and technologists during the last decade, is based on the use of supercritical gases as extractants and solvents for the extraction, separation, and purification of substances and also as a medium for various chemical reactions.[1] Although the first studies on the application of supercritical gases as solvents were published as early as the past century,[2] systematic fundamental and applied research in this field dates back to the 1970s, which is associated with the increasing urgency of energy saving and environmental protection problems. Among studies carried out hitherto on these lines, the vast majority are devoted to supercritical extraction (SE) of various substances both from the standpoint of the investigation of the physicochemical features of supercritical extraction and from the standpoint of its chemical-analytical and technological applications.

Supercritical extraction is a method for the extraction of components of solid or liquid mixtures into a supercritical gas phase, which plays the role of an extractant in this case. The supercritical gas (*supercritical fluid*) is a substance in a supercritical state, i.e. at a temperature and pressure above its critical point. By virtue of their low critical temperatures, carbon dioxide, ethane, ethylene, propane, sulphur hexafluoride, etc. have found the greatest number of applications in research and technological practice as extractants. Among them the greatest popularity is enjoyed by supercritical CO_2 because of its high solvent power in relation to many organic substances, ready availability, low cost, non-combustibility, and non-toxicity. A significant advantage of supercritical gases (SG) compared with the usual liquid solvents (extractants) is that the solvent power of such gases exhibits a marked dependence on temperature and pressure, which makes it possible to regulate extremely (i.e. by varying the temperature T or the pressure p) the selectivity of the supercritical extractants and also to achieve the complete regeneration of the extractant without resorting to reagent methods or distillation. Another attractive aspect of the application of supercritical gases is that high molecular diffusion coefficients (higher by 1–2 orders of magnitude than for the usual liquids) and low viscosities (approaching the usual gases in terms of order of magnitude) are characteristic of such substances.

Although supercritical extraction is a new and relatively expensive process, the results of a whole series of resarch studies have already found industrial applications and have been commercialised. For example, certain new technological processes based on supercritical extraction in the USA include the regeneration of the adsorbents and catalysts, the extraction of certain toxic organic substances from aqueous solutions and the soil, the elimination of asphaltenes from heavy petroleum fractions, the removal of sulphur from coal, the extraction of caffeine from coffee grains, the extraction of certain biologically active substances from plant raw material, etc. The range of industrial applications of supercritical extraction has been gradually expanding.

Supercritical extraction has been finding increasing applications in analytical chemistry as a selective method for the separation and concentration of components of complex mixtures of organic substances.

Bearing in mind that it is impossible to cover fully in a single article the present state of research into the field of supercritical extraction, which has recently acquired an interdisciplinary character, and also the fact that no reviews have so far been published on this topic in Russian scientific literature, the aim of the present study is to give an account of the main ideas underlying supercritical extraction and its practical importance and in addition to reflect certain latest tendencies in the development of this promising field.

II. The properties of supercritical gases as extractants

Supercritical gases occupy, as it were, an intermediate position between the usual gases and the usual liquids, combining the properties of both and possessing at the same time their own intrinsic properties. The supercritical state is a qualitative state of

matter in which the gaseous and liquid state become indistinguishable.[3] It is shown on the phase diagram (Fig. 1) that, on moving along the path (indicated by an arrow in Fig. 1) passing through the supercritical region, it is possible to achieve a transition from the liquid to the gaseous state and conversely without first-order phase transitions (in this instance this would be evaporation and condensation).

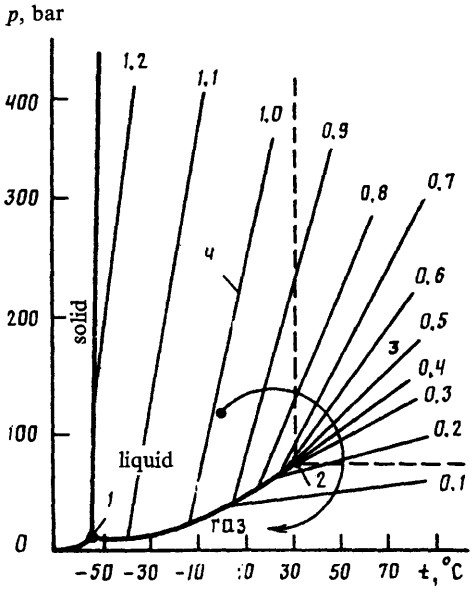


Figure 1. Temperature–pressure diagram for CO_2 with an indication of constant density lines: *1*, triple point; *2*, critical point (critical temperature −31.06 °C; critical pressure 73.8 bar); *3*, supercritical region; *4*, density lines.

One of the most important qualities of a supercritical gas as an extractant is its solvent power. It is determined by the molecular structure and density of the supercritical gas and can be characterised qualitatively by the solubility parameter δ (the square root of the cohesion energy density). This quantity can be rigorously calculated from thermodynamic properties by using the Hildebrandt theory.[3] The solvent power of a supercritical gas increases with increase in temperature at a constant density and with increase in density (pressure) at a constant temperature. The pressure dependence of the solubility parameter is illustrated in Fig. 2 for gaseous, liquid, and supercritical CO_2. Evidently δ for gaseous CO_2 is close to zero and at a temperature below the critical value (in the given instance $t = -30$ °C) the entire variation of δ with increasing pressure consists in an abrupt rise of δ until the attainment of a certain pressure p, which is caused by the condensation of CO_2. The parameter δ for liquid CO_2 differs only slightly from the value for organic solvents, for example solvents such as toluene, hexane, etc.[3,4] At a temperature exceeding the critical value (the cases corresponding to 32 and 70 °C are illustrated), increase in p does not induce a first-order phase transition and there is a possibility of a smooth regulation of the solvent power (δ) within wide limits by means of relatively small changes in temperature or pressure. The greatest changes in δ (as well as in the density—see Fig. 1) are observed in the vicinity of the critical point, since the compressibility becomes virtually unlimited at the critical point. The possibility of regulating the solvent power of a supercritical gas and hence the solubility of the components being extracted by varying the pressure or temperature is a unique characteristic quality of supercritical gases from the standpoint of their use as extractants.[5]

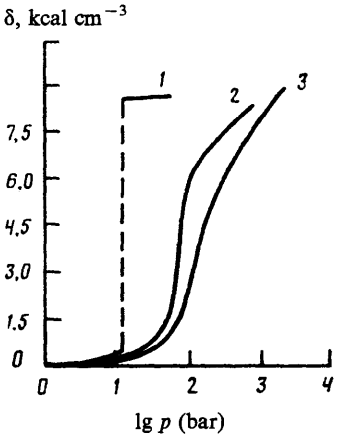


Figure 2. Dependence of the solubility parameter (δ, kcal$^{1/2}$ cm$^{-3/2}$) on pressure for CO_2 at different temperature (°C); *1*, −30; *2*, +32; *3*, +70.[1]

The solubility of the extracted components in a supercritical gas is determined by the characteristics of their partition between the phases in contact at equilibrium. Modern thermodynamics makes it possible to describe fairly reliably and in many instances with a high degree of accuracy the phase equilibria in various systems involving a supercritical gas. A detailed description of such problems may be found in the literature.[5–10] Here we shall deal only with the fundamental features important for the understanding of which factors determine the solubility of substances in a supercritical gas and the selectivity of the supercritical extraction.

We shall consider the relatively simple case of the equilibrium distribution of the components i between the solid (s) and supercritical (sp) phases. The equality of the fugacities of the ith component in the phases corresponds to the state of equilibrium:

$$f_i^s = f_i^{sp}. \quad (1)$$

The fugacities of the components can be determined using the fugacity coefficients ϕ_i:

$$f_i = y_i \phi_i p. \quad (2)$$

In Eqn. (2), p is the pressure and y_i the mole fraction of the component i in the supercritical phase or the vapour. For the

simplest case, where the solid phase consists of the component i, one can write[8]

$$y_i^{sp}\phi_i^{sp}p = \phi_i^s p_i^s \exp\int_o^p (V_i^s/RT)dp, \quad (3)$$

where p_i^s is the vapour pressure of the component i at a temperature T, ϕ_i^s the fugacity coefficient of the component i corresponding to the pressure p_i^s, V_i^s the molar volume of the component i, and ϕ_i^{sp} the fugacity coefficient in the supercritical phase. If the molar volume V_i^s is independent of p, then Eqn. (3) becomes

$$y_i^{sp}\phi_i^{sp}p = \phi_i^s p_i^s \exp\left(\frac{V_i^s(p-p_i^s)}{RT}\right). \quad (4)$$

Hence it is possible to find the solubility of the component i in the supercritical phase:

$$y_i^{sp} = \frac{p_i^s}{p}\left[\frac{\phi_i^s}{\phi_i^{sc}}\exp\left(\frac{V_i^s(p-p_i^s)}{RT}\right)\right]. \quad (5)$$

The multiplier in square brackets in Eqn. (5) is the intensification factor E, which shows by what factor the real solubility of the component i in the supercritical phase (y_i^{sp}) is greater than in an ideal gas (p_i^s/p):

$$E = \frac{\phi_i^s \exp\left(\frac{V_i^s(p-p_i^s)}{RT}\right)}{\phi_i^{sp}}. \quad (6)$$

The numerator in Eqn. (6) characterises the influence of pressure on the fugacity of the compound i, while the denominator (ϕ_i^{sp}) reflects the influence of the intermolar interactions in the supercritical phase and of the density. The quantity ϕ_i^{sp} may be found from equations of state such as the Soave–Redlich–Wang or Penn–Robinson equations.[3] It follows from Eqn. (6) that a component with a greater molar volume V_i^s is characterised also by a greater factor E for the same p and T and for identical intermolecular interactions in the supercritical phase. In terms of order of magnitude, the factor E is usually in the range 10^4-10^7 for substances of different types. Fig. 3 presents the dependences of E on the density of the supercritical CO_2 for a series of polar organic compounds with different functional groups.[11] Evidently the factor E varies in the series of these compounds approximately within the limits of one and a half orders of magnitude. At the same time, it has been shown[11] that the range of solubilities in the series of these compounds is much greater and corresponds to several orders of magnitude because the solubility is determined not only by the intensification factor, characterising the solvent–solute interactions, but also by the vapour pressure [Eqn. (5)]. The influence of the vapour pressure on the solubility and hence on the selectivity is illustrated in Fig. 4, which shows the dependence of the solubility of tetracyclic sterols having similar properties in supercritical CO_2 on the density of the latter. The solubility of cholesterol is greater by two orders of magnitude than that of ergosterol. This finding can be explained by the fact that the two compounds, having similar values of E, have very markedly different (by approximately two orders of magnitude) vapour pressures, that of cholesterol being higher, although they are both very low ($<10^{-10}$ bar).[12] Thus the selectivity of the supercritical extraction is proportional to the ratio of the vapour pressures although, the latter can in fact be negligibly low. With increase in p_i^s, the solvent–solute interactions, i.e. the factor E, make an increasing contribution to the selectivity.

The initial addition to the supercritical gas, for example to CO_2, of hydrocarbons and polar organic solvents is an extremely effective procedure for increasing the solubility of the extracted components in the supercritical phase and of the selectivity of the extraction.[5,13] This method has been widely used in research and technology because it significantly extends the limits of the applicability of supercritical extraction.[14] The most frequently employed additives (modifiers) of this kind in CO_2 are propane, hexane, alcohols (methanol, ethanol, octanol), acetone, tributyl phosphate, etc.[14] Such modifiers not only make it possible to increase the solubility and selectivity but in the vast majority of cases increase the dependence of the solvent power of the extractant on the pressure and temperature and make it possible to reduce the working pressure p and temperature T and also to reduce the amount of extractant consumed. The mechanism of the action of modifiers varies and depends on their nature. For example, propane, which has a high solvent power in relation to petroleum products, sharply increases their solubility in a CO_2–propane mixture compared with pure CO_2.[14] In contrast to supercritical CO_2, which is a lipophilic solvent with a very low dielectric constant ($\varepsilon = 0.5$ at $t = 50$ °C and $p = 250$ bar), polar organic substances are capable of forming donor–acceptor complexes of the extracted components, which affect the solubility and selectivity to a much greater extent than might have been expected on the basis of their fugacities alone.[13] Certain examples of an increase in solubility in the presence of polar modifiers are presented in Table 1. The last two rows of the table are noteworthy. They show that even ionic surfactants, in the given instance sodium 2-ethylhexyl sulphosuccinate, can be used as modifiers. Even ethanol-modified supercritical CO_2 is incapable of dissolving large amounts of hydrophilic substances. However, as can be seen from Table 1, in the presence of surfactants CO_2 is able to solubilise hydrophilic molecules as a result of the formation of reverse micelles or microemulsions.[1]

In many cases components entering into the composition of a complex mixture treated by the supercritical gas can play the role of modifiers. In this instance, being dissolved in the supercritical phase, some components increase the solubility of others, as happens, for example, on treatment of a naphthalene–benzoic acid mixture with supercritical CO_2.[15] A synergistic effect is observed in this case (Fig. 5), i.e. the solubility in the ternary system (two solutes, one solvent) exceeded the solubility in the binary system (one solute, one solvent).

III. Organisation of the supercritical extraction process

The organisation of the supercritical extraction process is illustrated schematically in Fig. 6.[16] The extractant (supercritical gas) passes in a continuous stream through the extractor (a mixer or a column apparatus), where it comes into contact with the solid or liquid mixture to be treated, extracting the soluble components. After emerging from the extractor, the extractant containing the dissolved target components is then subjected to a treatment, the main purpose of which is to isolate the target product from the extract and hence regenerate the extractant. This is achieved by a controlled decrease in temperature or pressure. Subsequently the parameters (p and T) of the regenerated extractants are adjusted to the required values and the extractant is again directed to the extractor, the circulation of the extractant being thereby achieved. Fig. 7 illustrated schematically the separation of components A and

B when component A is completely miscible with the supercritical gas. Evidently the complete separation of A and B can be achieved only when the extractant and component B are not infinitely miscible. A number of principal advantages and disadvantages of supercritical extraction as a technological process are presented below.[14,17,18]

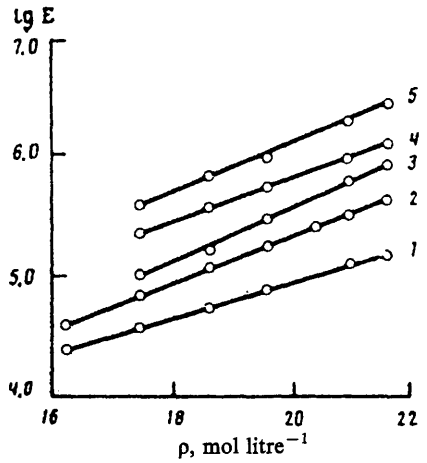


Figure 3. Dependence of the intensification factor E on the density (ρ) of supercritical CO_2 (t = 35 °C) for various substances: *1*, hexamethylbenzene; *2*, naphthol; *3*, phthalic anhydride; *4*, anthracene; *5*, acridine.[11]

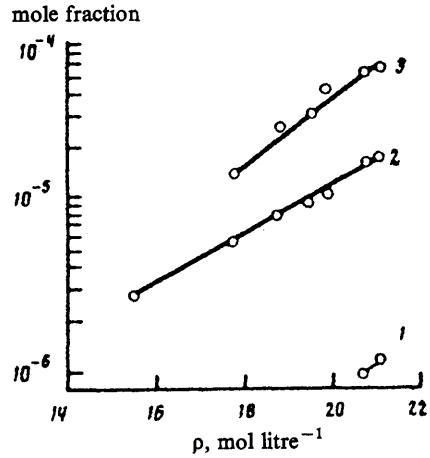


Figure 4. Dependence of the solubilities of various sterols in supercritical CO_2 (t = 35 °C) on its density: *1*, ergosterol; *2*, stigmasterol; *3*, cholesterol.[12]

Advantages: in terms of solvent power, supercritical gases are comparable to liquid organic solvents; the solvent power of supercritical gases and the solubility of the extracted components can be varied by altering p or T; it is possible to regenerate the extractant fully by altering p or T; high diffusion coefficients and low viscosities of supercritical gases; low working temperatures; low energy consumption in the process.

Table 1. The influence of modifiers on the solubilities of the extracted components in supercritical CO_2 at 35 °C.[13]

Extracted component	Modifier	F*
Acridine	Methanol (3.5%)	2.3
2-Aminobenzoic acid	Methanol (3.5%)	7.2
Cholesterol	Methanol (3.5%)	100
Hydroquinone	tri-n-butyl phosphate (2%)	300
ditto	Ethanol (5%)+surfactant** (0.5%)	>200
Tryptophan	Ethanol (5%)+surfacant (0.5%)	>100

* F is a parameter showing by what factor the solubility increases in the presence of the modifier.

** The surfactant employed was sodium di-2-ethylhexyl sulphosuccinate.

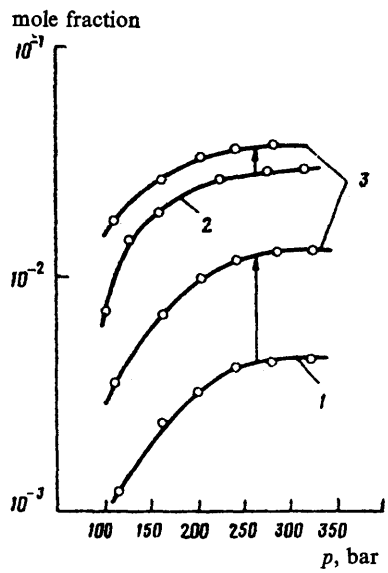


Figure 5. Mutual influence of naphthalene and benzoic acid in their extraction by supercritical CO_2 (t = 35 °C); dependence of the solubility in supercritical CO_2 on pressure in different systems: *1*, benzoic acid–CO_2; *2*, naphthalene–CO_2; *3*, (naphthalene + benzoic acid)–CO_2.[15]

Disadvantages: increased working pressure; high cost of equipment; unusual process conditions for many undertakings; complex character of the phase equilibrium in systems with supercritical gases.

IV. Applications of supercritical extraction

As shown by the analysis of the literature, among the wide variety of aspects of the technological applications of supercritical extraction, the aspects concerned with the protection of nature are nowadays of perhaps greatest interest because in this field the advantages of supercritical extraction make it extremely attractive for the solution of a wide range of applied problems.

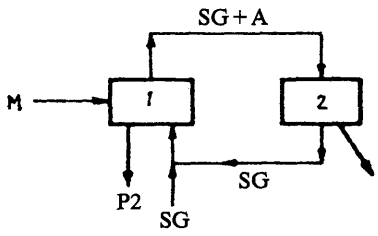


Figure 6. Schematic illustration of the supercritical extraction process: *1*, extraction; *2*, regeneration of the extractant and isolation of the products; M—mixture of components A and B undergoing separation: P1—product enriched in component A; P2—product enriched in component B.

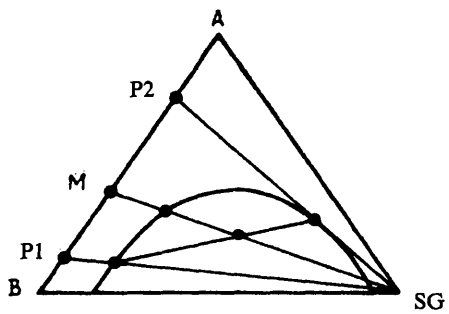


Figure 7. Schematic illustration of a binary mixture M of components A and B by supercritical extraction in conformity with the scheme presented in Fig. 6.

The processes based on the application of supercritical gases can be arbitrarily divided into three categories: single-stage separation, two-stage separation, and separation with simultaneous chemical conversion of the extracted components. In the single-state separation, the initial treated material is brought directly into contact with the supercritical gas, for example, in order to remove toxicants or to extract valuable components. In the two-stage separation, the initial treated material, for example water contaminated by organic toxicants, is brought into contact not with the supercritical gas but with an extracting phase of another type, usually a sorbent. Next, the sorbent is regenerated by being treated with the supercritical gas. In processes of the third category, the initial treated mixture is brought into direct contact with the supercritical gas, which functions not only as a solvent (extractant) but serves at the same time as a medium for the occurrence of chemical reactions, for example, such as oxidation of organic toxicants.

The single-stage separation is most suitable in those cases where the concentration of the extracted components in the mixture is relatively high. For example, processes involving the extraction of phenol, alcohols, aldehydes, and ketones from aqueous waste solutions by supercritical CO_2 and hydrocarbons have been developed for such cases.[19–23,27] The extraction of pyrethrin, for example, from plant raw material by means of supercritical CO_2 has proved extremely effective. Pyrethrin is extremely toxic to insects and is almost harmless to warm blooded animals. This substance is unstable and does not accumulate in the environment, in contrast to pesticides. The use of supercritical extraction for such purposes has made it possible to reduce almost by a factor of two the capital and operating costs compared with the usual multistage liquid extraction.[24,25] Another example of a single-stage process is the extraction of highly toxic organic substances, such as chlorine-containing pesticides and polychlorinated biphenyls from the soil and solid waste by supercritical CO_2.[24,26] The efficiency of the single-stage separation increases significantly when modifiers, increasing solvent power, are introduced into the supercritical gas.

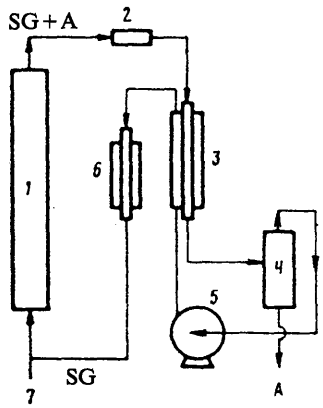


Figure 8. Schematic illustration of the sorbent regeneration process with the aid of supercritical extraction: *1*, apparatus in which the adsorbate is extracted from the sorbent by the supercritical gas; *2*, reductor; *3*, heat exchangers; *4*, separator; *5*, compressor; 6, heat exchanger; *A* = adsorbate.

The two-stage separation is extremely effective at low concentrations of the contaminant. In this case, supercritical extraction provides excellent possibilities for the regeneration of widely used sorbents such as activated charcoals and synthetic polymeric sorbents.[28–30] The usual regeneration methods, such as treatment with live steam and heat treatment, involve an extremely high energy consumption and are expensive. Compared with these methods, the use of supercritical extraction makes it possible, for example, to reduce by a factor of two the cost of regeneration of the sorbent in the purification processes for the waste waters from the industrial manufacture of pesticides involving the removal of contaminants such as atrazine, dinitrobutylphenol, alachlor, etc.[29]

An extremely important advantage of supercritical extraction is also the many-fold increase in the useful life of the sorbent, because it does not lose appreciably its properties even after many regeneration cycles. Fig. 8 illustrates schematically the regeneration of the sorbents by supercritical CO_2.[28]

The use of supercritical gases as a medium for chemical reactions has great potential possibilities. Supercritical water has attracted increasing attention of investigators and technologists in this connection. On passing to the supercritical state, the properties of water are radically altered and it becomes similar to non-polar organic solvents in terms of its solvent power. Supercritical water hardly dissolves in organic ionic substances and is completely miscible with hydrocarbons.[31] In supercritical water ($t > 374$ °C, $p > 218$ atm), organic toxicants can be oxidised by atmospheric oxygen to simple products such as CO_2, etc.[31] The study of the properties of supercritical water had made it possible to develop an effective process for the removal from waste waters of toxic organic components such as chlorine-containing pesticides, polychlorinated biphenyls, trichloroethane, perchloroethylene, etc.[31,32] The only reagent used in this process is compressed air. The degree of conversion of all the toxicants investigated into simple products as a result of oxidation was more than 99.99%, which exceeds significantly the degrees of conversion achieved in the combustion of toxic waste. The fact that, in contrast to combustion, the oxidation of, for example, chlorinated aromatic hydrocarbons in supercritical water does not involve the formation of dangerous toxicants such as dioxins and dibenzofurans is also important. Technical-economic estimates have shown that the cost of combustion exceeds significantly the cost of the process involving the use of supercritical water, which is associated with the lower consumption of fuel in the latter case. Fuel is necessary only in the initial stages of the process in order to establish the required temperature, which is then maintained as a result of the exothermicity of the oxidation reaction.

Another important example of the use of supercritical gases both as solvents and as reactants is the desulphurisation of coals by supercritical ethanol. Suphur-containing organic compounds are extracted into supercritical ethanol and are reduced there to products such as ethyl sulphide, and ethyl disulphide, thiophene, etc. Such treatment makes it possible to reduce the sulphur content in coal by a factor greater than 2.[24]

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Translated from *Uspekhi Khimii* **60** 2422–2447 (1991) U.D.C. 542.61:62-278:541.182.42/43

Extracting emulsions for the extraction of substances from aqueous media

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ABSTRACT. The characteristic features of the extracting emulsions used to extract and concentrate substances from aqueous solutions are examined. The influence on the properties of the extracting emulsions of the conditions in their preparation, of the properties of the disperse phase (the ionic strength and the pH of the aqueous solutions), the properties of the dispersion medium (viscosity, dielectric constants), as well as the presence of polar organic substances in the emulsions is discussed. The influence of the nanodispersion formed on mass transfer through the interface and on the properties of the extracting emulsions is demonstrated. The approaches to the mathematical description of the kinetics of the processes in extracting emulsions are discussed and it is shown that extracting emulsions with various properties designed for a wide variety of applications can be developed on the basis of the study of the physicochemical properties of such disperse systems.

Examples of the use of extracting emulsions in chemical engineering for the extraction of substances from aqueous media by membrane extraction into a multicomponent emulsion, for preliminary concentration in analysis, for therapeutic and prophylactic purposes in medicine, and for the protection of the environment are considered.

The bibliography includes 102 references.

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I. The membrane extraction method and extracting emulsions

Considerable interest in extracting emulsions, i.e. emulsions extracting or concentrating various substances, arose in connection with the first publications on membrane extraction into a multicomponent emulsion.[1,2]

Nowadays, together with the overall increased interest in liquid membranes,[3,4] a method of membrane extraction into a multicomponent emulsion has been developed for applications in various fields: for the isolation and concentration of substances from technological solutions, in analytical practice, in the solution of problems concerned with the protection of the environment, and for the detoxification of biological liquids involving the removal of harmful substances of exogenic and endogenic origin.[5–12]

The extraction and re-extraction stages in the membrane extraction process occur simultaneously in a system comprising three liquid phases. One of the phases (the liquid membrane) separates two solutions of different composition and immiscible with it: the initial solution (to be exhausted) and the re-extracting solution (the recipient) (Fig. 1). The membrane usually consists of an organic liquid, but systems are known with an aqueous membrane, used mainly for the separation of organic compounds.[13–19]

The membrane extraction method has many advantages compared with the usual extraction. One of the main ones is the reduction of the number of stages in the process. The combination of extraction and re-extraction makes it possible to achieve in a single stage the maximum possible, for the given system, differences between the concentrations of the extracted substance between the extracted and receiving phases. If the extracted substance in the phase F1 (Fig. 1) is bound in a weakly dissociating complex or forms an insoluble compound, then this ensures the most complete extraction from the initial phase F1.

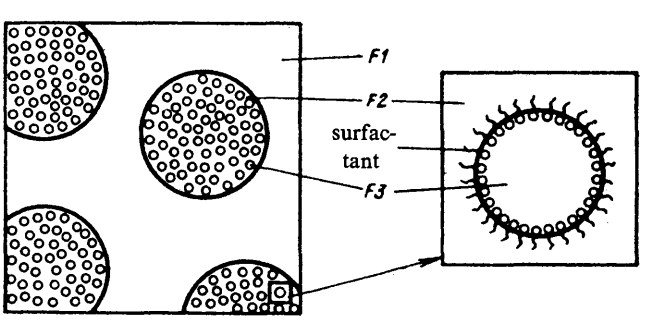


Figure 1. A multiple emulsion: F1 = solution to be extracted; F2 = liquid membrane (dispersion medium of the extracting emulsion); F3 = recipient solution (disperse phase of the extracting emulsion).

The degree of extraction in the membrane extraction process depends mainly only on the compositions of the initial and receiving solutions. The extractant in the phase F2 (Fig. 1) is merely a transferring agent, which interacts with the extracted substance

during its transport from the phase F1 to F3. Therefore the liquid membrane does not as a rule have to meet the requirements of a high capacity and high partition coefficients. The extractant-transferring agent determines mainly the rate and selectivity of the process. Thus in membrane extraction it is possible to use low concentrations of the transferring agents in the liquid membrane or to employ extractants which are relatively ineffective from the standpoint of two-phase extraction as transferring agents. This factor is attractive not only because of its economic aspect but also because of its ecological aspect.

Membrane extraction is a promising procedure for correcting the homeostasis and detoxification of biological liquids[8-11,20,21] and also for the extraction of metabolic products from enzyme solutions.[22,23] In this case, membrane extraction has an additional advantage associated with the possibility of preventing (or reducing to a minimum) the direct contact between the substances contained in the internal phase with the biological medium by virtue of the presence of the liquid membrane, consisting in the given instance of inert substances and, if necessary small amounts of the transferring agent. The amount and type of transferring agent are chosen to ensure, on the one hand, an acceptable rate of transport of the extracted substance through the liquid membrane and, on the other hand, so as not to traumatise the biological medium from which extraction takes place.

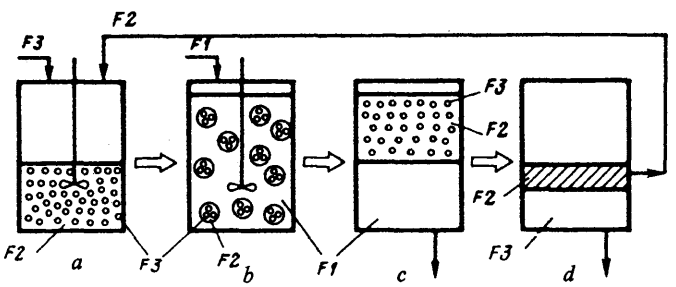


Figure 2. Schematic illustration of the membrane extraction process in a multiple emulsion: *a*, preparation of the extracting emulsion; *b*, bringing of the extracting emulsion into contact with the solution to be extracted; *c*, separation of the refined solution; *d*, separation of the extracting emulsion into layers.

In the case of extraction in a multiple emulsion, the process takes place in a system consisting of the extracting emulsion dispersed in the solution F1 to be extracted. The dispersion medium of the extracting emulsion F2 is the liquid membrane. The extracted solution F3 is dispersed in the liquid membrane F_2 with the aid of a surfactant (Fig. 1). The entire process consists of four stages (Fig. 2). In the first stage, the re-extracting aqueous solution is vigorously dispersed ($\omega = 200-2000\ s^{-1}$) in the organic phase containing the transferring agent and the emulsifier and an emulsion of the "water in oil" type is obtained (Fig. 2*a*). It is then brought into contact with the solution to be extracted under the conditions of "gentle" stirring ($\omega = 10-50\ s^{-1}$). This extracting emulsion is dispersed into individual globules and a multiple emulsion of the "water–oil–water" type is formed (Figs. 1 and 2*b*). At the end of the mass transfer, the extracting emulsion is separated from the refined product by means of gravitational separation into layers (Fig. 2*c*) and in the final stage the aqueous phase enriched in the target component and the organic phase are separated (Fig. 2*d*).

One of the characteristic features of the membrane extraction process in a multiple emulsion is the possibility of the constant renewal of the interface in the extracting emulsions during stirring, which is a positive factor in the extraction of substances in systems where interfacial films are formed. Such interfacial films, which retard the rate of diffusion of substances between phases, can be produced into systems containing both inorganic substances[24,25] and organic (protein) compounds.[26]

In analytical practice, the extracting emulsions can be used for the preliminary concentration of substances. Here not only the stability of the emulsions but also the distribution of water in the system, frequently leading to the "swelling" of emulsions (the transport of water into the extracting emulsion), which lowers the rate of concentration of the extracted substance, is very important. The use of kinetic factors for optimising the extraction time makes it possible, as will be shown below, to reduce to a minimum the negative effect of the swelling of extracting emulsions.

The region of possible applications of extracting emulsions is much wider than merely in the process involving membrane extraction in a multiple emulsion. Extracting emulsions can be used for the detoxification of various surfaces and media in the solution of ecological and medical problems. In particular, the employment of extracting emulsions as protective-prophylactic ointments, protecting (and cleaning) the skin against the action of harmful substances of different origin, in the first place the toxic substances present in industry, is a very promising application.[10,27] Extracting emulsions used for this purpose consist of thin films in which the contribution of the heterocoagulation resulting from the effect of the surface of the skin is enhanced.

II. Properties of extracting emulsions

The extracting emulsions must meet a number of requirements which are essential for their effective utilisation. These are stability throughout the period of application of extracting emulsions and minimal water transfer to the inner phase of the emulsions. It is also essential that the emulsions should be fairly stable throughout the long period of their storage before use. The emulsions must have definite properties depending on the specific process in which they are applied. Thus in technological processes, where the extracted component is concentrated in the inner aqueous phase, and the emulsions must then be separated into layers, the latter must be fairly stable throughout the extraction process, but after extraction they must be capable of separating rapidly into layers with the aid of the available methods. The emulsions used in medicine must be highly stable in order not to release the inner phase of the emulsion into the biological fluid.

In order to increase the capacity of the extracting emulsions, use is usually made of concentrated disperse systems, close to highly concentrated systems, with a volume fraction of the inner phase $\varphi = 0.6-0.7$. The view has been expressed in the literature that extracting emulsions with $\varphi > 0.5$ have a comparatively low stability,[28] but under certain conditions not only systems with $\varphi > 0.5$ but also highly concentrated emulsions with $\varphi > 0.74$ proved to be stable.[29]

An increase in the fraction of the inner phase above the theoretically possible value (φ_{theor}) for spherical particles of the same size (φ_{theor} is 0.741 for hexagonal packing, 0.686 for cubic centred packing, 0.524 for cubic packing, 0.340 for tetrahedral packing, and 0.64 for random packing[30,31]) involves the deformation of the drops of the disperse phase. Furthermore, real emulsions are polydisperse, which makes it possible to obtain stable emulsions with a high fraction of the disperse phase. The size distribution of the drops is an important characteristic of the extracting emulsion, which influences the stability of the system, its rheological properties, and other technological characteristics. The difference between the size distributions of the drops in emulsions having the same composition is one of the main causes of the discrepancies sometimes observed between the results of studies on membrane extraction in a multiple emulsion.

The properties of the extracting emulsions and in particular their stability are in many respects determined by the degree of dispersion of the inner phase.[28,32–34] The smaller the drop size, the higher the stability of the emulsion obtained. The influence of factors such as the type of stirring device,[28,38] the intensity of stirring, surfactant concentration,[33,34] etc. on the degree of dispersion has been noted.

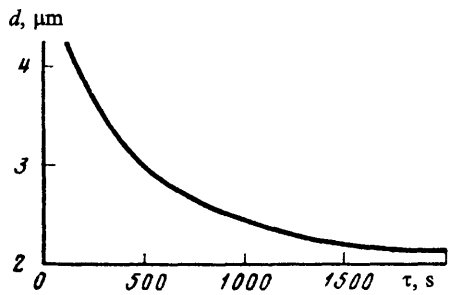


Figure 3. The effect of the emulsification time on the size of the drops of the inner phase of the emulsion of water in xylene (volume fraction of the inner phase $\varphi = 0.5$).[34]

Stirring for a period longer than the optimum time gives rise to little improvement in the quality of the emulsions.[33,34] The average drop size diminishes rapidly in the course of the first seconds of the emulsification process (Fig. 3).[34] With decrease in the size of the drops, their rigidity also increases and their size becomes comparable to the size of the eddies in the apparatus and there is no further dispersion. The viscosity of the emulsion diminishes during dispersion (Fig. 4).

The influence of the rate of stirring and of the surfactant concentration on the inner phase drop size is similar to the influence of the emulsification time (Fig. 3).[34]

As the temperature in the mixer is altered, there is a change in the surface tension, viscosity, and adsorption of the emulsifier. The decrease in viscosity and surface tension with increase in temperature improves the emulsification but under these conditions there is a sharp diminution in the degree of adsorption of the surfactant, which lowers the stability of the emulsions.

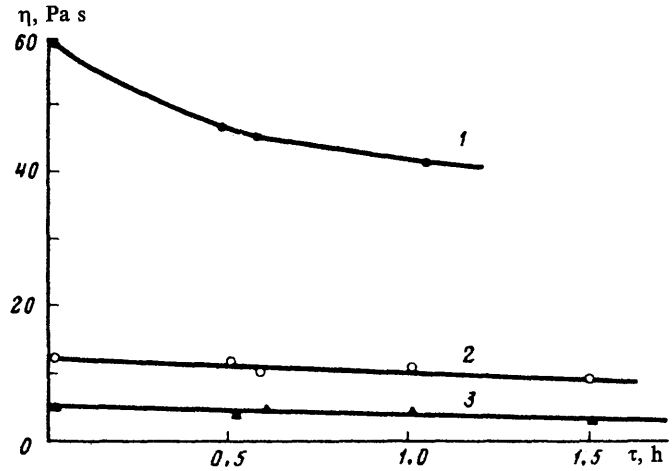


Figure 4. Dependence of the viscosity of the emulsion (η) on the dispersion time after the addition of the inner phase has ended;[34] temperature 25 °C; volume fraction of the inner phase: *1*, 0.65; *2*, 0.50; *3*, 0.40. Rate of displacement 3 s^{-1}.

With increase in the surfactant concentration, the stability of the adsorption layer is known to increase and hence there is an increase in the resistance of the emulsions to coalescence.[33] The dependence of the stability of the emulsions on the surfactant concentration show a maximum at 0.02 M (C_1) for hostacerin DGO and 0.45 M (C_2) for sorbitan oleate (Fig. 5).

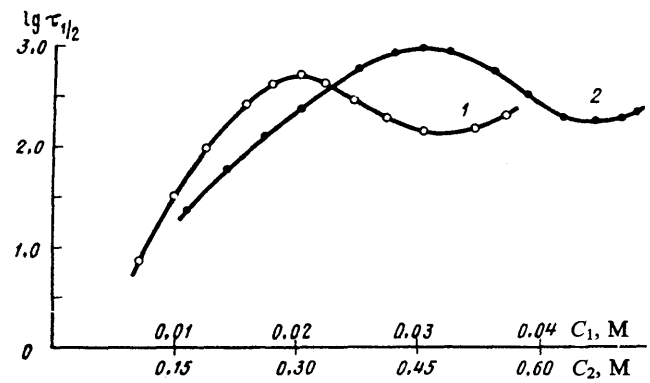


Figure 5. Dependence of the half-separation period ($\tau_{1/2}$) of the aqueous phase of the emulsion at 25 °C on the concentrations of hostacerin DGO (C_1, curve *1*) and sorbitan oleate (C_2, curve *2*). Fraction of inner phase 0.65. Isotonic buffer solution at pH 7.4 in liquid paraffin.

As mentioned above, the radius of the inner phase drops in emulsions initially diminishes with increase in the surfactant concentration and then remains constant,[34] which is associated with

the fact that the disperse system tends to the minimum interfacial energy possible for the given amount of the surfactant, so that, despite the high degree of dispersion of the inner phase, the drops coalesce until the attainment of an emulsifier content at the interface close to the limiting degree of sorption. When the surfactant is present in an amount sufficient for the stabilisation of all the drops of the interface formed as a result of the dispersion, the maximum stability of the emulsion is attained (under the given dispersion conditions).[35]

The increase in the viscosity of the emulsion is also associated with the decrease in the inner phase drop size (for φ = const.) (Fig. 6). After the attainment of the limiting degree of adsorption, the excess surfactant dissolves in the liquid membrane, the viscosity of the emulsions remaining virtually constant under these conditions.

At surfactant concentrations in the dispersion medium exceeding the critical concentration for the formation of non-spherical micelles (CCM-2), structure formation takes place in the organic phase and the viscosity of the emulsions increases with increase in the emulsifier concentration (Fig. 6).

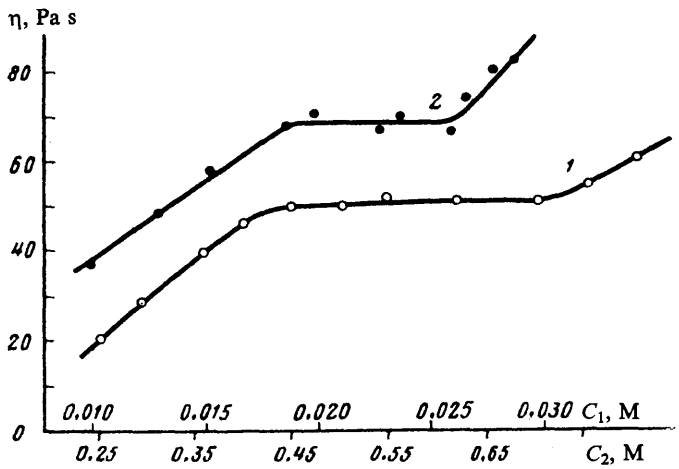


Figure 6. The influence of the concentrations of hostacerin DGO (curve *1*) and sorbitan oleate (curve *2*) on the viscosity of the emulsions at a rate of displacemnt of 3 s^{-1}. Fraction of inner phase 0.65; temperature 25 °C.

The study of the ξ-potential of the inner phase drops showed that, with increase in surfactant concentration above the value necessary for the complete saturation of the adsorption layer at the interface in the emulsion, the ξ-potential of the inner phase drops is seen to decrease. This lowers the repulsion energy between the disperse phase drops, which increases the rate of their coalescence and hence leads to a decrease in the stability of the emulsions.

Some increase in the stability of the emulsions at surfactant concentrations exceeding the CCM-2 in the liquid membrane is apparently associated with the formation of a heteroadsorption layer owing to the adsorption of the surfactant micelles at the interface.[36] When the repulsion energy of the adsorbed micelles exceeds their attraction energy, there is some increase in the stability of the emulsions.

Variation of the fraction of the inner phase in the emulsion leads to the variation of the specific interface. A definite position of the maximum in the dependence of the stability of the emulsion on the fraction of the disperse phase corresponds to each surfactant concentration (Fig. 7). The maximum stability corresponds to the complete saturation of the adsorption layer. For higher fractions of the inner phase at a specified surfactant concentration, the adsorption layer proves to be unsaturated and the stability of the emulsion is therefore diminished; for small fractions of the inner phase, when the interface in the emulsion is saturated to the maximum extent with surfactant molecules, the stability diminishes owing to the presence of an excess surfactant in the dispersion medium, i.e. an effect analogous to the dependence of the stability of emulsions on the surfactant concentration is observed (Fig. 5).

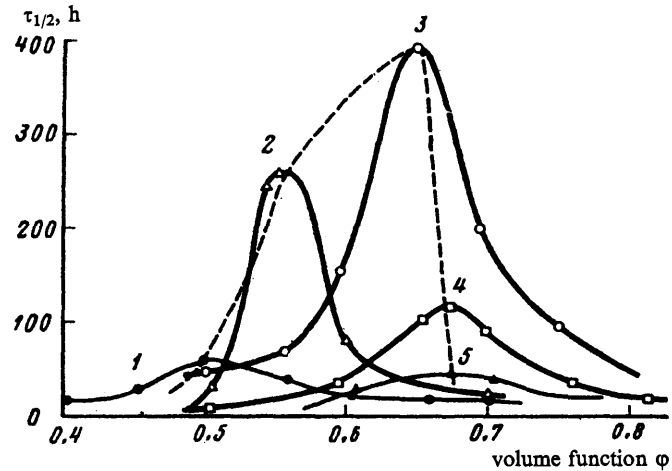


Figure 7. Dependence of the half-separation period of the inner phase of the emulsions at 60 °C on the initial fraction of the inner phase at different molar concentrations of sorbitan oleate: *1*, 0.24; *2*, 0.35; *3*, 0.45; *4*, 0.50; *5*, 0.55.

With increase in the surfactant concentration, the maximum in the stability of the emulsion shifts towards higher fractions of the inner phase.[37] At a surfactant concentration exceeding 0.02 M for hostacerin DGO and 0.45 M for sorbitan oleate, the stability maximum shifts towards higher fractions of the inner phase, but the absolute stability diminishes, the amount of surfactant necessary for the limiting degree of adsorption increasing sharply. For higher fractions of the inner phase, the shape of the drops deviates from the spherical and the drops are distorted, which reduces the stability of the extracting emulsions.

Thus in order to determine the quantitative composition of the most stable emulsion with the given qualitative composition, it is essential to take into account the interrelated influence of the fraction of the inner phase and the surfactant concentration.

The properties of the extracting emulsions can be varied by altering the composition of the dispersion medium, its viscosity, and its polarity. An increase in the viscosity of the outer phase of the emulsions can evidently ensure a certain kinetic stability of the

emulsion as a result of the decrease in the rate at which the thickness of the liquid film between the two surfaces diminishes as the drops of the inner phase approach one another. This fact can play a significant role in reverse emulsions. Fig. 8 presents the dependence of the half-separation time of the aqueous phase of the emulsion on the viscosity of the dispersion medium μ in the range of viscosities of hydrocarbon oils. Fig. 8 shows that the variation of the viscosity of the dispersion medium in the given range exerts an insignificant influence on the stability of the emulsions, but does influence appreciably their viscosity.[38] By altering the ratio of different oils in the organic phase of reverse emulsions, it is possible to alter the viscosity and other properties of the compositions without impairing the stability of the extracting emulsions.

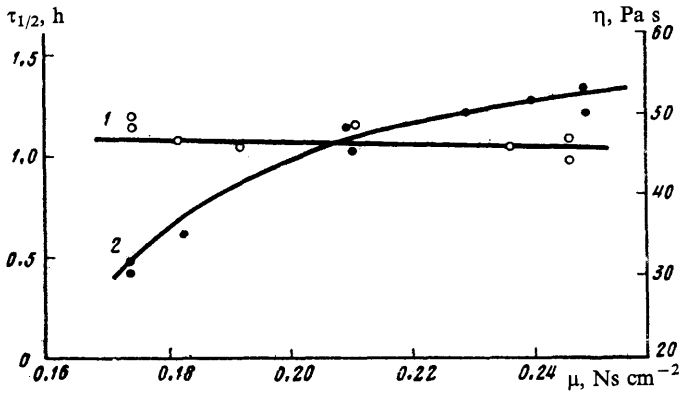


Figure 8. Dependence of the half-separation period of the aqueous phase (curve *1*) and of the viscosity of the emulsion (curve *2*) on the viscosity of the dispersion medium (μ).[38]

However, when the range of viscosities of the dispersion medium is widened, for example, by adding a hydrocarbon with a lower viscosity (decane), the stability of the emulsion is seen to decrease. Although in concentrated emulsions, close to highly concentrated ones, the thickness of the layers of organic phase is small (~20 nm), the hydrodynamic factor plays a fairly considerable role in the stability of the emulsions. Therefore, from the standpoint of the stability of the emulsions, it is useful to employ dispersion media with a fairly high viscosity and account must be taken of the fact that under these conditions the rate of diffusion of the target component falls in membrane extraction in a multiple emulsion.

The extractant-transferring agent forming part of the composition of the dispersion medium exerts a significant influence on the stability of the extracting emulsions. The extractants-transferring agents possess as a rule surface-active properties[24,39] and they therefore reduce the stability of the emulsions as a result of competitive adsorption at the interface. However, as shown previously, in the case of membrane extraction there is no need for high concentrations of the extractants-transferring agents in the liquid membrane and therefore in each specific case it is possible, as a rule, to select the necessary concentrations of the transferring agents both from the standpoint of the rate of extraction of the target component and from the standpoint of the stability of the extracting emulsion.

Apart from the above factors, the stability of the extracting emulsions is influenced significantly by the composition of the disperse phase. Among the factors playing the greatest role in their stability, mention may be made of the pH of the disperse phase, the ionic strength, and the presence of organic substances, which influence the polarity of the inner phase and the properties of the interface.

Fig. 9 presents the dependences of the half-separation period of the aqueous phase and of the viscosity of the emulsions on the NaCl concentration in the inner phase. With increase in the ionic strength of the solution constituting the disperse phase of the emulsions, both the stability and the viscosity of the emulsions increase. This is a positive factor in membrane extraction, since it makes it possible to increase the capacity of the emulsions with respect to the target component by increasing the content of the binding reagent in the inner phase.

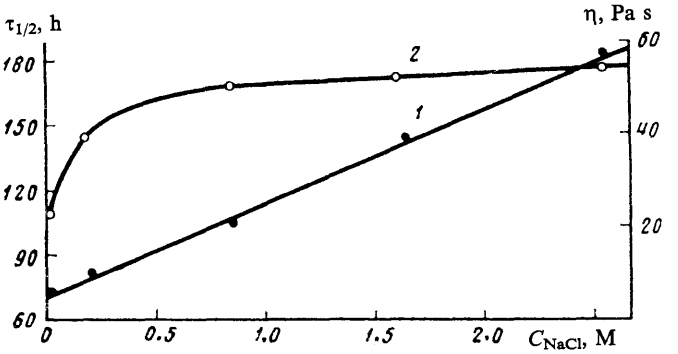


Figure 9. Dependence of the half-separation period of the aqueous phase at 60 °C (curve *1*) and of the viscosity of the emulsions at 25 °C (curve *2*) on the NaCl concentration in the inner phase of the emulsions.

Emulsions containing in the inner phase compounds creating alkaline or neutral media are frequently employed in membrane extraction. Fig. 10 presents the dependences of the stabilities and viscosities of the emulsions on the pH of the inner aqueous phase. In the region of neutral media, the half-separation time of the aqueous phase and the viscosity of the emulsions are virtually constant. The emulsions with alkaline and acid inner phases are characterised by a lower stability and viscosity. This has been attributed to the protonation of the emulsifier in the acid solutions and its hydrolysis in highly alkaline and acid media, which increases the hydrophilic–lipophilic balance (HLB) of the emulsifier and hence lowers the stability of the extracting emulsions.

Apart from other factors, the properties of the extracting emulsions may be appreciably influenced by the presence of organic substances which affect the polarity of the disperse phase. Figs. 11*a* and 11*b* illustrate the influence of the overall concentration of ethanol and diethyl ether ($C_{\text{alcohol+ether}}$), present in molar proportions of 4:1, on the stability and viscosity of emulsions.[35]

The increase in the overall concentration to ~3.0 M diminishes slightly the half-separation period of the emulsions. At concentrations of 3.5 M, there is a sharp fall in stability. This is associated with the fact that an increase in the content of ethanol and diethyl ether in the emulsion entails a decrease in the amount of the surfactant in the adsorption pair at the interface owing to the increase in the solubility of the surfactant in the phases. As a result, the stability of the emulsions falls sharply. Furthermore, an increase in the concentrations of ethanol and diethyl ether in the organic membrane diminishes the difference between the polarities of the phases so much that it becomes difficult to stabilise the system. Therefore at high concentrations of ethanol and diethyl ether in emulsions, an increase in the amount of the surfactant does not lead to an appreciable increase in the stability of the emulsions.

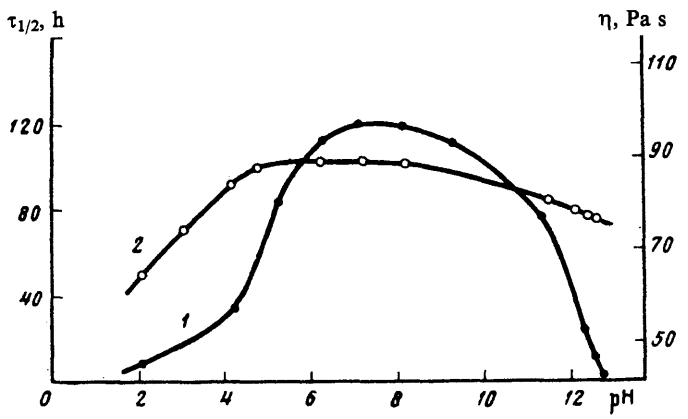


Figure 10. Dependence of the half-separation period of the aqueous phase at 100 °C (curve *1*) and of the viscosity of the emulsions at 25 °C (curve *2*) on the pH of the disperse phase.

It is noteworthy that, with increase in the contents of ethanol and diethyl ether (in the given concentration range), the viscosity of the emulsions decreases linearly (Fig. 11*b*).

Thus, depending on the type and concentration of the surfactants used to stabilise the system and also on the composition of the dispersion medium and the disperse phase, it is possible to obtain emulsions with different properties for each specific application.

III. The nanodispersion in the extracting emulsion

One of the most important phenomena which may occur at the interface in the extracting emulsion is the formation of a secondary emulsion made up of small particles of the order of 10–100 nm. The formation of such an emulsion is promoted by the presence of a surfactant and a cosurfactant in the system[40–42] and by the disequilibrium between the phases of the extracting emulsion, i.e. by the mass transfer of the components of the phases and the solvents through the interface. The formation of such dispersions in the presence of mass transfer has been investigated[25] in two-phase non-emulsion systems.

The spontaneous formation of an emulsion at the interface is possible when chemical reactions occur, including the formation of new surfactants, and also in the presence of aliphatic alcohols.[43–46] However, in the given instance, the authors observed the formation of larger drops—more than 200 nm in diameter.

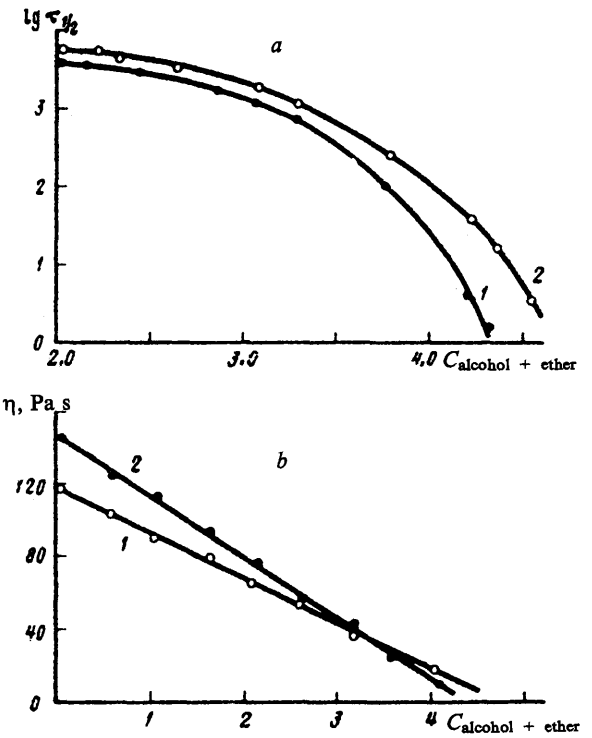


Figure 11. The effect of the overall concentration of ethanol and diethyl ether on the half-separation period of the aqueous phase (*a*) and of the viscosities (*b*) of emulsions stabilised by hostacerin DGO (line *1*) and sorbitan oleate (line *2*) at 25 °C.[35]

The formation of a secondary emulsion has been frequently referred to as microemulsification and the resulting emulsion was called a microemulsion. However, the term microemulsion has come to imply only thermodynamically stable disperse systems comprising particles 10–100 nm in diameter.[47,48] Furthermore, the diffusion coefficients of the microemulsion are much lower than those of the monomers—individual surfactant molecules. As the equilibrium shifts towards a decrease in the concentration of the surfactant monomer, there is no decomposition of the microemulsion drops.[49]

Thus, to solve the problem of classifying a particular emulsion, formed in the presence of diffusion of the substances in the heterogeneous system, as a microemulsion, one requires information about the particle size, the diffusion coefficients, and the thermodynamic stability of the system.

In the case of membrane extraction, the hypothesis of the formation of a microemulsion has been put forward mainly in connection with the transport of water.[50–52] However, the lack of

direct evidence enabled the authors to conclude that the hypothesis of the solubilisation of water by micelles or microemulsions in the course of its transport is invalid and they explain this phenomenon by the transport of water by individual surfactant molecules.[53,54]

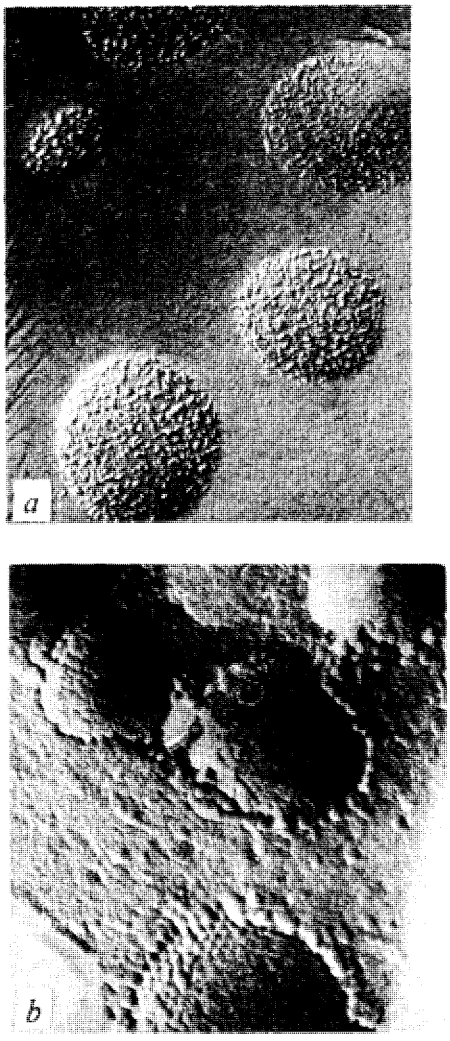


Figure 12. Photomicrographs of an emulsion containing an aqueous solution of ethanol and diethyl ether suspended in liquid paraffin and stabilised with sorbitan oleate: *a*, before extraction (×100 000); *b*, after extraction (×130 000).[57]

Data concerning the size distribution of drops in the emulsion before and after the membrane extraction of cholesterol have been published.[55,56] Photomicrographs of the Pt/C replicas of the cleavage plane of the emulsion, obtained by the freezing-cleavage method,[57] are presented in Fig. 12. The data obtained indicate the absence of a microemulsion from the initial emulsion before extraction and the subsequent formation of drops 17–25 nm in size in the course of the extraction process. The calculated effective diffusion coefficients of the substances forming part of the composition of such drops exceed by 2–3 orders of magnitude the molecular diffusion coefficients. Thus the small drops formed in the course of mass transfer in the extracting emulsion have two features of a microemulsion. The study of the thermodynamic stability of such systems is difficult since extracting emulsions are non-equilibrium systems.

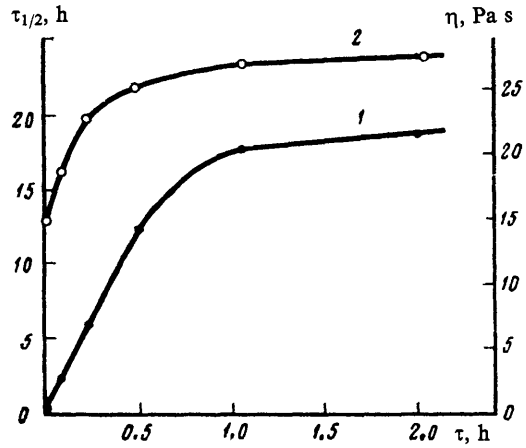


Figure 13. Dependence of the half-separation period at 70 °C (curve *1*) and of the viscosity of the emulsions at 20 °C (curve *2*) on the duration of the extraction of cholesterol.

In our view, for particles with diameters ranging from tens to hundreds of nanometers, one can use the term "nanodispersion", which implies both thermodynamically stable disperse systems (microemulsions) and thermodynamically unstable systems (solubilised micelles). The application of the concept of the "nanodispersion" makes it possible to designate clearly the fraction of small drops formed as a result of emulsification at the interface caused by the mass transfer.

The formation of the nanodispersion drops can influence significantly the kinetics and the quasi-equilibrium in processes occurring in extracting emulsions. The nanodispersion drops are distributed in the bulk of the liquid membrane and are concentrated at the interface, forming a structural-mechanical barrier (Fig. 12). This results in an increase in the stability of the extracting emulsions during extraction (Fig. 13) accompanied by an increase in their viscosity, apparently owing to structure formation in the emulsions and an increase in the cooperative interaction of the drops of the disperse phase. Fig. 14 presents kinetic curves for the separation of such emulsions into layers. The plots are characterised by the presence of two sections: rapid separation of a definite fraction of the inert phase slightly stabilised by the nanodispersion and slow separation of the remainder.

The formation of the nanodispersion is a positive factor when it is necessary to have emulsions which remain stable for a long time, for example, in medicine, in analytical methods, and in the preparation

of protecting creams, since the stability of the emulsions increases appreciably under these conditions. On the other hand, in the organisation of a technological process, where rapid separation of the extracting emulsion into layers is necessary in order to regenerate the extracted substance, the formation of nanodispersion is undesirable, since it entails an additional expenditure on the decomposition of the disperse system. An increase in the viscosity of the extracting emulsions increases the probability of paste formation (the coalescence of the globules), which prevents the normal operation of the technological equipment.

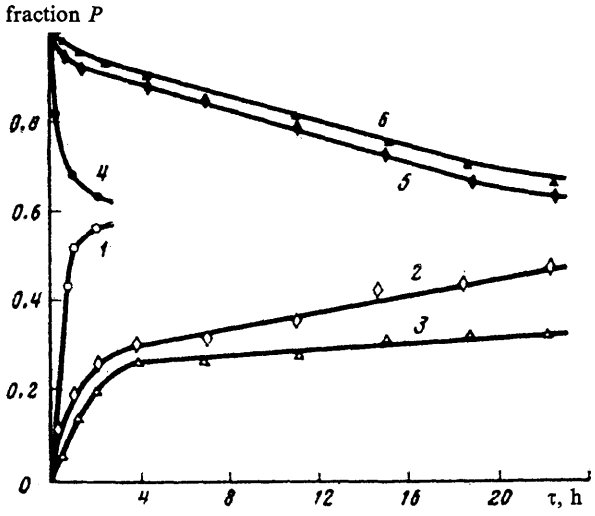


Figure 14. Kinetic curves for the separation of the extracting emulsions into layers (*1*–*3* aqueous phase; *4*–*6* organic phase) at 70 °C as a function of the duration of extraction of cholesterol. Extraction time (h): *1* and *4*, 0 (initial emulsion); *2* and *5*, 0.25; *3* and *6*, 1.

The formation of a nanodispersion is a positive factor also in the extraction of substances with surface-active properties, since the capacity of the extracting emulsions increases as a consequence of the increase in the degree of adsorption of the target component at the interface in the emulsion. The presence of a cosurfactant in the emulsions, for example, of ethanol and diethyl ether in the emulsions for the extraction of cholesterol (see Section V.3), promotes the formation of a nanodispersion as a result of the additional decrease in interfacial tension. By varying the type of cosurfactants and their concentration, the composition of the emulsions for the extraction of cholesterol was selected. For this emulsion composition, the specific interface increases by 55–65% and more,[56] which helps to increase the degree of extraction. The contribution of the adsorption of the target component at the interface to the overall capacity of such emulsions exceeds 50%.

The drops of the nanodispersion and the surfactant micelles can act as transferring agents in the liquid membrane of the extracting emulsions. A number of studies[58–60] have been devoted to the use of nanodispersions in the liquid membrane for the extraction of sodium and potassium picrates and proteins. The dodecyl ether of tetraethylene glycol is used as the surfactant and aliphatic alcohols are used as cosurfactants.

When extracting emulsions containing concentrated aqueous solutions in the inner phase are used, the drops of the nanodispersion can play the role of transferring agents for the solvent, leading to the transmembrane transfer of water to the inner phase (i.e. the swelling of the emulsions), which is an undesirable process. Some of the main factors which determine the rate of transfer of water are the type and concentration of the surfactants in the liquid membrane.[50,54,61] From the standpoint of the intensity of the formation of the nanodispersion, the use of sorbital ethers is undesirable,[54] since a high rate of transfer of water in emulsions stabilised by sorbitan oleate has been noted.[61]

The direction of the transmembrane transfer of water in a multiple emulsion is determined by the sign of the water activity gradients; when the sign is reversed, there is a corresponding change also in the direction of the transport of water.[38] It is noteworthy that the transmembrane transport of water to the inner phase of the extracting emulsions can be effected not only by the drops of the nanodispersion; the transport of water by the molecules of the surfactant and the transferring agent can also make a definite contribution.

In practice, when the extracted component is concentrated in the inner phase, use is made of extracting emulsions whose disperse phase contains concentrated aqueous solutions. For this reason, the swelling of the emulsions is the preferred process.

The emulsion swelling process does not as a rule reach equilibrium, since, as a result of the large difference between the osmotic pressures in the outer and inner aqueous solutions, the swelling of the extracting emulsions may be considerable. This leads to the breakdown of the emulsions in the extractor owing to the rapid coalescence due to the decrease in the degree of adsorption of the surfactant at the interface.

Thus the optimisation of the residence time of the extracting emulsion in the apparatus in order to concentrate the target component in the inner phase to the maximum extent is important.

IV. Mathematical description of the kinetics of the processes in extracting emulsions

An extensive literature has been devoted to the mathematical description of the mass transfer processes in heterophase liquid systems in both diffusional and kinetic regimes (see, for example, Refs. 3 and 62–64).

The description of the mass transfer in a multiple emulsion involves a number of characteristic features associated with the instability of the geometrical shape of the globules of the extracting emulsion and hence of the liquid membrane, the hydrodynamic set up in the latter, and the structure of the emulsion globules. The large specific interfaces in the extracting emulsions are responsible for the appreciable influence of adsorption not only on the extraction equilibrium but also on the rates of the processes in both diffusional and kinetic regimes.

The diffusion in a multiple emulsion is described using approaches based on the consideration of the non-stationary or quasi-stationary transport of the substances.

When quasi-stationary models are used, it is assumed that convective streams of the drops of the disperse phase arise in the liquid membrane owing to the sharp changes in the rate and

direction of the motion of the globules of the extracting emulsion caused by its dispersion in the solution being extracted. It has been noted that the mobility of the drops depends on their number and size and is fairly clearly correlated with the apparent viscosity of the emulsions.[65] Thus it has been suggested that the concentrations of the extracting component in each drop of the inner phase are equal at each instant.

In the given case, the globule of the extracting emulsion can be represented approximately by a hollow sphere (Fig. 15*a*), whose nucleus consists of the re-extracting solution, its composition being averaged over all the drops of the inner phase. Since concentrated emulsions, close to highly concentrated emulsions, are as a rule used for membrane extraction, the curvature of the liquid membrane is frequently neglected and the latter is treated as flat. The curvature factor can be taken into account with the aid of the relation

$$f_{int}/j=2\delta/d\ln[1/(1-2\delta d^{-1})],$$
$$j_{ext}/j=1-2\delta/d,$$

where j, j_{int}, and j_{ext} are the calculated fluxes through the flat membrane and through the inner and outer surfaces of the spherical membrane respectively, d is the diameter of the globule of the extracting emulsion, and δ is the thickness of the liquid membrane.

The coefficients of the mass transfer from the extracted solution, where it is effected by convective diffusion, into the globule of the extracting emulsion can be determined experimentally or estimated with the aid of the correlation equations published by Ivakhno et al.[66]

Molecular diffusion predominates in the drops of the disperse phase. Although this is a slower process, the mass transfer in the re-extracting solution is rarely the rate-limiting stage of the process, since the interface of the inner phase drops is large (10^6-10^8 ml^{-1}) and the re-extraction constants are usually small.

The models of the quasi-stationary transport do not always describe adequately the mass transfer in a multiple emulsion, especially during the final period of such mass transfer, although they may serve as a convenient mathematical approximation, adequate only along individual sections of the kinetic curves.[67]

Another version of the modelling of the extracting emulsion is based on the hypothesis that all the particles of the disperse phase have negligibly small dimensions, are uniformly distributed, and are fixed within a spherical globule with a radius R at specific reaction points (Fig. 15*b*). The target component or its complex with the transferring agent diffuses from the outer boundary of the extracting emulsion globule to its centre and, as soon as the diffusion front reaches the negligibly small drops of the inner phase, they are instantaneously saturated by the target component owing to extraction. Thus, at a distance r_f from the centre of the spherical globule of the extracting emulsion, there is a boundary between zones containing the inner phase saturated and unsaturated with the target component. The mathematical description includes the solution of the equation for the non-stationary diffusion in terms of spherical coordinates:

$$\frac{\partial C}{\partial \tau}=\frac{D}{r}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right); \quad r_f(\tau)\leqslant r\leqslant R.$$

The moving front (of reaction points) model was first proposed and a solution was obtained for one-dimensional diffusion by Marr and co-workers.[68] Later Ho and Li[69] solved numerically the equation with the aid of the perturbation method. The moving front model has been used to describe the transport of substances in multiple emulsions.[19,70–79]

A number of workers have noted the necessity to take into account the resistance to mass transfer in the boundary layer of the outer phase, particularly at the beginning of the process and in the case of a high concentration of the reactants in the inner phase.[80,81] This is apparently valid only in the case of liquid membranes with a low viscosity. For extracting emulsions based on viscous hydrocarbon oils in the absence of slow reactions, the rate-limiting stage of the process is as a rule diffusion in the liquid membrane. Thus in the extraction of lysine in a multiple emulsion (see Section V.1), the resistance to mass transfer in the bulk of the globule exceeds by a factor greater than 500 the resistance in the outer boundary layer.[38]

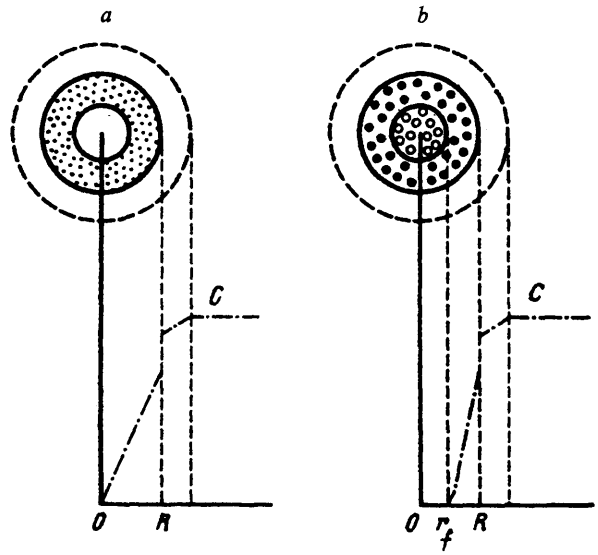


Figure 15. Models of the globules of extracting emulsions: *a*, hollow sphere; *b*, moving front. The dot-dash line represents the profile of the variation of the concentration (C) of the diffusing substance; R = radius of the extracting emulsion globule; r_f = radius of the reaction front in the globule.

The moving front model describes adequately the kinetics of membrane extraction in the case of highly viscous emulsions where the intraglobular convection is suppressed. In practice mainly concentrated emulsions, close to highly concentrated ones, are used, i.e. disperse systems with a high viscosity (see Section II) and therefore in such cases the moving front model is preferred.

The concentrations of the target component $C(t)$ in the solution being extracted have been calculated[38,82] for the membrane extraction of lysine using a model of a moving front with quasi-stationary diffusion (Fig. 16). It was shown that the non-stationary model describes adequately the experimental kinetic curve throughout the process, whereas the quasi-stationary model describes it only in the initial instants.

The mathematical adequacy of the linear functions arises because the complex functions can be fitted by a linear relation along the initial sections of the kinetic curves regardless of the real nature of the mass transfer. The main difference between the non-stationary and stationary models is observed far from the points used for the identification of the model parameters. In the mathematical description of the kinetics of membrane extraction in a multiple emulsion, it is therefore necessary to consider the kinetic curve from the initial instant up to the attainment of quasi-equilibrium in the system.

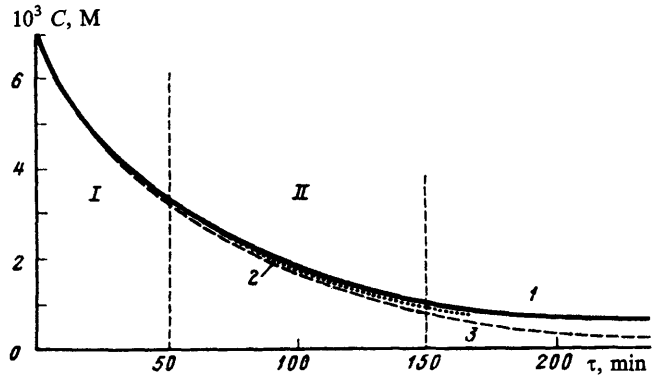


Figure 16. Comparison of the experimental kinetic curve (*1*) with relations calculated on the basis of the moving front (curve *2*) and stationary diffusion-controlled transport (curve *3*) models; *I*, tabulated value of the Fisher statistic f_t = 9.55; calculated Fisher statistics—f_2 = 0.23, f_3 = 0.23; *II*, f_t = 9.12; f_2 = 0.32; f_3 = 1.13; *III*, f_t = 9.12; f_2 = 0.23; f_3 = 13.83.

Information about the nature of the diffusion processes in the liquid membrane can be provided by the "physicochemical probing" method proposed by Frank-Kamenetskii and consisting in the determination of the degree of the power relation between the mass transfer coefficient β and the diffusion coefficient D.[82,83]

The moving front model describes mainly the membrane extraction process in the diffusion regions of the reaction. Special difficulties arise in the transitional region of the reaction, where it is necessary to take into account the influence of the rates of not only diffusion but also of chemical reactions. The analytical solution of the equations for the mathematical description of the kinetics narrows the range of their applicability, since the adoption of certain assumptions is frequently required.

In the given instance, it is best to use a universal, numerical method, which, in contrast to the analytical solutions, makes it possible to obtain an adequate description of the process with constants having a definite physical significance.[84]

In the development of the given model, the following assumptions were made: the diffusion of the components in the liquid membrane is non-stationary; the chemical reactions in the extracting emulsion globule take place at a finite rate and may be both reversible and irreversible; the globule of the extracting emulsion is spherical and is regarded as a pseudohomogeneous medium. For each system component, the following equation is valid:

$$\varepsilon \frac{\partial C_i}{\partial \tau} = D_i\left[\frac{\partial^2 C_i}{\partial r^2} + \frac{2}{r}\frac{\partial C_i}{\partial r}\right] + R_i(\mathrm{C}),$$

where i = 1, ..., N, N is the number of system components, and r = 0, ..., R.

The solution of the above system of equations yields the distribution of the concentrations at any instant and at any point in the system. The system may be solved by employing the method of matrices in combination with the run-through [machine pass] and linearisation methods. In the dimensionless form, we have

$$\hat{\varepsilon}\frac{\partial \bar{C}_i}{\partial T} = \frac{\partial^2 \bar{C}_i}{\partial X^2} + \frac{2}{X}\frac{\partial \bar{C}_i}{\partial X} + R_i(\mathrm{C}),$$

where $X = r/R$, $\bar{C}_i = C_i/C_0$, and $T = (D/R^2)\tau$ for the following initial and boundary conditions:

$$X=1,\ \bar{C}_i=1 \text{ when } T=0,$$
$$d\bar{C}/dX=k\Delta\bar{C} \text{ when } X=1,$$
$$d\bar{C}/dX=0 \text{ when } X=0.$$

The given differential equation is converted into a system of algebraic equations:

$$AC_{i+1}^{k+1} + BC_i^{k+1} + EC_{i-1}^{k+1} = F,$$

where A, B, E, and F are the coefficients of the system of equations which are solved by the run-through method requiring a minimal amount of calculations.

It is noteworthy that, when the specific interface is large and the thickness of the liquid membrane is small, the presence of a surfactant can alter the diffusion coefficient of the target component in the liquid membrane, the partition coefficient between the phases, the reaction rate constant, etc. compared with the corresponding values obtained for a two-phase system of similar composition. The nanodispersion, formed on mass transfer through the interfaces in the multiple emulsion, can also exert a significant influence on the given quantities. This must be taken into account in the determination of the parameters of the mathematical models in independent experiments.

The mathematical description of the kinetics of membrane extraction in a multiple emulsion can include the optimisation of the process either from the standpoint of the attainment of a high degree of concentration (since the molecular diffusion of the target component or of its complex with the transferring agent is appreciably faster than the transmembrane transfer of water leading to the swelling of the emulsion) (see Section III) or from the standpoint of a more effective separation of the substances.[85] Harrington's method, using the so called desirability function as the optimisation parameter, may be used for these purposes.[86]

In the extraction of lysine in a multiple emulsion,[38,82] it has been shown that the maximum efficiency of the lysine concentration process is obtained at time τ_{opt}, which is not the same as the time of attainment of quasi-equilibrium in the system (Fig. 17), since, at times exceeding τ_{opt} in the membrane extraction process, the

concentration of the target component in the inner phase begins to fall because the swelling of the emulsion predominates.

The optimisation of the mass transfer process in extracting emulsions makes it possible to achieve best results in the concentration or extraction of the target component.

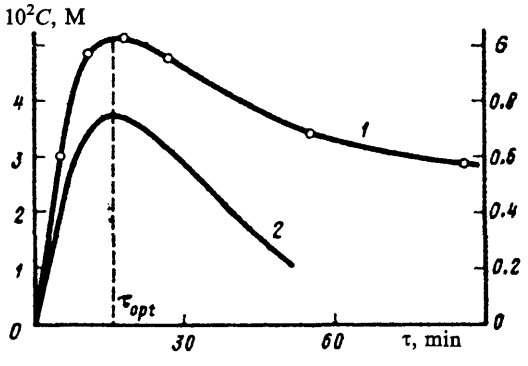


Figure 17. Dependence of the concentration of lysine in the inner phase of the emulsion (curve *1*) and of the generalised desirability function (curve *2*) on the duration of extraction with optimisation of the process.

V. Examples of the practical use of extracting emulsions

1. Application of extracting emulsions in technological processes

Various practical applications of the membrane extraction method in the extraction of numerous metals have been described in the literature: Cu, Ni, Co, Zn, Cr, U, and Hg as well as organic compounds. Detailed reviews of these studies in recent years may be found in the literature.[3,87–89]

Fig. 18 presents as an example a schematic illustration of the experimental-industrial apparatus for the extraction of copper.[5] This process makes it possible to extract more than 99% of the metal. The residual concentration does not exceed 2–7 g m^{-3}, i.e. is 20–30 times lower than in the single-step liquid extraction under comparable conditions. The concentration factor varies from 10[66,90] to 500 and above.[91–94] The emulsifier is usually sorbitan oleate and, more rarely, sorbitan stearate, polyamines, etc. Various hydroxyoximes, β-ketones, and carboxylic or alkylphosphoric acids are used as transferring agents.[66] The inner phase of the emulsions contains 0.5–2.5 M sulphuric acid solution, while the concentration of the sulphuric acid in the extracted solution is not more than 10^{-2} M.

As an example of the extraction of organic substances, one may quote the membrane extraction of aminoacids from enzyme solutions in the microbiological industry.[38,95,96] The extraction of aminoacids proceeds most effectively from weakly concentrated aqueous solutions, especially from dilute liquid waste and wash solutions. Thus the above process can assist in a more complete extraction of aminoacids, in the reduction of their losses, and in the creation of almost waste-free technologies. In one contact step, it is possible to achieve residual concentrations of the order of hundredths of a gram per litre.

The process is of special interest for the extraction of aminoacids sparingly soluble in water, for example tryptophan, since in practice one deals with relatively low concentrations of such aminoacids in aqueous solutions.

A technological scheme has been developed for the recovery of aminoacids (lysine, tryptophan) from their aqueous solutions with the aid of membrane extraction in a multiple emulsion (Fig. 19). The scheme includes the following stages: the preparation of the extracting emulsion, membrane extraction in the multiple emulsion, decomposition of the extracting emulsion after extraction, the evaporation of the solution of the inner phase of the emulsion, and the crystallisation of the aminoacid from the concentrate followed by its washing and drying and the preparation of the commercial product. The ethanol used to wash the aminoacid is periodically redistilled. When the process is carried out in accordance with the above scheme, the aminoacid is freed from other substances present in biological waste: pigments, inorganic salts, etc.[38]

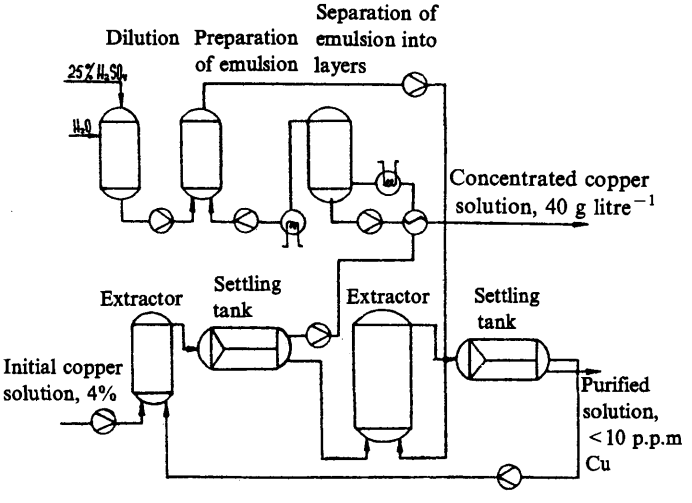


Figure 18. Schematic illustration of the apparatus for the extraction of copper in multiple emulsions.[5]

2. The use of extracting emulsions in analysis

Extracting emulsions can be used for the preliminary concentration of substances for the purpose of their subsequent analysis.[12] These processes may be of special interest in the analysis of the state of the environment, where the test substances are present at very low concentrations unsuitable for traditional analytical methods. Concentration is achieved by allowing a large volume of the test liquid to flow through the cell with the extracting emulsion. Problems of stability are then solved as a rule by selecting the appropriate composition of the extracting emulsion. The situation is more complex as regards the diffusion of water into the extracting emulsion. The swelling of the extracting emulsion impairs the efficiency of the concentration, particularly in extraction from media with low concentrations of the solutes.

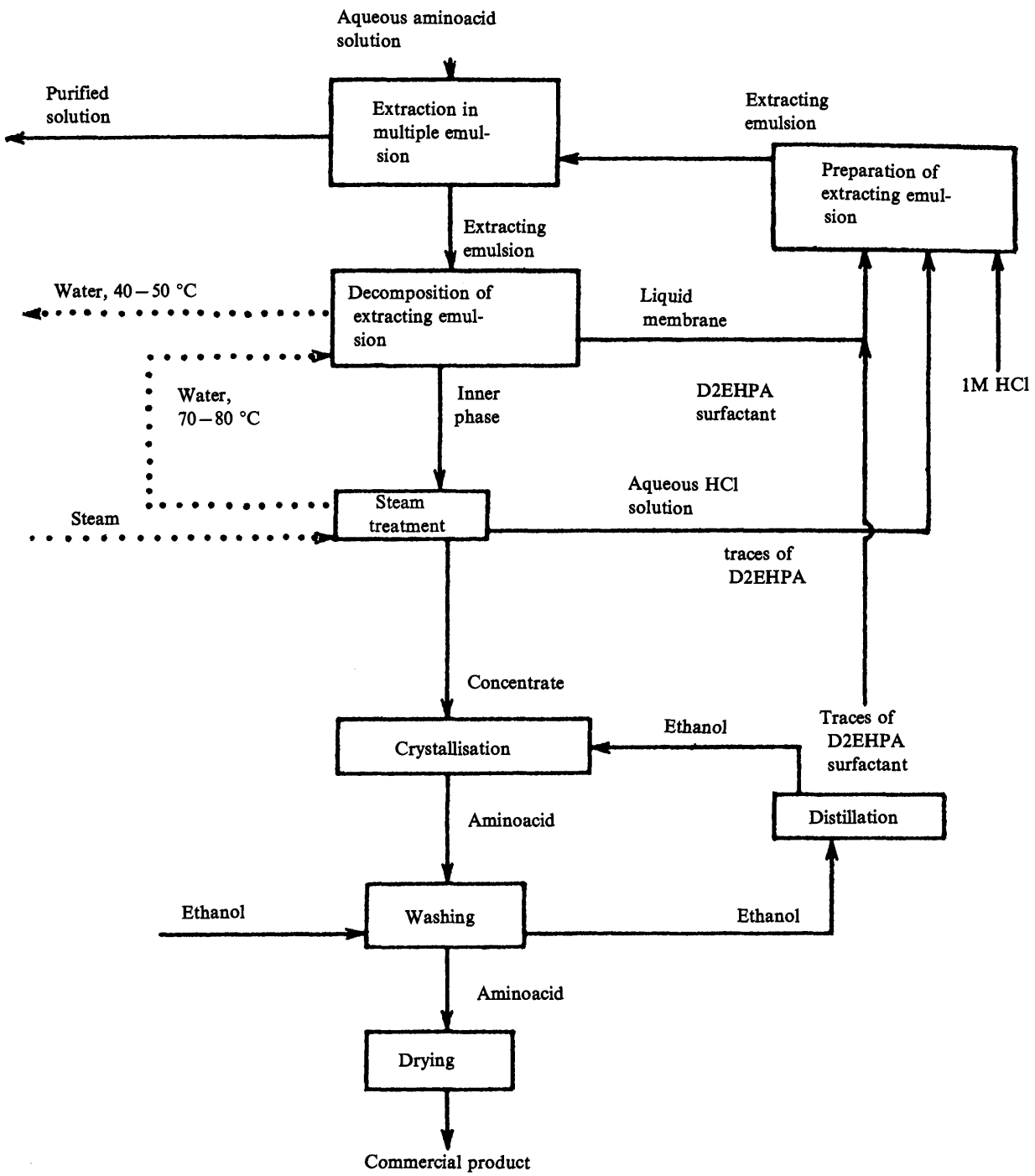


Figure 19. Technological scheme for the isolation of aminoacids (lysine and tryptophan) from their aqueous solutions.

The effect of swelling can be reduced by optimising the contact time on the basis of kinetic relations, as stated above, and also by employing polymeric surfactants. Examples of the use of extracting emulsions in analysis can be found in the literature[12,97] and the use of the extraction of mercury,[98] lead, and cadmium[12] for analytical purposes has been described.

3. The use of extracting emulsions for the detoxification of biological media

Extracting emulsions can find applications in the detoxification of biological media—for the extraction of poisons of exogenic and endogenic origin.[8–10,21,99,100] When inert liquids are used as the

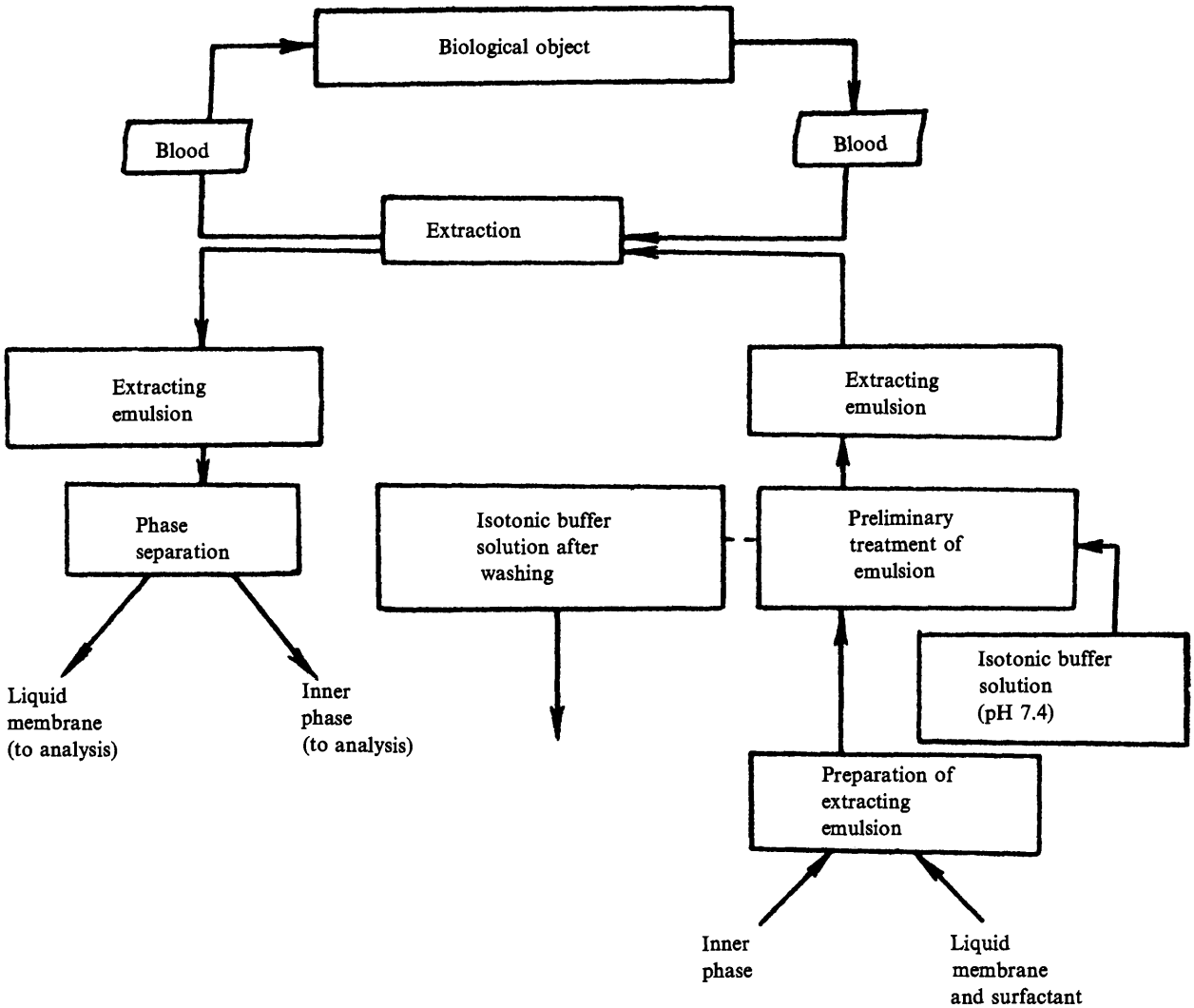


Figure 20. Schematic illustration of membrane extraction from blood using extracting emulsions.

dispersion medium (liquid membrane), it is possible to carry out extraction directly from the blood.

It is noteworthy that many components of biological liquids possess surface-active properties and the contribution of the adsorption component to the capacity of the emulsion can therefore be fairly large; for example it exceeds 50% in the extraction of cholesterol. From this standpoint, membrane extraction in a multiple emulsion has an additional advantage, since extracting emulsions are characterised by a large specific interface (10^6-10^8 m^{-1}). There exist various procedures for increasing the interface, for example as a result of the formation of a nanodispersion, which increases the capacity of the extracting emulsions in the extraction of substances with surface-active properties.

Emulsions containing ethanol and diethyl ether have been developed for the extraction of lipids, including cholesterol and its ethers.[21,35,99] Such emulsions extract cholesterol and lipids into the liquid membrane and sorb them at the interface. In emulsions of this kind, the mass transfer of ethanol and diethyl ether across the interface entails the formation of a nanodispersion. The conditions under which the formation of a nanodispersion is a maximum were selected by varying the concentrations of ethanol and diethyl ether as well as their ratio. The specific interface then increased by 55–65% which resulted in an increase of the degree of extraction of cholesterol owing to adsorption on the interface in the extracting emulsion.[56]

Emulsions containing saponins have been developed for the extraction of non-etherified cholesterol from biological liquids in order to reduce its content in the organism under the conditions of atherosclerosis.[9,21] A water-insoluble equimolecular complex of cholesterol and the saponin is formed in the inner phase of such emulsions. It is almost totally insoluble in water and precipitates. Owing to the haemolytic activity of saponins, preliminary washing of the extracting emulsions with an isotonic buffer solution before extraction from the blood is necessary. After such treatment, the emulsions have no toxic activity since the liquid membrane reliably isolates the saponins present in the disperse phase.

Fig. 2 illustrates schematically the membrane extraction from the blood using extracting emulsions. Blood circulates between the organism and the apparatus in a manner similar to the haemodialysis or haemosorption processes.[10,101] After extraction, the emulsion can be separated into phases in order to determine the concentrations of the substances extracted from blood.

4. Application of extracting emulsions as protection-prophylactic creams

The method of membrane extraction in a multiple emulsion can serve as a basis for the creation of prophylactic creams to protect the surface of the skin against various toxic substances.[11,27,102] Such creams are in many cases more effective than the traditional ones. The difference between them and the existing ointments consists in the fact that the creams extract the sensitisers from the surface of the skin and fix them within their bulk. Traces of the sensitiser on the surface of the skin can also be absorbed by the cream which prevents their accidental incidence on the unprotected sections of the skin.

A process analogous to membrane extraction in a multiple emulsion then takes place. Here the solution of the sensitiser or the upper layer of the skin constitutes the external phase being extracted. Irreversible or reversible reactions involving the binding of the toxic substance may occur in the inner phase. In the latter case, it is necessary to endeavour to make sure that the equilibrium constant of the reversible reaction is as large as possible in order to maintain a minimal concentration of the extractant-transferring agent in the liquid membrane. A fairly wide range of reagents can be used in the inner phase of the emulsion cream, since they are separated from the skin by an inert liquid membrane and do not therefore come into direct contact with the skin.

It is noteworthy that the cream can be not only protecting but also therapeutic and prophylactic, since it can be deposited on the skin already containing a sensitiser, which is extracted from the skin into the emulsion cream.

An important condition for the efficacy of the cream is the maximum extraction of the toxic substance from the organic membrane in contact with the skin into the inner aqueous phase or its fixation in the bulk of the liquid membrane. This is achieved by the strong binding of the sensitiser in a weakly dissociating complex in the inner phase and also by employing low concentrations of the extractant-transferring agent in the organic membrane. Creams whose action is based on this principle prevent the penetration into the skin of not only sensitisers (i.e. substances including dermatitis) but also of other harmful substances (i.e. substances leading to damage of the organism on penetration into the latter through the skin), which is of increasing interest owing to the impairment of the ecological situation.

An important characteristic of the protecting cream is its stability. In this case the emulsions obtained must be even more stable than those employed in technological processes and even in extraction from blood, since in the application of the cream the emulsion is present as a thin layer on the surface of the skin and under such conditions the role of heterocoagulation processes becomes more marked.

A similar approach to the creation of extracting protecting creams served as a basis for the development of a number of specific compositions of prophylactic creams designed against harmful organic and inorganic substances, in the first place sensitisers: heavy metals, chromium, antibiotics, aldehydes, ketones, etc.[11,27,102]

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Translated from *Uspekhi Khimii* **60** 2448–2462 (1991) U.D.C. 628.3:546.27

The current state of the problem of the elimination of boron from waste waters

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ABSTRACT. The advances in the extraction of boron-containing substances from waste waters and natural brines are examined and surveyed. The current prospects for the solution of the problem of creating an ecologically clean technology for the purification of industrial liquid waste with recovery of valuable components are described. The results of studies on the problem, obtained under experimental and industrial conditions, are discussed.

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I. Introduction

The disturbance of ecological equilibria in the biosphere has raised at the present time a series of fairly acute questions associated with the protection of the environment, which necessitates more stringent requirements as regards the protection of water, soil, and the atmosphere. The requirements have become more stringent both as regards the purity of the liquid waste discarded into water-containing areas and their amount.

The industrial waters, sludge, and mother liquors in modern factories processing boron-containing raw material contain an appreciable quantity of boron. This fact poses a serious problem in many industries concerning the extraction and utilisation of boron-containing products.

The use of modern methods for the extraction of boron from waste waters makes it possible to improve the technological processes and to solve problems of the recovery of boron and of the preservation of natural resources.

In nature, boron is encountered in the form of more than 80 independent materials. In the dissolved state in water, boron is present as salts of boric and polyboric acids and also as free orthoboric acid.

The data concerning the toxicity of boron compounds are fairly contradictory and the toxicities of many boron-containing substances have been hardly investigated. Soluble boron compounds are classified as polytropic poisons, prolonged action of which can induce chronic intoxification and diseases of the nervous system.

The limiting permissible concentrations (LPC) in water-containing areas used in fish farming are 0.1 mg litre^{-1} in terms of B_2O_3 and 0.017 mg litre^{-1} in terms of boron and in sanitary-domestic water it is 0.5 mg litre^{-1} in terms of boron. A norm for the LPC of boron in drinking water has not been laid down, but a concentration of 1 mg litre^{-1} has been recommended in the USA.

Thus the current interest in the problem of the extraction of boron from waste waters is associated, among others, with economic problems and the protection of human health.

The methods for the processing of natural types of boron-containing raw material involve a series of a wide variety of technologies for the extraction of boron from aqueous solutions, such as precipitation of boron in the form of sparingly soluble compounds, coprecipitation, extraction with organic solvents, sorption on selective sorbents, separation by electro-ion-exchanger membranes, etc. These methods are at present being developed.

II. Reagent methods for the extraction of boron from waste waters

The reagent methods for the purification of waste waters are based on the precipitation of boron in the form of sparingly soluble compounds and are fairly effective in the case of high concentrations of boron-containing substances in the treated liquid waste.

Treatment of the waste waters obtained in the processing of boron-containing raw material with lime water makes it possible to reduce appreciably and stabilise the concentration of boron. In this case it is possible to reduce the concentration of boron trioxide from 2.5–2.7 to 0.20–0.25%. When lime water is added, calcium borate crystallises from boron-containing solutions. The composition of the borate $x\mathrm{CaO}.y\mathrm{B_2O_3}.z\mathrm{H_2O}$ depends on the precipitation conditions. Thus borates with the ratios $x:y:z$ = 2:3:13 and 1:1:6 are formed at 25 °C, borates with the ratios 2:3:9 and 1:1:4 are formed at 80 °C,[1–3] while at 95 °C borates with the ratios 2:1:1, 2:3:7, and 1:3:5, and, after the introduction of a seed, also 4:5:7, 2:3:5, and 2:7:8 were isolated.[4] From the standpoint of subsequent use, calcium diborate hexahydrate $\mathrm{CaO}.\mathrm{B_2O_3}.6\mathrm{H_2O}$ (1:1:6) is of greatest interest. The borate is preciptiated via the reaction:

$$2\mathrm{H_3BO_3} + \mathrm{Ca(OH)_2} + \mathrm{aq} \rightarrow \mathrm{CaO}\cdot\mathrm{B_2O_3}\cdot n\mathrm{H_2O} + \mathrm{aq}.$$

It is essential to note that the precipitation process is influenced significantly by the temperature, the amount of lime water, and the pH.[5,6] In order to obtain the borate with the 1:1:6 composition, it is essential that the temperature should be not higher than 25–30 °C. The optimum temperature is 22–27 °C. In order to obtain a borate with a stable composition and involving the maximum extraction of boron from the solution, the pH of the reaction medium should be in the range 11.4 ± 0.20.[3] Furthermore, it has been found that the range of grain sizes and the chemical composition of calcium diborate depend on the content of impurities in the solution being purified and in the lime water. The purification of the lime water should ensure the content of the inadequately slaked component not greater than 0.2% and 0.015% Fe_2O_3 for an overall 10% content of active CaO.

In the course of the precipitation of the 1:1:6 borate, a small amount of amorphous variable-compositon calcium borate is produced. The amount of B_2O_3 in the amorphous component of the precipitate is relatively constant and the B_2O_3:CaO weight ratio is in the range 0.85–1.05. In the crystalline product, this ratio is always close to the theoretical value of 1.24.[6] The yield of the boron obtained in the amorphous phase is up to 10–15% of its content in the solution.

In the course of the preparation of commercial calcium diborate, the crystal growth stage is rate-limiting, the maximum size of the crystals not exceeding as a rule 50 μm. The concentration of boron oxide in the liquid phase diminishes from 1.5 to 0.15–0.17% after mixing the reactants for 1–3 min at 25 °C, i.e. it is reduced virtually to the equilibrium value.

It is notable that, in the purification of waste waters with a high B_2O_3 content, the precipitate contains, other conditions being equal, a greater amount of the crystalline phase. A similar effect has been obtained also in the presence of a definite amount of a seed in the reactor.

A reactor design ensuring the separation of finely disperse impurities from the crystalline phase during the synthesis of calcium diborate has been developed.[4] The yield of the commercial borate is in this case 96.8 ± 0.5%, the calcium borate being homogeneous in its chemical composition and in terms of its grain size.

The presence of boron-containing kerosene and polyacrylamide (PAA) hydrocarbons in waste waters does not affect the efficiency of the extraction of boric acid.[7] However, the crystals of calcium borate preciptiated from a solution containing these organic impurities are acicular in shape and a tendency towards the agglomeration of the crystals and loss of the regular form corresponding to the internal structure of the crystal is observed. This can be accounted for by the fact that the impurities influence the crystallisation process through a change in the structure of the solution and through adsorption on the faces of the crystals, inducing a change in the rate of their growth.

The coprecipitation of calcium and copper borates makes it possible to isolate up to 93–95% of boron from a solution containing 0.2–0.4% B_2O_3. After preciptiation, the solution contains 0.03% B_2O_3 and the precipitate contains 22.4% B_2O_3, 18.3% CuO, 36.3% CaO, and 23.1% H_2O. Somewhat poorer results are obtained in the coprecipitation of calcium borate with other microimpurities—manganese and cobalt.[8]

A decrease in the content of boric acid in the water being purified can be achieved by isolating at 95 °C dicalcium borate $2CaO.B_2O_3.H_2O$, the solubility of which is low. For this purpose, waste waters containing up to 0.25% B_2O_3 are treated with lime water, the measured amount of the latter, recalculated in terms of CaO, amounting to 130–170% of the stoichiometric amount[9] according to the reaction equation:

$$2Ca(OH)_2+2H_3BO_3=2CaO\cdot B_2O_3\cdot H_2O+4H_2O.$$

The residual content of B_2O_3 in the waste water is 0.03–0.04%.

It is essential to note that the extraction of boron from waste water by precipitating sparingly soluble calcium borate is widely used on the industrial scale.

The mother liquors in the boric acid industry, containing 1.3–1.6% B_2O_3, 21–23% $MgSO_4$, and 0.2–0.6% H_2SO_4, are also treated with magnesium oxide.[10] In this case, magnesium borates having the composition $xB_2O_3.yMgO.zH_2O$ are precipitated. At 95 °C, for a MgO norm amounting to 4.5 mol per mole of B_2O_3 and for a stirring time of 2 h, more than 90% of the boron is precipitated and the filtrate contains 0.26% B_2O_3 after separating the precipitate. Treatment of the mother liquors with ammonia and carbon dioxide or ammonium carbonate makes it possible to obtain ammonium borosulphate and magnesia:

$$4H_3BO_3+(NH_4)_2CO_3=(NH_4)_2B_4O_7+CO_2+6H_2O,$$

$$4MgSO_4+4(NH_4)_2CO_3+10H_2O=$$

$$=3MgCO_3Mg(OH)_2\cdot 9H_2O+4(NH_4)_2SO_4+CO_2.$$

The precipitated magnesium carbonate is separated from the solution and the latter is neutralised with H_2SO_4 and dried, which affords ammonium borosulphate containing 6% B_2O_3, 70% $(NH_4)_2SO_4$, and 20% $MgSO_4$.

It is essential to note that the magnesium and manganese borate precipitates can be used to prepare boric acid. Calcium borate is employed as a substitute for boric acid in many chemical processes. It has also been suggested that the precipitate, formed when boron-containing waste waters having the composition 7% B, 15% B_4C, 60% B_2O_3, and 18% of carbon black are allowed to stand, be subjected to a high-temperature treatment in order to obtain boron carbide.[7]

Waste waters containing 40–50 g $litre^{-1}$ of boric acid can be used in the manufacture of boron dyes.[11] For this purpose, they are treated with sodium carbonate in an amount necessary for the formation of the tetraborate:

$$4H_3BO_3+Na_2CO_3=Na_2B_4O_7+CO_2+6H_2O,$$

and for the formation of a product in which the ratio $Na_2CO_3:Na_2B_4O_7.10H_2O$ does not exceed 10.

In aqueous solutions, boric acid forms complexes with tartaric and trihydroxyglutaric acids. Thus boron can be isolated from very dilute solutions by precipitation in the form of salts with these acids.[12]

The methods for the extraction of boron from waste waters by precipitating sparingly soluble borates are fairly simple to apply and are widely used on the industrial scale. However, the use of these methods is justified in weakly mineralised systems in which the concentration of B_2O_3 is at least 0.3–0.5%. The presence of alkali metal chlorides and sulphates in the solution lowers the qualitative parameters of the process. One of the deficiencies of the method is the impossibility of attaining a high degree of elimination of boric acid from the liquid waste.

III. Extraction of boron from aqueous solutions on inorganic sorbents

On precipitation of certain metal hydroxides from aqueous solutions, boron ions are entrained to some extent. Coprecipitation is explained by the formation of the corresponding metal borates.

The limits of the practical applicability of the given method are between 1 and 3 g litre^{-1} in terms of B_2O_3. The upper limit is set by the duration of the protecting effect of the sorbent and the lower by the formation of eluates dilute in boron on regeneration of the sorbent, which hinders the extraction of boron from them on further treatment.

The sorbents employed are the alkali metal hydroxides $Al(OH)_3$, $Fe(OH)_3$, $Sn(OH)_4$, $Ti(OH)_4$, $Mn(OH)_4$, $Ni(OH)_2$, $Mg(OH)_2$, and $Zn(OH)_2$.[13–16] The degree of coprecipitation of boron with these hydroxides increases with enhancement of their basic properties. Thus, at a boron concentration of 0.31 g litre^{-1}, the amounts of boron coprecipitated are 90% by $Ni(OH)_2$, 60% by $Mg(OH)_2$, $Al(OH)_3$, and $Fe(OH)_3$, and 25% by $Zn(OH)_2$. This suggested the following exchange mechanism: borate ions$\rightleftarrows OH^-$ ions of the hydroxides. However, $Zn(OH)_2$ sorbs much less boron than had been suggested and $Cu(OH)_2$ does not sorb it at all. This can be accounted for by the occurrence, together with ion exchange, of a chemical interaction involving the formation of borates, which is confirmed by studying the influence of the concentration of borate ions on the sorption of boric acid. When the boron concentration in solution was altered from 0.31 to 31 g litre^{-1}, the amount of boron coprecipitated changed from 0.037 to 0.806 g litre^{-1} for $Zr(OH)_4$ and from 0.099 to 3.534 g litre^{-1} for $Ni(OH)_2$. The IR spectra of the hydroxides precipitated from boric acid solutions at different concentrations permit the conclusion that the interaction of a nickel salt with boric acid involves the formation of nickel borate, which is coprecipitated together with $Ni(OH)_2$, the structure of the borate resembling that of ulexite $CaNa[B_5O_6(OH)_6].5H_2O$, while in the case of the hydroxides $Al(OH)_3$ and $Zr(OH)_4$ ion exchange takes place.

Data have been published[5,6] concerning the preparation of borate concentrates from petroleum waters (0.25–0.46 g litre^{-1} in terms of B_2O_3) with the aid of $Mg(OH)_2$, MgO, and heat-treated dolomite ($MgCO_3$ + $CaCO_3$). When boron was extracted with magnesium hydroxide, the sorption capacity was 0.3% in terms of B_2O_3, which is of virtually no practical interest. Using magnesium oxide and heat-treated dolomite as sorbents under static conditions with a sorbent : solution ratio of 1 : 100 and for 8 h contact, it is possible to extract 50–70% of B_2O_3, the degree of extraction being independent of the degree of mineralisation of the brines. Under dynamic conditions, it is possible to achieve almost complete extraction of boron (up to a residual content of 20 mg litre^{-1} of B_2O_3). However, the cost of magnesium oxide is fairly high and it is therefore desirable to use heat-treated dolomite. The process parameters have been established:[17] ratio of solid and liquid phases S : L = 1 : 100, temperature 30–45 °C, pH 9. Under these conditions, the degree of elimination of boron is 90%.

A method has been developed for the elimination of boron from highly mineralised natural solutions,[18] involving their treatment with chromium hydroxide in an amount of 2–12 g per 100 ml of the solution at pH 8.5. The sorbent is supplied in two lots in equal portions, after which the solution is stirred for 30 min. For a settling time of the suspension of 30 min, the efficiency of the extraction of boron reaches 65%. The nature of the anion in the initial chromium salt and its concentration have almost no effect on the extraction of boron in the pH range 6.8–12.[19]

A sorbent consisting of granulated magnesium-nickel hydroxide (MNH) has been synthesised.[20] Its comparison with zirconium hydroxide shows that under static conditions the rates of equilibration on the MNH sorbent are almost twice as high but the capacity of the zirconium hydroxide is greater. The experiments carried out under dynamic conditions shows that, in the sorption of boron from concentrated brines, preference should be given to zirconium hydroxide.

A technology has been developed for the extraction of boron by a sorbent based on zirconium and magnesium-nickel hydroxides, involving a multicycle procedure, in which the solutions are brought into contact with the sorbent, the sorbent is regenerated with an alkaline solution, and boron is isolated from the eluates by means of compounds of univalent or divalent metals with formation of sparingly soluble borates and the mother liquor.[21] The mother liquor from the preceding cycle is brought into contact with the sorbent before its regeneration in the next cycle.

Zirconium hydroxide, obtained directly in the boron-containing solutions, was proposed as the sorbent.[23] This hydroxide gives rise to a fairly high degree of precipitation of boron. Thus, after a fourfold precipitation, the degree of extraction of boron from a solution containing about 1 g litre^{-1} of B_2O_3 in 98.5%. The boron is extracted from the residue by being converted into borax with sodium hydroxide and by leaching the deposit with warm water. The sorption properties of granulated zirconium hydroxide (GZH) have also been investigated[23] by freezing and by the gel-sol methods. Boron was extracted from waste waters with an overall degree of mineralisation of 4.2 g litre^{-1} and a high concentration of boric acid at pH 5. The capacities of the sorbents obtained by the above procedures are 44.9 and 38.2 mg g^{-1} respectively.

Stable polynuclear derivatives of zirconium nitrate exhibit an enhanced ability to react with borates.[24] H_3BO_3 is sorbed under static conditions, the equilibration time being 30 min. The ratio of the solid and liquid phases is 1 : 30. For a H_3BO_3 content in the liquid waste between 0.5 and 2.5 g litre^{-1}, the percentage extraction of the acid is independent of its concentration. The greatest sorption effect is observed at pH 9 and reaches 90% in one cycle. It has been established that heating assists sorption.

Studies on the sorption of boron by granulated metal hydroxides from boric acid solutions and natural magnesium chloride brines under static conditions at boron concentrations between 0.05 and 0.25% in terms of B_2O_3 have shown that[25] the optimum sorption conditions are attained at pH 3.5–4.0 and temperatures in the range 35–40 °C. In terms of their equilibrium sorption capacity, the metal hydroxides can be arranged in the following sequence: Zr^{4+} (in NaCl solution) > Al^{3+} > Zr^{4+} > Fe^{3+}.

Zirconium hydroxide has the maximum capacity and this sorbent has been tested also under dynamic conditions. The maximum capacity is attained at a flow rate of the solution being purified of 0.2–0.5 ml min^{-1}, at 25–30 °C, and at pH 3.5–4.0.

According to Nikolaev's study,[26] the efficiency of the capture of boron from water by different hydroxides at pH 8.2–8.3 is characterised by the following sequence:

$$ZrO_2 > La_2O_3 > SiO_2 > TiO_2 > Fe_2O_3,\ Al_2O_3.$$

The presence of certain ions has a fairly appreciable influence on the extraction of boron by metal hydroxides. For example, the presence of sodium and lithium chlorides promotes an increase in the capacity of zinc, nickel, iron, aluminium, and tin hydroxides with respect to borate ions. This can be accounted for[27] by the influence

of the above electrolytes on the structure of the boron ions in solution. At the same time, the absorption borate ions diminishes in the presence of anions in the following sequence: $NO_3^- > Cl^- > SO_4^{2-}$. With increase in the boron concentration in the initial solution, the influence of anions diminishes appreciably.[28–32]

The extraction of boron by aluminium and iron hydroxides has been investigated in fair detail.[33] The concentration and nature of the hydroxides, the contact time, and the pH of the reaction medium were adopted as the principal factors governing the process. Aluminium hydroxide has been obtained by adding aluminium sulphate to a sample of the waste water and iron hydroxide was prepared by adding iron chloride. The maximum boron extraction effect is observed at pH 7.0–9.0 and is attained at the instant of the formation of the hydroxides, i.e. the separation of the suspension in order to extract the spent hydroxide is best performed in a contact clarifier or on a contact filter. With increase in the hydroxide concentration, the coprecipitation effect also increases, but such relations are not highly linear and the copreciptiation effect increases up to a certain limit.

The removal of boron from natural brines[34] is most effective when the Al_2O_3 sorbent is used in an amount corresponding to 0.5–20% relative to the mass of the brine. The suspension containing the sorbent is heated to 60–80 °C and stirred at this temperature for 30–60 min. The residual boron content in the brine is less than 50 mg litre^{-1} and the degree of extraction reaches 87–97%. The sorbent is separated from the solution by allowing it to settle, after which the boron is desorbed with a 10% mannitol solution. Solutions of glycerol, sorbitol, and a number of other substances can be used as desorbing agents. A procedure for the elimination of boron compounds from magnesium chloride brines with activated alumina or activated bauxite has been proposed.[55] When the ratio of the Al_2O_3 content to the mass of the brine is 1:4, the degree of purification is 91%.

Studies[36] on the sorption properties of the ash formed after the combustion of coal are of interest. Since the ash contains sodium, potassium, calcium, magnesium, aluminium, and iron ions, the hydroxides of the above metals are formed at elevated pH and bind the borate ions.

Thus we may note that the most effective inorganic sorbent is zirconium hydroxide, which, however, suffers from a serious deficency—low mechanical strength, which is an obstacle to its employment in industry. Aluminium hydroxide also exhibits a high efficiency in extracting boron.

The method involving the coprecipitation of boron with metal hydroxides makes it possible to attain high degrees of elimination of boron from waste water, but it is less critical as regards the content of dissolved alkali metal salts. However, one must add that the above method is technologically complex: the rates of filtration are low and a constant regeneration of the carrier deposit is required, which involves the consumption of acids and alkalies. The deposits as a rule contain boron at a low concentration, their composition is not constant, and they require additional processing. The process has not been applied widely on an industrial scale.

IV. Sorption of borate ions on anion-exchange resins

The methods for the extraction of boron with the aid of ion-exchange materials are applicable mainly to weakly mineralised aqueous solutions with a fairly low content of B_2O_3 (up to 2–3 g litre^{-1}).[9] The need to apply ion-exchange methods arises in the extensive purification of waste waters and also in the extraction of boron for analytical and chromatographic purposes and for the separation of isotopes.

The studies on the sorption properties[37,38] of anion-exchange resins of neutral and weakly basic types in relation to the extraction of boron from waste waters have shown that weakly basic anion-exchangers of the polycondensation type, containing hydroxy-groups as well as primary, secondary, and tertiary amino-groups, are more selective with respect to boron. Up to 80% of boron is extracted from pure solutions of boric acid containing 0.28% B_2O_3, but the attainment of this degree of purification requires a long contact time.

The presence of metal salts in the solutions lowers the degree of extraction of boron. This fact as well as the low exchange capacity of the sorbents suggest that mixed and highly basic sorbents may be more promising, but these do not exhibit selectivity with respect to borate ions.

There are insufficient literature data and recommendations concerning the application of USSR-produced ion exchangers. For example, the AV-17 anion-exchange resin has been suggested for the isolation of boric acid from heat exchangers, aqueous salt solutions, and waste waters.[39–42] The AV-17 anion-exchange resin in the OH-form has been used for the extraction of boron from heat exchangers of the power reactor of an atomic power station.[43] The degree of purification reached 99.5% and the dynamic capacity of the resin was 100–120 g litre^{-1}. It has been established[44] that, with increase in the concentration of boric acid by a factor of 10, the degree of sorption of boron increases by a factor of 2–4, while a temperature rise from 18 to 50 °C lowers the degree of extraction of boron, especially for dilute solutions. The resin is regenerated with a potassium hydroxide solution and the eluate is treated in an electrodialysis cell with cation-exchange and dipolar membranes, which results in the extraction of 98% of borate ions.

The sorption capacity of the AV-29 anion-exchange resin with respect to boron is 507 mg litre^{-1} when the resin comes into contact with a solution whose pH is 6.[45] Compared with the AV-17 anion-exchange resin the efficiency of the AV-29 resin is higher by a factor of 1.7.

According to the data of Samberskii, et al.,[46] the capacity with respect to boron increases in the following sequence of anion-exchange resins: AV-17 × 8, AV-29, AN-2F, EDE-10P, AN-31, i.e. with increase in the content of hydroxy-groups in the resin. In the presence of salts, the capacity of the sorbents falls sharply (especially that of the AV-17 anion-exchange resin) owing to the high ion-exchange affinity for the Cl^- and SO_4^{2-} ions. The influence of cations on the sorption of boron diminishes in the sequence $K^+ > Na^+ > Zn^{2+} > Mg^{2+}$, which is apparently caused by the different capacities of the cations for hydration. Thus the presence of even small amounts of NaCl and $ZnCl_2$ diminishes sharply the capacity of the resins with respect to boron.

The complex-forming sorbents ANB-11 and ANB-11m are highly effective in the extraction of boron from mineralised waters.[47,48] The static capacity of the above anion exchangers is 80 mg litre^{-1} and the optimum pH at which the boron-containing waters and the sorbents are brought into contact is 7. The presence of salts hardly affects the sorption process. Sorbents distinguished by a satisfactory kinetic parameter, which are readily regenerated with HCl, have undergone industrial tests.[49] In order to increase the degree of purification, the sorption is carried out on anion-exchange resins subjected to preliminary treatment with methanol.

Studies directed towards the search for ion-exchange materials selective with respect to borate ions are of practical interest.

In order to increase the sorption capacity with respect to boron, anion exchangers of the aminoepoxide type have been modified chemically which increased the concentration of hydroxy-groups.[50] Anion exchangers of the aminoepoxide type[51] and the epoxyamino-type, B-8, B-257,[52] and SB-1[53] have been obtained in this way. The experimental data for the extraction of boron from natural concentrated magnesium chloride brines, obtained under static conditions, showed that B_2O_3 concentrations in excess of 1 g litre^{-1} and a solution temperature of 40 °C are optimum for the sorption of boron. The equilibrium capacity of ion exchangers under these conditions is 110 mg h^{-1}. However, at a B_2O_3 concentration below 1 g litre^{-1}, the sorbent capacity falls sharply and the ion-exchange purification becomes inefficient.

For example, the SB-1 ion-exchange resin, containing in its structure hydroxy- and amino-groups which are selective with respect to boron, can be used for the effective extraction of boron from solutions at a concentration of 2–3 g litre^{-1} of B_2O_3, but, owing to the instability of the borate ions, boron cannot be extracted as far as the limiting permissible concentrations (LPC). The study of the pH dependence of the sorbent capacity with respect to boron showed that the maximum occurs at pH 7.4–8.8 and the total dynamic exchange capacity of the resin is 160 mg of B_2O_3 per gram of the resin. The degree of extraction of boron is 82% for an initial B_2O_3 content of 1.2–3.22 g litre^{-1}.[54] When the SB-1 ion-exchange resin is compared with the zirconium-hydroxide based inorganic sorbent GZH, whose properties were discussed in the previous Section, it is noteworthy that the latter sorbent permits a more extensive purification of the solutions, while the SB-1 sorbent has a higher mechanical strength by an order of magnitude.[55] The equilibrium pH depends on the content of salts in the solution. In the presence of a high salt content, the sorption pH differs from the initial value by more than 1–2 units, while in the presence of a low salt content the pH is 8.5–9.5, which is attributed to the "buffer" capacity of the impurities.

Resins with active catechol groups exhibit a fairly high capacity with respect to borate ions. On this basis, the ANPK-31 sorbent has been synthesised. It consists of the AP-31 anion-exchange resin modified with catechol.[56] At pH 7.5, this resin extracts 60 mg of boron per gram of the resin.

A technology has been developed for the preparation of a sorbent.[57] It is based on the use of chitosan (a chitin hydrolysis product), which is a glucosamine polysaccharide. Fe_3O_4 grains coated by the chitosan solution bind boron into complexes with chitosan. The efficiency of the purification is 70%. This method of purification has been validated by industrial tests.

The interaction of boric acid with polyhydroxy-compounds, which include aliphatic and cyclic diols and triols and polyhydric alcohols and phenols, has been fairly thoroughly investigated hitherto. One of the sorbents exhibiting a high selectivity is poly(vinylene glycol) (PVG),[58] which is a linear insoluble powdered polymer. Its capacity is 91.4 mg of B_2O_3 per gram of the sorbent, an increase in the pH of the solution from 3.5 to 8.5 increasing the degree of extraction of boron. An increase in the content of alkali metal and magnesium salts also improves the sorption of boric ions. However, PVG has not come to be widely used owing to its operating properties and also because it is impossible to obtain concentrated solutions in the desorption process.

Much attention has been devoted to the preparation of polymerised sorbents with aminopolyol groups capable of extracting selectively boron compounds from aqueous solutions at B_2O_3 concentrations from 0.5 to 1 g litre^{-1} and above.[59] An example of such a sorbent is the Amberlite XE-243 resin, which exhibits a high selectivity with respect to boron in neutral and alkaline media. In an acid medium, the resin capacity falls sharply. These capacities are 1.74, 1.5, and 0.7 mequiv. litre^{-1} respectively. The presence of NaCl and $MgCl_2$ does not affect the efficiency of the process, which is carried out in weakly alkaline medium. The resin has been recommended for the extraction of borates from natural brines.

Sorbents have been synthesised using tris(hydroxymethyl)amino-methane as the aminopolyl.[60] The capacity of these sorbents reaches about 70 mg of H_3BO_3 per gram of the resin for sorption from solutions containing 1 g litre^{-1} of boric acid and 50 mg per gram of the resin for sorption from solutions with a high solvent content. The optimum sorption pH is 7. The presence of salt hardly affects the capacity of the sorbents with respect to boron, so that it is useful to use them for the extraction of boron from solutions against a strong salt background. The character of the interaction of borate ions with the sorbent based on *N*-methylglucosamine is similar. However, when these sorbents are used in chloroform, the sorption maximum shifts to a more alkaline region. The resins are readily regenerated with hydrochloric acid and less effectively with hard water and alkali. The sorption process takes place less effectively in the presence of magnesium sulphate. The presence of $MgCl_2$ increases the capacity of the resin with respect to boron which is apparently associated with the salting-out of boron into the sorbent phase. The presence of NaCl, KCl, and LiCl hardly affects the resin capacity. It has been established that the process kinetics depend very significantly on the boric acid concentration in the solution.

It is noteworthy that the capacities of all the sorbents based on phenol-containing resins are lower than those of Amberlite XE-243 and its analogues. The optimum complex-forming sorbent is the resin based on *N*-methylglucosamine. Furthermore, a major advantage of polymerisation sorbents compared with the poly-condensation phenol-containing resins is their high chemical stability.

The suggestion that an activated charcoal impregnated with the Methylene Blue dye be used for the purification of boron-containing waste waters is of interest.[61–63] A fairly high efficiency of the purification of boron-containing waste waters has been achieved using Filtrasorb activated charcoal. The degree of purification was 90% for an initial boron concentration of 5–30 mg litre^{-1}.

The extraction of boron with a mixture of organic and inorganic sorbents merits attention.[64] The method involves the treatment of the anion-exchanger with a solution of zirconium oxalate and then with ammonia at pH 9–10. The sorbents prepared on the basis of the AV-17–12P, AN-2F, and PD7-10G anion-exchange resins are fairly effective in the removal of boron-containing substances from water (65%). However, the technology of their preparation is complex.

Thus one may conclude that the sorption method has a number of evident advantages and permits a fairly extensive purification of the solution without its secondary contamination. The disadvantages of the sorption technology, which complicates its practical application, are the absence of the industrial production of sorbents with the required qualities, low rates of sorption, and low economic parameters of the process.

V. Extraction of boron with organic solvents

The extraction of boron with organic solvents is one of the highly effective and selective procedures. Studies have shown that the most effective extractants for borate ions are hydroxylated organic

compounds. In the general case, the greater the number of hydroxy-groups in the structure of the organic substance, the greater its efficiency. The concentration of hydroxy-groups can be increased either by diminishing the molecular weight of monohydric alochols or by increasing the number of hydroxy-groups in the molecule by going over to polyols. As a consequence of this, two main trends have arisen in the study of the extraction of boron—extraction with monohydric and polyhydric alcohols.

Studies on a series of alcohols have shown that the efficiency of the extraction of boron with alcohols falls with increase in their moelcular weight. In terms of decreasing efficiency of the extraction of boron by alcohols, the latter can be arranged in the following sequence: 1-butanol, isobutyl alcohol, 1-pentanol, isopentyl alcohol,..., 1-octanol,..., isododecyl alcohol.

With increase in the concentration of the salting-out agent, for example $MgCl_2$, in the aqueous phase, the above sequence is in general retained, but alcohols with the iso-structure become much more effective than the alcohols with the normal structure. In concentrated $MgCl_2$ solutions, the efficiency of the alcohols with a branched structure then increases with increase in the length of the carbon chain. The alcohol efficiency sequence changes: iso-octyl alcohol,..., isopentyl alcohol, isobutyl alcohol, 1-pentanol, 1-butanol, 1-nonanol.

Thus, in the extraction of boron from bischofite brines, the most effective organic extractants are iso-octyl and isopentyl alcohols. In order to increase the efficiency of the isolation of boron, a mixture of several organic compounds is frequently used. For example, a boron extractant consisting of a mixture of aliphatic alchols (60–70% of isopentyl alcohol, 20–25% of isobutyl alcohol, and 5–10% of propylbutyl alcohol) has been proposed[65] for the extraction of boric acid. The extractant is selective with respect to boron and is immiscible with water. The maximum degree of extraction of boron is 99% and it can be attained for a boron content in the initial solution of 1 g litre^{-1}.

Table 1. The partition coefficients of boric acid in extraction with 2-substituted β-diols.

No of extractant	K_p		
	pure boric acid solution	boric acid solution saturated with NaCl	boric acid solution saturated with $MgCl_2$
(I)	13.8	39	14.9
(II)	14.6	–	58
(III)	20	40	30
(IV)	31	42	–
(V)	30	37	53

A fair amount of attention is being devoted to studies on the extraction of boric acid from aqueous solutions of diols. A fairly high degree of extraction of boron is attained[66] using 2-propylheptane-1,3-diol (I), 2-butyloctane-1,3-diol (II), 2-isopropyl-6-methylhexane-1,3-diol (III), 2,2,4-trimethylpentane-1,3-diol (IV), and 2,2,5-trimethylhexane-1,3-diol (V).

The best diluents for extractants (I) and (II) are chlorohydrocarbons, toluene, (kerosene can also be used), while the best diluent for extractants (IV) and (V) is chloroform. Table 1 presents the equilibrium partition coefficients K_p of boric acid in extraction with 0.5 M solutions of extractants (I)–(V) in chloroform for a 0.1 M solution of boric acid without electrolytes and against the background of saturated sodium and magnesium chloride brines at 20 °C. With increase in the extractant concentration in the diluent, the degree of extraction rises. The maximum partititon coefficient is observed for a tenfold molar excess of the extractant. A decrease in the boric acid concentration in the solution extracted to 0.31 g litre^{-1} does not diminish the degree of extraction when extractants (I)–(IV) are used, but the degree of extraction falls somewhat (from 96.78 to 90.26%) in the case of extractant (V). The extractants investigated extract boric acid over a wide pH range. However, at pH values in excess of 8, the degree of extraction of boron falls sharply, especially in the case of extractants (IV) and (V). The organic solvents are re-extracted with a solution of alkali.

A promising extractant, Yarrezin-B, which is an aminophenol-formaldehyde polymer, has been developed[67] for the extraction of boron. The extractant has undergone industrial tests.

Alkylcatechols and hydroxymethyl derivatives of alkylphenols have been proposed as extractants.[68] In the presence of added aromatic amines, these substances extract boron from neutral and weakly acid solutions. They are re-extracted with solutions of inorganic acids.

Studies directed towards the search for effective boron extractants are being continued. It is noteworthy that extraction is a promising method for the removal of boron from brines, having advantages such as ease of automation, high rate of the process, continuous operation, and high purity of the product obtained. However, the method also suffers from serious disadvantages, which limit its application: complexity of the equipment and partial solubility of the organic extractants in water, which leads to the loss of expensive reagents and create an ecological problem.

VI. Thermal methods for the elimination of boron-containing substances from waste waters

Thermal methods for the extraction of boron from industrial liquid waste are of definite interest in some cases. We shall consider below some of them.

The method based on evaporation ensures the complete utilisation of boron-containing compounds and the liquidation of boron-containing liquid waste. After evaporation, the cooled solutions are treated with seeding crystals, increasing thereby the degree of salting-out of boric acid. This technology has been developed for the etching and moulding of a foil, where the content of boric acid is 10 g litre^{-1}.

The waste waters from electroplating industry, containing fluoroborates, are also treated by evaporation. The improvement of this method compared with that described above consists of the fact that the waste waters are treated beforehand with an alkali metal hydroxide until the attainment of pH 8 and the precipitated metal hydroxides are separated. This prevents encrustation of the apparatus.

Evaporation is frequently used in the purification of boron-containing waste waters from atomic power stations.[69] Radioactive waste waters containing boric acid at a concentration less than 2.4% are treated with soda-lime until the attainment of pH 6.8–7.7. The

liquid waste is then concentrated by evaporation until a boric acid concentration of 25–54% is reached. The distillate is cooled and discarded into a water-containing area, while the concentrated liquid waste is directed to a settling tank where boric acid crystallises on cooling. In order to reduce the pH and intensify the crystallisation process, the still residue is treated with oxalic acid. The supernatant liquid is treated with a solution of potassium permanganate and is directed to the evaporation apparatus.

A procedure for the purification of waste waters containing boron compounds and organic substances has been proposed.[70] It consists of the fact that the water is heat-treated in the presence of steam in an amount permitting the conversion of a major proportion of the boron into H_3BO_3. The method makes it possible to regenerate heat and boric acid, but is highly energy consuming.

In the general case, thermal purification methods are energy consuming, while in combination with other methods they greatly complicate the technology.

VII. Other methods for the isolation of boron from aqueous solutions

A fairly considerable amount of attention has been devoted to the extraction of boron from aqueous systems by electrochemical methods and by reverse osmosis. These procedures are of interest for the preparation of highly pure boron-containing products and also when it is necessary to eliminate boron compounds thoroughly from aqueous systems.

Liquid membranes based on β-diols, placed between two semiconducting partitions, have been proposed[71] for the extraction of boric acid. The β-diols employed were 2-butyloctane-1,3-diol, 2-propylheptane-1,3-diol, and nonane-1,3-diol dissolved in heptane, benzene, chlorobenzene, and isopentyl alcohol. The degree of extraction of boric acid from solutions increases linearly from 45 to 87% with increase in the concentration of the diols in the liquid membrane from 10^{-3} to 10^{-1} M and the current density is 0.5–10 mA cm^{-2}. In all cases, the highest percentage extraction of borate ions through the membrane is observed when isopentyl alcohol is used as the solvent for the liquid membrane, while the smallest effect is obtained when benzene is employed. Studies[72] on the influence of the pH in the electrodialysis of boron-containing waters showed that the optimum pH for the process is in the range 9.1–9.6.

By varying the composition of the liquid membrane, it is possible to achieve fairly complete extraction and concentration of boric acid from aqueous salt solutions. Electrochemical purification is also carried out with the aid of ion-exchange diaphragms, consisting of films of an ion-exchange resin and a filler. The diaphragms have a low hydrodynamic permeabilty and in water their intrinsic electrical conductivity is also low.[9] Apart from concentrating boron-containing solutions, electrolysers with ion-exchange membranes can find applications in the selective electrochemical decomposition of a boron-containing raw material.

A technology has been proposed[73,74] for the purification of boron-containing waste waters formed in the nickel-plating process. It involves reverse osmosis. In the first stage at pH 6, nickel is separated, after which the second purification stage is carried out. The boric acid concentrate obtained in the second stage is utilised.

Heterocyclic polymeric materials, including fluorinated and modified polyamides, are used[75] as the membrane material in the elimination of boron from waste waters by reverse osmosis. Thus, when a polypiperazineamide membrane is used at a pH of the medium of 8.4, the degree of extraction of boron is 83%, while at pH 11 the efficiency increases to 95%.

A cascade of reverse osmosis apparatus has been used for the extraction of boric acid from the waste waters generated by atomic power stations.[76] The process is carried out at pH 5–6.5 and at the ambient temperature.

A membrane, obtained by depositing a cellulose acetate film on a polyamide film, has been developed.[77,78] The active surface of the polyamide film was subjected to preliminary treatment with compounds selected from the $CaMoO_4$, $CoWO_4$, $PbWO_4$, $CaWO_4$, etc. group. The selectivity of this membrane is higher by 11.3% and its productivity is higher by 14.5% than those of the usual double membrane.

The employment of the electrochemical method as well as the reverse osmosis method for the extraction of boron compounds from aqueous solutions requires further study and improvement of the design of the electrolysers and of the quality of the membranes.

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As can be seen from the data presented above, boron is extracted from aqueous systems by means of a series of methods. The choice of the method of purification depends significantly on the concentration of boric acid in the waste water.

The elimination of boron from water by coprecipitation with gel-like metal hydroxide deposits entails costs associated with the regeneration of the deposits. This method has not been applied widely in technology.

The extraction of boron by organic compounds is a fairly effective and selective method when the boric acid content is in excess of 3 g $litre^{-1}$ and has a number of advantages. However, the method suffers at the same time from serious disadvantages, which limit its application: complexity of the equipment and partial solubility of the organic extracts in water, which creates an ecological problem.

The procedure based on evaporation is energy consuming and when combined with other methods appreciably complicates the technology.

The methods for the extraction of boron with the aid of ion-exchange materials of different kinds have been developed mainly for aqueous solutions with a relatively low (up to 2–3 g $litre^{-1}$) boric acid content. The low exchange capacities and the lack of selectivity of the majority of resins in relation to boron compounds make their practical use fairly complicated.

The commonest method for the extraction of boric acids from waste waters is the reagent method involving the precipitation of boron by lime water in the form of the sparingly soluble calcium borate. The method has proved itself in aqueous systems with concentrations of 1.3–1.5% in terms of B_2O_3.

It is essential to note that the usefulness of a method for the extraction of boron from waste waters must be considered for each specific case.

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Translated from *Uspkekhi Khimii* **60** 2463–2468 (1991) U.D.C. 66.066–278:532.711

Micellarly enhanced (reagent) ultrafiltration

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ABSTRACT. The few data available in the scientific and technical literature on a new method for membrane separation—micellarly enhanced or reagent ultrafiltration (RUF)—are presented. Three versions of reagent ultrafiltration are considered in which sols are separated on a membrane. Data are presented concerning the influence of the characteristics of the disperse phase on the ultrafiltration process.

The bibliography includes 17 references.

Membrane separation and the usual filtration are frequently regarded as identical technological processes. The series of procedures filtration, microfiltration, ultrafiltration, and reverse osmosis are outwardly similar because of the presence of a partition and a common driving force—the pressure gradient. However, in this series the size of the retained particles diminishes (from micrometres to angstroms), the pressure gradient increases, and the specific productivity of the partition falls rapidly. Furthermore with increase in dispersity, for example, in the sequence coarse suspensions/emulsions–sols/microemulsions–lyophilic colloid systems (polymer and surfactant solutions), the influence of the sieve effect diminishes and the role of the aggregative behaviour of the disperse phase in the solution (its interaction with the surface of the membrane) increases appreciably.

The objects to be separated, for example industrial waste waters, very often consist of inhomogeneous mixtures containing a vast amount of an indifferent inorganic electrolyte and the contaminant proper, the amount of which can be very low but is nevertheless much greater than the limiting permissible amount. In particular, liquid radioactive waste consists of aqueous solutions of salts with an overall ionic concentration amounting to hundreds of milligrams per litre. Under these conditions, the contaminating components (radionuclides) cannot be determined in terms of weight concentrations and only the radioactivity is measured. Such systems can be conveniently separated by micellarly enhanced or reagent ultrafiltration (RUF). This membrane separation method, which can combine a high productivity with a low working pressure and the ability to eliminate ionic components from water with selective separation of the components, is based on the conversion of dissolved low-molecular-weight components into a new associated molecular or colloid state with subsequent separation on a macroporous membrane of the associated species produced.

Reagent ultrafiltration can be applied in several versions.[1]

1. The addition to the solution of a water-insoluble organic compound which interacts with the required component according to the extraction mechanism. The resulting emulsion is separated on a porous membrane subject to appropriate requirements.

2. The addition to the solution of surfactants which lead to additional purification at a concentration above the critical concentration for micelle formation (CCM) as a consequence of the physical adsorption of the contaminant on the surfactant micelles.

3. The addition to the solution of water-soluble polyelectrolytes with functional groups which are able to combine with the required components via an ion-exchange complex formation, etc. mechanism. The solution remains homogeneous and its separation is achieved in accordance with the laws governing the ultrafiltration of solutions of high-molecular-weight compounds.

4. The addition to the solution of a freshly prepared sol on the particles of which the required component is bound as a result of physical adsorption.

5. The conversion of the dissolved ionic species of the components into a molecular and subsequently a colloid phase in the course of the hydrolysis as a result of the addition of alkali to the solution. The electromembrane method of hydrolysis is a variety of this version.

6. The addition to the solution of chemical reagents whose interaction with the reqired component converts the latter into an insoluble form. The formation of a deposit should be stopped at the colloid phase formation stage.

We should like to emphasise that there may not in fact be a distinct boundary between the above versions, i.e. the solution of the given problem may require different versions to supplement one another.

At the present time, certain versions of the RUF have already undergone a far reaching theoretical development and have even found industrial application, whereas others are only being investigated.

This review deals with the application of the last three versions, where sols are subjected to membrane separation and it is therefore necessary to take into account the stability of the system and the size of the colloid particles in the concentration process.

It is known[2,3] that a deposit begins to be formed on supersaturation of the system and that the process can be divided arbitrarily into three stages: (1) the formation of nuclei of critical size; (2) the growth of particles (the particles are aggregates of the nuclei); (3) precipitation and ageing of the deposit.

The precipitation reaction in the colloid range of dispersity can be stopped in different ways: by introducing into the reaction mixture various stabilisers (surfactants, polymers), which on being sorbed on the surfaces of colloid particles prevent their further aggregation, by altering the temperature, pH of the reaction medium, etc. The choice of specific conditions and additives for controlling the dispersity of the colloid system is determined by the nature of the disperse phase and the solvent.

The ultrafiltration process is greatly influenced by the particle size, which depends on its turn on the mechanism and kinetics of the process leading to the formation of the new phase. The formation of the new phase begins either as a result of the fluctuation generation of a nucleus of critical size (homogeneous fluctuation of crystallisation centres) or following the introduction into the system of ready made nuclei from outside (heterogeneous formation of crystallisation centres).

According to the Gibbs–Thomson equation, we have for a critical nucleus of spherical shape

$$r_{cr} = \frac{2\sigma V}{RT \ln \gamma},$$

where r_{cr} is the critical radius of the nucleus, σ the interfacial tension, V the molar volume of the new phase, R the gas constant, T the temperature, and γ the critical degree of supersaturation. For non-electrolytes, $\gamma = c/c_0$, c is the concentration of the test substance in the supersaturated solution, and c_0 the equilibrium solubility of the macrocrystals. For strong electrolytes, $\gamma = ab/L$, where a and b are the activities of the cations and anions and L is the solubility product. It follows from this equation that the lower the degree of supersaturation, the higher the values of r_{cr} and the appearance of the critical nucleus therefore becomes increasingly more difficult with decrease in the degree of supersaturation of the system.

Depending on the conditions, there is a possibility of both homogeneous and heterogeneous formation of nuclei.[2,4,5] Furthermore, depending on the degree of supersaturation, the process can proceed in the same system via both the nucleus formation mechanisms. This has been demonstrated by Mikhnevich.[3] When the degree of supersaturation in the system diminishes, crystallisation becomes possible only on increasingly larger particles. Finally, if r_{cr}, defined by the Gibbs–Thomson equation, becomes greater than the size of the impurity particles, "spontaneous" formation of nuclei on the latter begins. The energy necessary for such a heterogeneous process is then found to be lower than the energy of the homogeneous formation of nuclei of the same size.

The next stage of crystal growth is determined by two processes:[6] the supply of the substance from the bulk of the solution to the surface of the crystal (diffusion) and incorporation of molecules in the crystal lattice (surface reaction). The growth rate is determined by the rate of the slower of the two processes. Crystal growth processes controlled by either diffusion or the surface reaction are therefore distinguished. The rate of the surface reaction is independent of the hydrodynamic conditions and is determined by the state of the surface of the growing crystal. Experiments have shown that, when small amounts of other substances, capable of being sorbed on the surface, are added, they may influence significantly the rate of growth and shape of the crystals. As regards the rate of supply of the substance, one may claim that it depends on the stirring. As the stirring becomes more intense, the rate of crystallisation increases but only up to a certain limit, at which the rate-limiting factor is the surface reaction.

Between the establishment of supersaturation in the system and the appearance of the first traces of the new phase which can be distinguished in one way or another, there is a definite time interval called the induction period. During this period, crystallisation centres are formed vigorously. The duration of the induction period τ_i varies markedly depending on the nature of the deposit and for a given deposit is a function of the initial degree of supersaturation.[7] Thus, for $BaSO_4$ and AgCl deposits having approximately the same molar solubilities, we have, for equal initial concentrations,

$$\tau_i(BaSO_4) \gg \tau_i(AgCl).$$

According to Nielsen's studies,[8] where the crystallisation of $BaSO_4$ was investigated, the induction period τ_i, the total number of grown crystals N, and the average rate of formation of nuclei N/τ_i were determined, the number of crystals N remains approximately constant up to a concentration $c \simeq 0.01$ M and then increases sharply: N/τ_i increases in proportion to the concentration raised to the power 18. Evidently in this case there is a change from the heterogeneous to the homogeneous mechanism of the formation nuclei. The size of the nucleus (18 ions or 9 molecules), the critical degree of supersaturation ($\gamma_{cr} = 630$), and the interfacial tension ($\sigma = 90$ erg cm^{-2}) were calculated from the data presented.[9]

Thus, on the basis of the foregoing, one may postulate that, by altering the degree of supersaturation of the system, the rate of supply of the test substance, and the rate of the surface reaction, it is possible to achieve control of the induction period and the dispersity of the colloidal phase and hence also of the particle size. Then, having stabilised the system obtained, the ultrafiltration process can be carried out. The barium chromate colloid system has been obtained by this method. It is important to note that sometimes, when the precipitation process is carried out without satisfying the technological requirements, colloid systems are formed in settling tanks.[10] In this respect, a result which is undesirable for a given process may prove positive for reagent ultrafiltration.

It has been suggested[11] that sodium sulphide, forming disperse systems with contaminants, be used as the reagent for the isolation of mercury, lead, and cadmium ions. As a result of the formation of colloid systems, it became possible to remove them by means of ultrafiltration.

When the fourth version of reagent ultrafiltration is carried out, satisfactory results are achieved at low concentrations of the contaminant, which is sorbed on the colloid particles. This can naturally limit the application of the given method. However, it proved effective for the elimination of caesium-137 from liquid radioactive waste from atomic power stations.[12] Copper ions Cu^{2+} and the $[Fe(CN)_6]^{4-}$ ions were introduced into the caesium-containing liquid waste. The reaction resulted in the formation of a colloid system in which caesium was sorbed on the colloid particles retained by subsequent ultrafiltration. The degree of extraction of caesium-137 was 99% and the consumption of the reagents was 2% of the amount required for the precipitation.

The fifth version of reagent ultrafiltration, where the colloid particles are obtained by hydrolysis, can find extensive application if it proves possible to shorten the hydrolysis time, i.e. to increase the rate of reaction. It is known that, at a concentration of the component isolated in excess of 10^{-3} M, the hydrolysis proceeds with formation of polynuclear complexes in several stages, including the formation of monomers and dimers, their polymerisation, the appearance of amorphous colloid particles, and their subsequent transformation into a crystalline form. Any of the atoms forming part of the polymer chain can be hydrolysed twice and three times, which leads to the branching of the chain. The identification of the species formed is exceptionally difficult, but for practical applications only one parameter is important—their size, which after the addition of alkali has ceased may increase owing to coagulation and may lead to the loss of resistance to aggregation by the colloid system. There are several methods for preventing this phenomenon: the addition of surfactants and a change of temperature.[13]

The results achieved in the removal of iron and chromium from solutions are presented in Figs. 1 and 2 and the influence of surfactants on this process is illustrated in Fig. 3.

Hydrolysis with the aid of electroadjustment of the pH of the solution, i.e. the gradient-free micellarly enhanced ultrafiltration method, is a variety of the fifth version. In this procedure, the question of the resistance of the system to aggregation is even more

acute, but at the present time the method has not yet been investigated.

Membrane separation is evidently determined in many respects by the stability of sols as regards an increase in concentration, by the size and charge of their particles, and by the hydrodynamic conditions in the apparatus. The creation of optimum hydrodynamic conditions is especially important for diminishing the phenomenon of concentration polarisation.

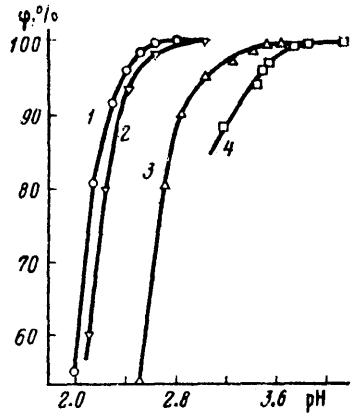


Figure 1. Dependence of the selectivity of the purification (φ) on the pH of the medium for an iron solution; [Fe] (mg litre^{-1}) in the initial solution:[1] *1*, 1000; *2*, 300; *3*, 60; *4*, 25.

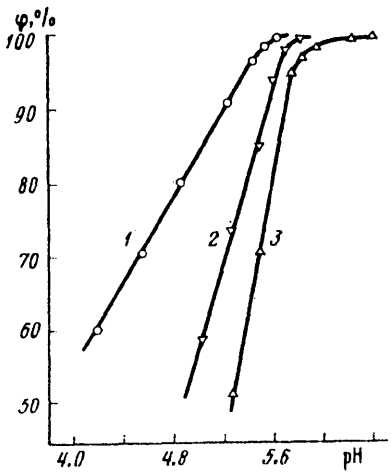


Figure 2. Dependence of the selectivity of the purification on the pH of the medium for chromium solutions; [Cr] in the initial solution (mg litre^{-1}):[1] *1*, 500; *2*, 350; *3*, 100.

The change in the properties of hydrosols during their concentration from 3.5 to 43% has been investigated[14] by the ultrafiltration method. It was noted that during concentration there is an increase in the viscosity of the sol, which exerts an appreciable influence on the rate of ultrafiltration, especially on increasing the concentration above 35%. This is explained by the fact that, for a given size of the particles and taking into account their hydration shells, the closest packing is attained under these conditions. The shells of the stabilising counterions begin to overlap, so that a slight increase in the concentration of the sol entails an appreciable increase in viscosity. Ultimately this leads to a lower stability of silica sols in relation to gel formation.

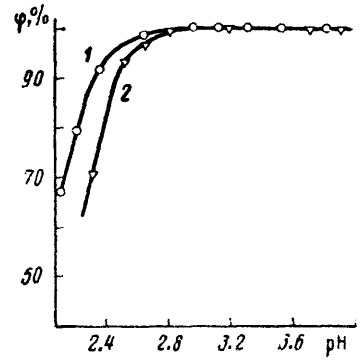


Figure 3. Dependence of the selectivity of the purification on the pH of the medium for the iron–surfactant system; [Fe] in the initial solution (mg litre^{-1}):[1] *1*, 1000; *2*, 100; the surfactant concentration was 100 mg litre^{-1} in both cases.

Studies[15] of the influence of hydrodynamic conditions and of the diameter of the SiO_2 sol particle on the rate of ultrafiltration showed that, on vigorous stirring of the disperesions, whereupon a gel layer made up of the sol particles is not formed on the surface of the membrane, the rate of filtration is constant and independent of the particle diameter. A highly concentrated sol (106 kg m^{-3}) is an exception. In the absence of stirring, the rate of filtration increases with increase in the particle diameter, which can be explained by the increase in the porosity of the gel layer. An increase in pH diminishes the resistance of the gel layer as a consequence of the increase in the repulsion between the sol particles. In these experiments, the size of the colloid particles was less than the size of the membrane pores. However, in practice one may encounter opposite cases where the colloid particles, penetrating into the pores, irreversibly contaminate the membrane. In order to solve this problem, it has been suggested[16] that the particles capable of penetrating into the membrane pores be aggregated until particles which are retained on the surface of the membrane are obtained. An increase in the size of the particles and the presence of a charge on their surface have positive influence on the rate of filtration.

Certain aspects of the ultrafiltration of colloid systems have been described by Bryk and Tsapyuk.[17]

Studies in the field of the ultrafiltration of colloid systems are just being activated, but it is already possible to formulate preliminary results: (1) the irreversible contamination of the membrane is caused by particles whose size is smaller than the pore size; (2) the charge on the colloid particles, by virtue of which there is a possibility of

their electrostatic repulsion from the membrane, is very important; (3) by controlling the conditions in the formation of the colloid system, it is possible to achieve the best ultrafiltration conditions by an appropriate combination of the size and charge of the particle; (4) it is important to set up the optimum hydrodynamic situation over the membrane, the elimination of stagnant zones being of primary importance.

Reagent ultrafiltration increases markedly the applications of the membrane separation methods. It becomes possible to use highly productive processes for the purification of liquid industrial waste, which could be achieved previously only by reverse osmosis, and to eliminate selectively contaminating components from the waste without involving the salt ballast, which is especially important in the handling of radioactive and electroplating waste. A new method has arisen for the fractionation of components of liquid mixtures which may become analytical after appropriate further developments. Finally, new approaches to the utilisation and processing of toxic concentrates are appearing.

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Translated from *Uspekhi Khimii* 60 2469–2483 (1991) U.D.C. 502.678.7 + 628.16

Ecological aspects of the extreme purification of water

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ABSTRACT. The influence on the eco-system of the products of the large-scale technology for the preparation of ultra-pure water required for the electronic and radiotechnical industries is examined. The distillation, ion-exchange, and membrane methods are subjected to a comparative analysis. It is shown that the membrane method for the extreme purification of water is ecologically the most desirable. The methods for the elimination of nitrates from drinking water are examined.

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I. Introduction

The preparation of ultrapure water has become one of the most urgent problems in chemistry and chemical engineering in connection with its definite role in the manufacture of electronic devices, integrated circuits, microprocessors, and specially pure substances.

The construction of transistors, integrated circuits, and microprocessors involves a multiplicity of operations with chemical treatment, after which the articles have to be washed with water of the highest purity. There is a direct relationship between the purity of water and the information capacity of integrated circuits. In particular, in order to obtain 64 kbytes of information, the content of organic carbon must not exceed 500 μg litre^{-1} and the attainment of 4 Mbytes requires the use of water in which the concentration of organic carbon is not more than 30 μg litre^{-1}. Even more stringent requirements must be met as regards the content of inorganic substances and micro-organisms. It is therefore not fortuitous that the widely familiar study by Shockley, who first obtained a transistor in 1951, was published simultaneously with the work of Reents and Kahler, who were the first to use a mixed bed of cation-exchange and anion-exchange resins for the extreme purification of water.[1]

The progress in electronic engineering and the synthesis of specially pure chemical and pharmaceutical preparations have helped to convert the ion-exchange technology for the manufacture of specially pure water into a large-scale process. With the aid of this technology, the problem of the conditioning of water for industry can be solved fairly easily. However, it was found subsequently that the ion-exchange method and the ion-exchange technology based on it constitute an "ecological boomerang", since the waste waters from ion-exchange apparatus contain a mass of mineral substances which exceeds by an order of magnitude the mass of impurities extracted from natural waters.

The return to the method of multistage vacuum distillation, developed by Kohlrausch,[2] did not lead to success, although the first impression was that the method and the technology based on it do not involve the discarding of substances into the environment. The paradox of the purification of water by distillation consisted in the fact that the high energy consumption leads to the contamination of the environment not in the region of the operation of the given apparatus but in the regions where there are thermal electric power stations whose gaseous waste is emitted into the atmosphere and spreads over long distances. The results of the ecological analysis of these methods have led to the alarmist attitude for our time.

At the same time, a new aspect of the solution of the ecological problems in the preparation of high purity water has arisen. This is associated with the use of membrane methods for the separation of substances and the membrane technology based on them. Hitherto many specialists have been sceptical about the possibility of replacing distillation and ion-exchange methods for the purification of water by membrane methods, pointing out at the same time the limitations of the baromembrane methods (microfiltration, ultrafiltration, and reverse osmosis), which do not permit the preparation of water purer than distilled water, or of electromembrane methods (electrodialysis with ion-exchange membranes) in view of its limited possibilities in the elimination of organic non-electrolytes with low dissociation constants. However, they failed to take into account the fact that, firstly, there exists a mechanism of the electroosmotic transport of molecules through ion-exchange membranes as a result of the forces arising from the coupling with fluxes of ions (ion–dipole interaction) and, secondly, that there is a possibility of combining various baromembrane and electromembrane methods whereby one can set up a sequence of operations leading to the preparation of ultrapure water. A feature distinguishing membrane purification methods from other procedures is the approximate equality of the mass of the substances entering the liquid waste and the mass of the substances extracted from natural waters when the latter are purified. The ecological usefulness of a particular membrane method also depends on the operating costs, among which the cost of the electrical energy is of main importance. At the present time there are membrane methods, applied under laboratory or even industrial conditions, which permit intensive purification of water with a very low electrical energy expenditure. In the immediate future, there will be a need to increase the information capacity of the integrated

circuits and microprocessors and this will entail both an extensive and an intensive growth of the production of ultrapure water, which has already reached a large scale. The ecological blunders in this kind of technology have therefore become completely inadmissible and this has determined the aim of the present publication. Furthermore, while the problem of the preparation of ultra-pure water is specific, at the same time it has significant general features in common with the solution of other problems in ecological chemistry.

II. The distillation method for the intense purification of water

The purification of water by distillation has been known since ancient times,[3] but interest in the preparation of ultrapure water did not arise until the past century. After G Kwinke observed that the specific conductance of pure water increases on storage, Kohlrausch and Heidweiler[2] applied in the concluding purification stage consecutive vacuum distillations using vessels made of old Jena glass. After 60 days of successive vacuum distillations, water with a specific conductance of 4.2×10^{-8} S cm^{-1} (specific resistance 23.8 MΩ cm) at 18 °C and 6.09×10^{-8} S cm^{-1} (specific resistance 16.4 MΩ cm) at 25 °C was obtained. The preliminary purification was carried out using the freezing out method proposed by Nernst. The principal physical parameters of the water obtained in these experiments are quoted in monographs and textbooks of physical chemistry, although Kohlrausch himself believed that he had not obtained ultrapure water. However, he discovered how to estimate the electrical conductivity of ideal water on the basis of the van't Hoff theory. Calculation showed that ideally pure water should have a specific conductance of 3.8×10^{-8} S cm^{-1} (specific resistance 26.4 MΩ cm) at 18 °C. A novel method for the determination of the physicochemical parameters of ultrapure water without its purification was developed by Harned and Hamer.[4] They measured potentiometrically the ionic product of water using a hydrogen indicator electrode and a silver/silver chloride reference electrode. The electrolyte was a standard solution of potassium hydroxide and potassium chloride. By extrapolating the electrode potentials obtained to zero ionic strength, Harned and Hamer[4] obtained the following numerical value of the ionic product of water:

$$K_w\ (25^\circ\mathrm{C}) = [\mathrm{H^+}][\mathrm{OH^-}] = K\cdot[\mathrm{H_2O}] = (1.008+0.001)\cdot 10^{-14}, \quad (1)$$

where K is the dissociation constant of water. With the aid of the Ostwald dilution law

$$K = c\alpha^2/(1-\alpha), \quad (2)$$

where α is the degree of dissociation of a weak electrolyte and C its concentration, it is possible to calculate the degree of dissociation from which the equivalent molar conductance can then be evaluated by means of the familiar Arrhenius relation:

$$\alpha = \Lambda/\Lambda_\infty \quad (3)$$

The values obtained are sufficient to calculate the specific conductance $\varkappa$ and the specific resistance ρ:

$$\varkappa = 1/\rho = \Lambda\cdot c \quad (4)$$

It was found[5] that the specific resistance of ideally pure water at 18 °C is 26.6 MΩ cm^{-1}, while at 25 °C it falls to 18.25 MΩ cm. We shall now introduce the dimensionless specific resistant ρ^*, which is equal to the ratio of the experimental specific resistance ρ to the calculated specific resistance of ideally pure water ρ_{lim}:

$$\rho^* = \rho/\rho_{\mathrm{lim}} \quad . \quad (5)$$

Using calculated resistances for the temperatures at which the experimental measurements were made as ρ_{lim}, we are able to estimate the degree of purity of water which is independent of the temperature of the measurement. In particular, Kohlrausch[2] was able to obtain water having $\rho^* = 0.8947$, which is 89.47% of the specific resistance of ideally pure water.

At the present time the distillation method is used widely to desalinate sea and ocean waters, using various evaporators of the thin-film type improved to achieve instantaneous ebullition, hygroscopic and hydrophobic evaporators, and distillation on membranes. The water obtained by single distillation has an intrinsic cost between 3 and 13 roubles per m^3. A relatively high consumption of metals accompanied by a relatively low quality of the purified water (the content of inorganic impurities is approximately 1 mg litre^{-1} and that of organic substance is approximately 4 mg litre^{-1}) is characteristic of distillation apparatus. An increase in the number of purification stages leads to an exponential increase in the cost of the water, so that multistage distillation is used for the preparation of specially pure water only under laboratory conditions.[6]

The distillation method creates the illusion that it is ecologically clean, since at the site where the apparatus operates no discharge of harmful substances is observed, while in the liquid waste the mass of substances is not greater than the mass of substances extracted from natural waters. Nevertheless distillation must be classified as a harmful technology because of its exceptionally high energy consumption. Therefore in order to analyse the ecological effects of distillation, it is essential to estimate the ecological effects of the production of electrical energy.

Since the fraction of electrical energy generated by thermal power stations is 80%, we shall confine ourselves to the analysis of the gaseous waste in the combustion of a non-renewable organic fuel. It has been established that the generation of 1 kWh of electrical energy by the combustion of coal entails the discharge into the atmosphere of 14 g of slag, 80 g of ash, 1000 g of carbon dioxide, and 14 g of sulphur dioxide (21 g of sulphuric acid).[7] We may draw attention to the production of sulphur dioxide, the discharge of which exceeds the permissible amount for the turnover of sulphur in nature.[8] When the limiting permissible concentration (LPC) of sulphur oxides is exceeded, asthma, bronchitis, and emphysema are contracted.[9] It is also known that sulphur dioxide disturbs the photosynthetic process by decomposing chlorophyll.[9] Acid rain, containing sulphuric acid, destroys forests and fish, increases the corrosion of metals, and destroys ancient monuments.

The discharge of nitrogen oxides into the atmosphere has both positive and negative effects on the eco-system. The positive influence consists in supplementing the store of bound nitrogen, which is formed in limited amounts as a result of the functioning of nitrogen-fixing bacteria (on leguminous plants), fungi, and seaweed and is also derived from the molecular nitrogen in the atmosphere under the influence of electric discharges. However, the negative effect of the discharge of nitrogen oxides into the amtosphere is much more significant. On interaction with hydrocarbons in the presence of sunlight, such oxides give rise to peroxyacetyl nitrate and ozone. The reaction is an example of synergism, where certain contaminants react with one another in the environment and form secondary even more toxic compounds. Both peroxyacetyl nitrate

and ozone induce lachrymation and also exert an irritant effect on the respiratory pathways in man. Furthermore, both products are toxic to plants, since ozone intensifies the respiration of leaves and plants are destroyed through exhaustion, while peroxyacetyl nitrate blocks the Hill reaction in photosynthesis, which also leads to the destruction of plants caused by the low intensity of the synthesis of nutrient substances.[8]

Apart from sulphur and nitrogen oxides, the waste from thermal electric power stations contains also solid waste, slags, and dust and soot particles which nowadays occupy many millions of hectares of land which used to be arable. As the structure of the fuel–energy balance changes, in particular, with increasing contribution by nuclear power, the situation may alter fundamentally.

Since it is virtually impossible to take into account all the factors leading to the contamination of the environment on distillation of water because of their different influences, Mazo[10] suggested that analysis be restricted to the discharge of sulphur and nitrogen oxides, which are converted respectively into sulphuric and nitric acids. Account was also taken of the fact that the generation of 1 kWh of electrical energy leads to the discharge of 0.5 of an equivalent of sulphuric and nitric acids. The coefficient of the contamination of the environment, as a result the purification of water, can be expressed by the ratio of the mass of the acids formed to the volume of water V treated annually:

$$Cd = \sum_i m_i/V + \sum_k m_k/nV \,, \qquad (6)$$

where Cd is the coefficient of the contamination of the environment, m_i the mass of the contaminants entering the environment during the operation of the technological set up, m_k the mass of the contaminants entering the environment during the establishment of the technological set up, and n the duration of operation of the technological cycle. Eqn. (6) expresses the coefficient of the contamination of the environment as a quantity proportional to the rates of the reactions generating the products contaminating the environment. As a result, the contamination coefficient is given by the sum

$$Cd = \sum_i \frac{\partial C_i}{\partial \tau} \,, \qquad (7)$$

in which C_i is the concentration of the harmful substances produced and τ is the reaction time.

In order to be able to compare the different contaminants in the environment, it has been suggested[11] that norms be laid down for the limiting permissible concentrations (LPC). By introducing the dimensionless concentration

$$C_i^* = \frac{C_i}{C_{lim}} \,, \qquad (8)$$

representing the ratio of the concentration of the harmful component to its limiting permissible concentration C_{lim}, we obtain the following expression for the rate of production of the component contaminating the environment:

$$\frac{\partial C_i}{\partial \tau} = C_{lim} \frac{\partial C_i^*}{\partial \tau} \,. \qquad (9)$$

Here one should bear in mind that the product obtained may also react chemically. In one case it is assimilated by the eco-system, being converted into a harmless component or mixture of components, while in another it is converted, like nitrogen oxides, into a component even more dangerous to life (synergism). In both cases, account must be taken of the rate of reaction of the component:

$$\frac{\partial C^*}{\partial \tau} = K_1 - K_2, \qquad (10)$$

where k_i is the rate constant for the reaction leading to the formation of the component contaminating the environment and K_2 is the rate constant for the reaction leading to the consumption of this component. Eqn. (10) was formulated solely for zero-order reactions. For $K_1 \leqslant K_2$, i.e. when the reaction product does not contaminate the environment, it is possible to assess the ecological situation as favourable, because in this case nature fully processes the harmful waste.

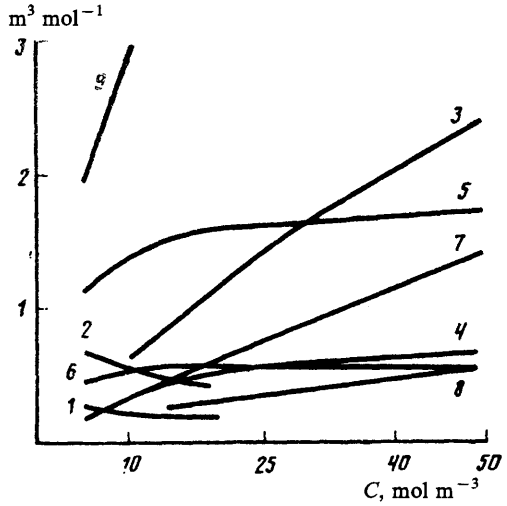


Figure 1. Dependence of the coefficient of the pollution of the environment on the salt content in the initial water subjected to extreme desalination by various methods: *1*, ion exchange (cation exchange–decarbonation–anion exchange–deionisation by a mixed bed); *2*, ion exchange with processing of waste water by electrodialysis; *3*, electrodialysis and ion exchange; *4*, ion exchange softening–electrodialysis–ion exchange; *5*, reverse osmosis–decarbonation–ion exchange; *6*, ion exchange softening–reverse osmosis–decarbonation–ion exchange; *7*, multichamber evaporation–ion exchange; *8*, ion exchange softening–multichamber evaporation–ion exchange; *9*, reverse osmosis–electrodialysis with ion exchange membranes and grains–ion exchange in a mixed bed.[10]

Fig. 1 presents the result of the calculation by Eqn. (7) of the coefficients of the pollution of the environment in the purification of water.[10] Analysis of the data presented in the figure shows that ion-exchange technology is ecologically less desirable than distillation technology, but the quality of water obtained by ion exchange is significantly higher than that produced by distillation.

III. The ion-exchange method for the preparation of ultrapure water

Ion exchangers are solid or liquid substances containing ions capable of exchanging with other ions of the same charge sign present in the solution where the given ion exchanger is insoluble.[12] Ion exchange was first used for the treatment of water with the aid of modified activated charcoals,[13] but, owing to their low stability in alkalies, the technology did not come to be widely employed. Furthermore, the natural and synthetic inorganic ion exchangers had a comparatively low exchange capacity. After Adams and Holmes[14] established in 1935 that the phenol-formaldehyde resin obtained by polycondensation has a much higher capacity compared with the known ion exchangers, commercial production of cation exchangers for the purification of water was organised in Germany. Less than a decade was needed to synthesise phenol-formaldehyde cation exchangers with sulpho-groups. D'Alelio[12] synthesised a sulphonated copolymer of styrene and diviylbenzene—the first monofunctional highly acid cation exchanger. Anion exchangers of the weakly basic and strongly types were soon synthesised. The present stage of the use of ion exchange for the purification of water began from that moment. The preparation of ultrapure water begins with cation exchange. The initial highly acid cation exchanger must be in the acid form and the cation exchange reaction then leads to the formation of the corresponding acids:

$$RH+NaCl=RNa+HCl\ ,$$
$$2RH+Ca(HCO_3)_2=R_2Ca+2CO_2+2H_2O\ ,$$
$$2RH+MgSO_4=R_2Mg+H_2SO_4\ .$$

The reactions are carried out so long as the cation exchanger in the acid form remains in the column. After the conversion of the cation exchangers into salt-forms, they must be regenerated. Chemical regeneration of cation exchangers with acids is usually employed in technology. The reason for the ecological undesirability of ion exchange for the intensive desalination of water arises from the necessity for the ion exchanger chemical regeneration reactions:

$$RNa+HCl=RH+NaCl\ ,$$
$$R_2Ca+2HCl=2RH+CaCl_2\ ,$$
$$R_2Mg+2HCl=2RH+MgCl_2\ .$$

Cation exchangers with the ionogenic sulpho-group have the maximum affinity for multicharged ions. The reason for this is both the direct and stronger electrostatic interaction of the multicharged counterions with the fixed ions and the strengthening of the hydrogen bond formed by the molecules of the water of hydration, the counterions, and the fixed ions. The sorbability series is as follows:

$$Fe^{3+}>Ca^{2+}>Mg^{2+}>Na^{+}>H^{+}\ .$$

The desorption of calcium and magnesium ions, the absorption of which is described by a convex isotherm, requires an appreciable excess of acids for regeneration. The complete regeneration of the cation exchanger in the sodium-form requires a 2.5-fold excess of acids. The desorption of doubly charged ions from an ion exchanger requires an even greater excess of acid and the regeneration is therefore carried out without restoring fully the capacity of the acid-form,[15] although this does not eliminate the need for the use of an excess of acid. As a result, the waste water from cation-exchange columns contains after regeneration an appreciable excess of acids together with sodium, calcium, and magnesium salts.

After cation exchange, the water is decarbonated to remove carbon dioxide, which is followed by anion exchange. The anion exchange process is carried out successively, initially on weakly basic and then on highly basic anion exchangers. The weakly basic anion exchangers contain primary, secondary, or tertiary amines as ionogenic groups which function effectively only in an acid medium. Therefore anion exchangers of this type sorb strong acid anions:

$$R'OH+HCl=R'Cl+H_2O\ ,$$
$$2R'OH+H_2SO_4=R_2'SO_4+2H_2O\ .$$

The necessity to use weakly basic anion exchangers is associated with the ease of their regeneration (the consumption of alkalies on the regeneration process is greater than the stoichiometric amount by a factor of 1.2–1.5). However, weakly basic anion exchangers hardly sorb weak acids, in particular silicic acid. An important feature is that highly basic anion exchangers function virtually in any pH range and sorb silicates from natural waters. On the other hand, highly basic anion exchangers are much more difficult to regenerate (the consumption of reagents is 5–10 times greater than the stoichiometric amount).

An exceptionally important step in the development of the ion-exchange method in the technology for the preparation of highly desalinated water was the application by Reents and Kahler[1] and almost simultaneously by Kunin and McGarvey[16] of a mixed bed of granulated cation and anion exchangers. The following reaction takes place in this case:

$$RH+ROH+NaCl=RNa+RCl+H_2O\ .$$

The proximity of heteropolar ion exchangers and the presence of a product with a low dissociation constant lead to a virtually irreversible reaction, which permits the complete demineralisation of water. Both a strongly acid cation exchanger and a strongly basic anion exchanger must be used for the complete demineralisation.

Since the electrochemical regeneration of a mixed bed of ion exchangers[17] has not come to be widely used, an obligatory stage is the separation of the components of the mixed bed. This operation is usually carried out by supplying water in the direction from below upwards. The cation exchanger, which is more dense, then settles downwards, while the anion exchanger forms the upper layer. After this, the cation exchanger and the anion exchanger are regenerated with acid and alkali respectively, the amounts consumed exceeding the stoichiometric amount by a factor of 2–3.

It is also important to draw attention not only to the necessity for an excess of the regeneration reagents but also for the necessity to double the mass of the reagents relative to the mass of the impurities extracted from natural water, because the cation and anion exchangers are regenerated separately. The cations of each electrolyte are sorbed on the cation exchanger and the anions are sorbed on the anion exchanger. They are regenerated in the same way. Altogether this leads to an increase in the mass of inorganic substances in waste waters by a factor of 3–15 depending on the quality of the initial water and the required degree of desalination.

Ultrapure water cannot be obtained by ion exchange without the preliminary sorption of organic susbtances.[15] Activated charcoals or anion exchangers of the macroporous and isoporous type are used for this purpose. Best results in the sorption of humates and fulvates from natural waters are obtained by the successive employment of weakly basic and highly basic anion exchangers. In particular, their successive adsorption on the USSR-produced anion exchangers IA-1 and AB-17P in the preliminary purification stage makes it possible to avoid the poisoning of the ion exchangers by humates and fulvates.[18] As a result of this, the principal units in the technology for the production of ultrapure water involve preliminary purification specific to a particular type of natural water, the adsorption of organic substances, cation exchange, decarbonation, anion exchange, and ion exchange in a mixed bed of cation and anion exchangers. Some of these operations can be repeated several times.[15]

After all these purification stages, the water is characterised by the lowest concentrations of impurities, approaching ideality in this respect. In the Soviet literature, a single term has not been established for the limiting quality of water and the concepts of ultrapure, specially pure, and highly pure water are used together with the term "deeply" desalinated water. The very term ultrapure water arose in the French language literature (l'eau ultrapure), while in the English language literature two terms exist—ultrapure water and high purity water. We have given preference to the term ultrapure water because it is most widely used in the world's scientific literature.

The question arises what characteristics shoudl utlrapure water possess? In view of the absence of a Government Standard (GOST) for ultrapure water, use is made of OST 11 029.003-80, where brands A, B, and C are distinguished in terms of their quality. The highest quality water of brand A must have a specific resistance not less than 18 MΩ cm at 20 °C, a permanganate oxidisability less than 0.5 mg O_2 litre^{-1}, a silicic acid content less than 0.01 mg litre^{-1}, iron and copper contents less than 0.002 mg litre^{-1}, not more than 2 microparticles per ml, and not more than 1 colony of microorganism. In the USA, the type 1 ASTM standard corresponds to water with a maximum specific conductance of 0.06 μS cm at 298 K (specific resistance 16.67 MΩ cm), a content of organic substances not more than 1 mg kg^{-1}, a content of dissolved gases not more than 200 mg kg^{-1}, a residue after evaporation not greater than 0.1 mg litre^{-1}, the absence of a positive response to the test for silicates, a maximum content of heavy metals of 0.01 mg kg^{-1}, and not more than 150 particles in 1 kg.

The development of the ion-exchange technology ensuring the preparation of water of the very highest quality by the most economical method, involving simple apparatus and permitting the attainment of virtually any required productivity of the latter, for a long time created the illusion that the problem of the preparation of ultrapure water has been solved. Difficulties arose when an attempt was made to organise a waste-free circulating water supply, which in our time has become absolutely essential, since the general ecological situation has become very much more acute. From the standpoint of the protection of nature the question arose whether or not the ion exchange technology transfers impurities to pure rivers and water-containing areas and whether or not the soil, air, and subterranean waters suffer as a result. It is known that water (rain and snow) precipitated on the surface of the soil in the active water exchange zone, where waste is in fact mainly stored, enters river water after approximately 17 years. Calculations show that in the immediate future the amount of chlorides of anthropogenic origin will exceed by a factor of 4 the natural background. By the end of the century, the antropogenic concentration of sulphates will exceed by a factor of almost 7 the concentration in 1980 and the LPC for commercial water-containing areas. The conversion of organic contaminants into mineral ones in the course of the biological purification of water does not in essence alter the fundamental situation. As a consequence of this, the discharge of mineralised waters, including regenerators of ion-exchange filters, is forbidden in the comparatively water-deficient Ukraine and individual sections of the Northern Donets and the Dneper.

We draw attention to the fact that, since the mass of mineral substances in the liquid waste from ion-exchange apparatus after chemical regeneration is more than three times greater than the amount of such substances extracted from natural waters, the degree of mineralisation of subterranean and river waters will increase after a certain time. Since the initial water will become more mineralised, this will entail the consumption of a greater mass of chemical reagents for regeneration. This will lead in its turn to an even greater pollution of the environment and ultimately to an additional increase in mineralisation. The reaction producing mineral substances will change from a zero-order process to a first-order process; since the production of mineral substances under such conditions is proportional to the concentration, we have

$$\frac{\partial C_i}{\partial \tau} = K_i C_i \,, \tag{11}$$

and this leads to an exponential increase in the concentration of mineral substances in subterranean waters and rivers:

$$C_i = C_{0,i} \cdot \exp(K_i \tau) \,. \tag{12}$$

Such a system may be characterised as an ecological boomerang, since not only an increase in the productivity of the devices using the ion-exchange method but also their functioning with a constant productivity entails a continuous impairment of the quality of the initial water and an exponential growth of the waste discharged as a function of time. The creation of the ion-exchange technology can be regarded nowadays as an ecological mistake with unforseeable harmful consequences involving a change in the environment, which vitiates the planned benefit and generates more problems than it solves. This entails a double tragedy, since it will be necessary to seek means not only for the liquidation of the waste discharged into natural waters but also for the solution of all the new problems arising in this connection (human diseases, destruction of fish farming, etc.). The "unpredictability" of the pernicious consequences is due to the inadequacy of the preliminary research and the underestimation of the impact on the environment and human beings.[8] Fig. 1 shows why ion exchange is an ecologically undesirable technology for the extreme purification of water.

IV. The membrane method for the extreme purification of water

The ecological undesirability of distillation and ion exchange necessitated the search for alternative methods leading to the solution of the problem of the preparation of ultrapure water. We shall consider the possibility of using membrane methods for the solution of the problem. Membrane is the term which has come to

be applied to a body whose extent in terms of two coordinates significantly exceeds its extent in terms of the third (a one-dimensional disperse system). The word membrane comes from the latin word meaning pellicle, shell, or partition. When generalised thermodynamic forces are applied to a membrane, mass fluxes arise.[19] Transport processes following the application of a chemical potential gradient (dialysis), a pressure gradient (microfiltration ultrafiltration, reverse osmosis), and an electric potential gradient (electrodialysis) are distinguished.

Baromembrane methods can be most usefully applied in the first stage of the purification of water. Natural water is initially filtered to remove coarsely dispersed impurities, after which it is subjected to microfiltration to remove finely dispersed impurities and bacteria.[20] In the next stage, colloid impurities, high molecular-weight and oligomeric compounds, and viruses are eliminated by means of ultrafiltration.[21,22] Using UAM-100 and UAM-150 ultrafiltration membranes, it was possible to remove about 80% of organic substances from water.[23] Next, reverse osmosis is used to purify water.[21,24]

In particular, when filter elements of the rolled up type with the MGA-95 cellulose acetate membranes are used, reverse osmosis makes it possible to obtain water with a specific resistance of 0.02–0.07 MΩ cm containing 0.25 mM silicate, exhibiting a permanganate oxidising capacity not more than 3.1 mg O_2 litre^{-1}, and showing the complete absence of microflora. On the other hand, one should immediately abandon the illusion that reverse osmosis makes it possible to obtain ultrapure water directly. Studies have shown that by this procedure it has not yet been possible to attain the state of distilled water formed after a single distillation and having a specific resistance of 0.1–0.3 MΩ cm. On the other hand, the role of reverse osmosis in increasing the ecological compatibility of the purification of water is so great that even its combination with ion-exchange deionisation by means of filters containing a mixed bed of granulated ion exchangers has come to be widely used.[25,26]

Extreme desalination of water treated by reverse osmosis can be achieved by electrodialysis using ion-exchange membranes. This can be best carried out in two steps. In the first step of the electrodialysis, the aim is to obtain water with a specific resistance of about 1 MΩ cm, while in the second the aim is to achieve a specific resistance of the order of 18 MΩ cm. Several versions of the procedure can be selected for the preparation of water with such a specific resistance. The first version represents electrodialysis employing ion-exchange membranes and a small distance between the membranes.[27] The intermembrane distance of 0.5 mm used by Tezikov and Saldadze makes it possible to obtain water in the required condition but at a relatively high coefficient of hydraulic resistance, requiring additional expenditure of electrical energy. The reason for the increase in the efficiency of desalination with decrease in the inter-membrane distance was investigated by laser interferrometry[28] and it was shown that the overlap of the boundary diffusion layers of the solution at the interfaces with the membranes plays a decisive role. For large intermembrane distances, there remains a zone in the middle of the desalination section in which no concentration changes occur. The second version, electrodialysis with the desalination section between the membranes filled with a mixed bed of granulated ion exchangers, was proposed by Walters, et al.[29] Glueckauf[30] investigated the function of the grains in electrodialysis with an ion-exchanger filled intermembrane section and found that heteropolar contacts between the anion-exchange grains and the cation-exchange membrane, on which water undergoes irreversible dissociation with formation of hydroxide ions migrating along the circuit and regenerating continuously the ion exchanger, play the main role. Subsequently anion exchange takes place between the hydroxide-form of the anion exchanger and the impurities in the water. Correspondingly water also decomposes the contacts between the cation-exchange grains and the anion-exchange membrane, hydrogen ions migrating along the chain of cation exchanger grains, regenerating them continuously. This is followed by ion exchange between the cationic impurities in the water and the hydrogen ions. Complete deionisation takes place because the desorption products (hydrogen and hydroxide ions) recombine to water—an electrolyte with a low dissociation constant. The impurity cations and anions migrate respectively along the chains of grains to equipolar membranes and are removed through them by the electric current to adjoining sections where the concentration takes place. In their study of the mechanism of transport through pairs of equipolar $\overrightarrow{C-C}$ and $\overrightarrow{A-A}$ grains (C and A denote cation-exchanger and anion-exchanger grains respectively and → indicates the direction of the direct current from the anode to the cathode) and also through heteropolar $\overrightarrow{C-A}$ and $\overrightarrow{A-C}$ grains, Gnusin and Grenenyuk established a series of fundamental features of the mass transfer.[31] They believe that equipolar contacts do not introduce significant changes into the distribution of local concentrations in the solution, whereas the C–A contacts concentrate the electrolyte in capillary gaps. The electrolyte concentrated in the capillary gaps is distributed by convection throughout the bulk of the solution in the desalination section, reducing fundamentally the efficiency of the process. This is the reason for the attempts to find a way of eliminating the C–A contacts. A solution was found using monolayers of alternating cation- and anion-exchanger grains placed in an inert grid.[32] The replacement of the inert grid by an ion-conducting grid makes it possible to reduce the energy expenditure to 0.2 kW h m^{-3}.[33]

Only electrodialysis with ion-exchange membranes and with the desalination sections between the membranes filled with a mixed bed of granulated ion exchangers can be used for the membrane preparation of ultrapure water in the final stage: in the regime with periodic circulation[34] and in the direct-flow continuous regime.[35] Many years after these investigations similar studies were performed in the USA by the Millipore Corporation[36] and in France.[37] As in the earlier studies,[34,35] the attainment of a specific resistance close to the limiting value was noted.[36,37] However, in addition to what was already known, it was stated[36] that the secondary contamination of water by solid particles is not observed. Thus the sequence of steps in the preparation of ultrapure water by membrane methods consists of filtration, microfiltration, and ultrafiltration stages, reverse osmosis, electrodialysis with ion-exchange membranes and a layer of granulated ion exchangers, and electrodialysis with ion-exchange membranes and the intermembrane space filled with a mixed layer of granulated ion exchangers.

In the membrane purification of water, there is no increase in the mass of substances in waste water compared with the mass of the extracted impurities. In the concentration sections, the mass is doubled and the concentration of inorganic substances is equal to the mass extracted, which imparts to membrane methods appreciable advantages over ion exchange and distillation. To some extent the future of membrane methods, which have been officially declared to be technologies for the XXIst century,[38] depends on the fraction of electrical energy which they consume. Estimation of the ecological compatibility of combined membrane methods yields the lowest coefficients of the pollution of the environment (Fig. 1), which

enables one to predict their successful development. On the other hand, we may draw attention to the large amount of scientific labour required by membrane methods[19] and also the necessity for qualified staff to use them. Theoretical studies in the field of mass transfer through membranes, which make it possible to create mathematical models optimising the membrane technology, have become particularly urgently required.

V. Removal of nitrates from natural waters

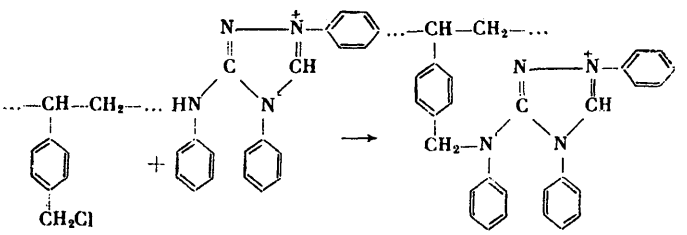
Apart from the tasks involving the general extreme purification of water, there are those concerned with local elimination of components which constitute a risk to human health. Among the problems which have given rise to particularly great alarm in society is that of the removal of nitrates from drinking water. Nitrates enter water as a consequence of the large-scale use of mineral fertilisers containing them. Mineral fertilisers began to be employed after Leibig developed in 1840 the theory of the mineral nutrition of plants, according to which man irreversibly extracts nitrogen compounds from the soil but their deficiency can be made good by nitrogen-containing inorganic salts (nitrates). The nitrates not assimilated by plants enter natural waters, which leads to two types of illness. The first is methaemoglobinemia induced by the oxidation of haemoglobin to methaemoglobin, which is incapable of chemisorbing oxygen. It has been established that an increase in the content of nitrates, nitrites, aniline, and nitrobenzene leads to methaemoglobinemia. Methaemoglobinemia is particularly dangerous for embryos and suckling infants, whose blood contains up to 85% of foetal haemoglobin, which is more susceptible to the action of nitrates than the haemoglobin of an adult human being. The second type of illness is caused by the reduction of nitrates to nitrites in the intestine followed by the reaction with amines, which converts them into carcinogenic nitrosamines. The content of nitrates in natural waters used for drinking has therefore been limited to 50 mg litre^{-1} in the countries of European Economic Community and in 1994 it is planned to reduce the limiting permissible concentration to 30 mg litre^{-1}.

Unfortunately the use of nitrates can no longer be avoided, since this would require a threefold increase in the arable land. It is therefore essential to determine nitrogen-containing substances in the soil in order to introduce fertilisers in controlled amounts. The use of a large mass of fertilisers, which cannot be immediately assimilated by soils and plants, is particularly dangerous. The membrane method for the controlled release of substances is therefore especially promising.[39] The Rose-Nelson pump, consisting of three sections separated by one semipermeable membrane and one impermeable elastic membrane, may serve as the simplest example of the use of this method. One of the three sections contains water, whilst the other, adjoining section contains the salt. The osmotic flux through the semipermeable membrane into the salt-filled section increases the osmotic pressure in the latter and, in the presence of the elastic membrane, leads to an increase in the volume of the section. The elastic membrane slowly forces out of the section the fertiliser solution or any preparation, including therapeutic preparations. One may foresee the wide scale future employment of this membrane method for the introduction of fertilisers into the soil. In the introduction of nitrate fertilisers, it is very important to select an appropriate time for this purpose. The best time for the feeding of plants is the vegetative period. Unfortunately at the present time the necessary agrochemical expertise involving the use of fertilisers is lacking and this leads to the limiting permissible concentration being appreciably exceeded in the drinking water in many regions, which require special methods for the elimination of nitrates from natural waters.

We shall consider the possibility of the elimination of nitrates from natural waters by biological and biotechnological methods. For the microbiological removal of nitrates, it is essential to create anaerobic conditions, which is in principle possible directly in the soil but requires not only the participation of bacteria but also of organic substances. For example, under laboratory conditions the anaerobic elimination of nitrates is carried out in the presence of ethanol and sodium phosphate. Such requirements cannot be satisfied in practice. The biotechnological method, in which bacteria convert nitrates into molecular nitrogen, has already found an application and has been proposed by the name Biodenit by the "Energy Equipment for Heidelberg Joint Stock Company". However, the application of this method leads to the production of a large amount of biomass and side products, which is also unacceptable for the conditioning of water in order to obtain drinking water yet alone for its intense purification. The ion-exchange method for the removal of nitrates from drinking water has come to be widely used. Its effective application required anion exchangers selective with respect to nitrates. There are two versions of the synthesis of selective ion exchangers. The first involves the introduction into the polymer of an ionogenic group with a specific strong interaction with a particular ion. The classical example is provided by the synthesis of the potassium-selective cation exchanger by Scogside,[12] who obtained it by introducing into the polymer hexanitrodiphenylamine (dipicrylamine), which is used as a reagent for the precipitation of potassium.

The second procedure involves the regulation of the properties of the polymers, promoting an increase in selectivity. For example, the introduction of the cross-linking agent diphenylbenzene in the polymerisation of styrene increases the selectivity of the ion exchangers as a result of the decrease in the water content. The reduction of the water content is accompanied by a decrease in the number of water molecules between the fixed ion and the counterion in the ion exchanger and an intensification of the electrostatic interaction. Electrostatic interactions involving ions of different radius and bearing different charges differ fairly markedly, whereas the energies of the hydrogen bonds formed by water molecules between the fixed ion and the counterion are similar.

A nitrate-selective anion-exchanger was obtained by the reaction of the chloromethylated styrene-divinylbenzene copolymer with 1,4-diphenyl-2-phenylaminodihydrotriazole (nitrone):[40]

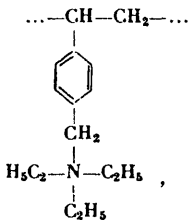


The isotherms of the exchange of chloride and sulphate ions for nitrate ions obtained by Frölich and Weber[40] show the high selectivity of the above anion exchanger in relation to nitrate ions. The nitrone anion exchanger is regenerated chemically with a 5% solution of sodium chloride. After many repetitions of these cycles,

no losses in exchange capacity were observed. The traditional type of highly basic anion exchanger made of the styrene-divinylbenzene copolymer and comprising the benzyltrimethylammonium elementary unit (AV-17) exhibits a higher selectivity in relation to sulphate ions. The selectivity sequence is as follows:

sulphate > nitrate > chloride > bicarbonate

The replacement of methyl groups in the fixed ion by ethyl groups alters the selectivity sequence in the anion exchanger



and the latter becomes more selective in relation to nitrates.

The membrane methods for the removal of nitrates from natural waters are ecologically more promising. However, the membranes synthesised at the present time exhibit a selectivity of 86% with respect to nitrate ions, while the selectivities with respect to chloride and sulphate ions are 94 and 90% respectively. Furthermore, in reverse osmosis the membranes retain also cations. In particular, the selectivity with respect to calcium ions reaches 96%.[42] Therefore reverse osmosis makes it possible to demineralise water at the present time but does not allow the selective extraction of nitrates from it.

Electrodialysis with ion-exchange membranes is especially promising for the removal of nitrate from drinking water.[42] The use of a mixed layer of ion exchangers for the filling of the desalination sections permits the intense elimination of nitrates from water, but, as in reverse osmosis, it is not possible to achieve the selective removal of nitrates from water. Therefore the membrane method has still not solved the problem of the selective transport of nitrates through membranes and the ion-exchange extraction of nitrates with the aid of the nitrate-selective ion exchangers is most useful.

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Translated from *Uspekhi Khimii* **60** 2497–2527 (1991) U.D.C. 547.717'898.07

Nitrogen- and sulphur-containing macroheterocycles and their complexes. New low molecular models of enzymes†

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ABSTRACT. Methods of synthesising *N,S*-containing macroheterocycles and their complexes with cations, anions and organic molecules are discussed. Complexes of copper(II) ions with thiazamacrocyclic ligands as low molecular structural models of the active centres of "blue" proteins are considered. The possibility of transporting metal ions through membranes by thiaza-crown compounds and the application of complexes of them in catalysis has been shown. Promising directions for using nitrogen- and sulphur-containing macroheterocycles in modelling enzymes are discussed.

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I. Introduction

The vigorous development of the chemistry of macroheterocyclic compounds which has been observed in recent years is explained by the discovery of crown ethers and their ability to form stable complexes selectively with ions of the alkali and alkaline earth metals.[1–3] Further investigations in this area have shown that the macroheterocycles bind not only metal cations but also anions and even neutral organic molecules, forming complexes of the "host–guest" type.[2,3]

The study of nitrogen-sulphur-containing macroheterocycles and complexes of them as models of biological systems and processes occurring *in vivo* involving compounds of nitrogen and sulphur has become urgent. In particular, complexes of thiaza-crown compounds with copper(II) ions attract attention as models of copper proteins ("blue" proteins). The active centre of "blue" proteins is a complex of a copper(II) ion in an environment of nitrogen and sulphur atoms. It is characterised by spectral and oxidation–reduction properties unusual for copper(II) compounds. Investigation of the analogous physicochemical characteristics for complexes of macroheterocycles containing nitrogen and sulphur with copper(II) ions has shown that they are identical in this respect to a copper-containing "blue" protein. Copper proteins are important metal-containing enzymes for living organisms. They participate in electron-transfer, the metabolism of compounds and they catalyse oxidation–reduction functions of cell respiration. The study of copper(II) complexes with polythiazacrown compounds is urgent due to their use as low molecular models of metalloenzymes.

The metalloenzymes are highly organised systems possessing high substrate selectivity and catalytic activity. The further development of synthetic enzymes ("synzymes")[5,98] is only possible on continuing from simple monomolecular systems to oligomolecular systems, particularly to associates, bound by non-covalent interactions, i.e. by transferring from molecular chemistry to supramolecular chemistry.[4,5]

The development of supramolecular chemistry to date already enables the recognition and selective interaction of a macrocyclic receptor with various substrates to be effected.[5] This interaction is effected in two ways. Complex-formation may occur within the cavity of a macrocycle, when the receptor is able to "envelop" a substrate and retain it through the formation of many non-covalent bonds. Biological analogues of these endoreceptors may be found in the active centres of enzymes where a substrate insignificant in size is bound within the cavity of a large protein molecule. Another type of substrate binding uses the outer surface of the receptor. In this case complex-formation of the exoreceptor with the substrate occurs by surface–surface interaction. The biological analogy for this may be the protein–protein interactions occurring on the antigen–antibody interface, leading to immunological recognition processes.

N,S-Containing macroheterocycles display the properties of both endo- and exoreceptors in that they selectively bind cations, anions and organic substrates. The further development of the chemistry of nitrogen- and sulphur-containing macroheterocycles and their investigation as enzyme models may become the chief instrument for studying the structure and biological properties of many biopolymers.

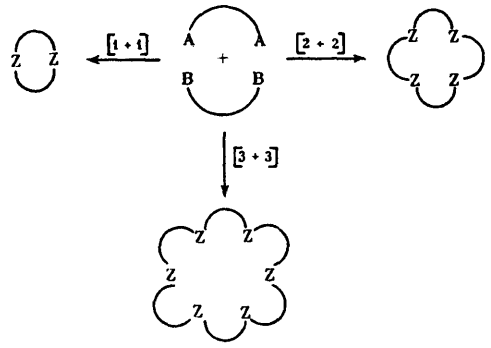
II. Synthesis of *N,S*-containing macroheterocycles

1. Aliphatic polythiaza crown compounds

The formation of macrocyclic compounds is complicated by the presence of secondary linear polycondensation products since the oligomers formed as intermediates may later take part in both intra- and intermolecular reactions at the same time. One further difficulty is the occurrence of cyclisation at several stoichiometric levels

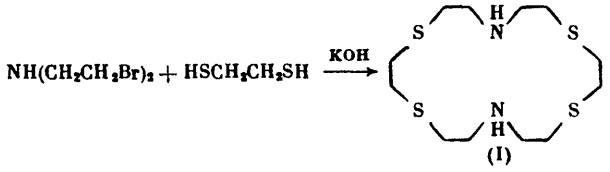
†Awarded first prize at the competition for reviews organised by section No. 4 "Organic and Hetero-organic Synthesis" of the Inter-departmental Scientific-Technical Bureau on the priority directions of chemical science and technology.

simultaneously. If one molecule of each starting material partakes in the formation of the macromolecule, that is designated a [1 + 1] condensation. There are also [2 + 2] and [3 + 3] condensations.



High dilution methods and template reactions are mainly used to prevent side reactions.

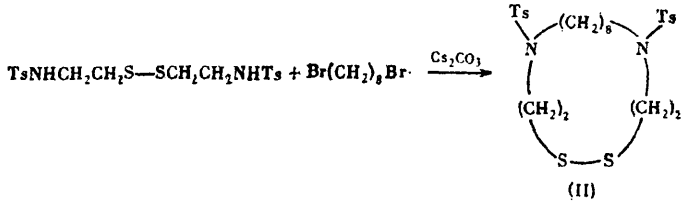
For example, the reaction of bis(2-bromoethyl)amine with ethane-1,2-dithiol takes place under conditions of high dilution by a [2 + 2] condensation.



(I)

The yield of 1,4,10,13-tetrathia-7,16-diazacyclo-octadecane (I) was 45%.[6,7]

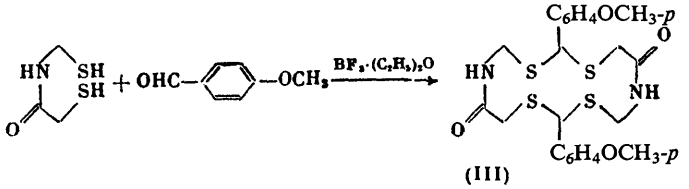
The macrocyclic disulphide (II) is obtained by the reaction of ditosylated cystamine with 1,8-dibromooctane in DMF in the presence of Cs_2CO_3.[8]



(II)

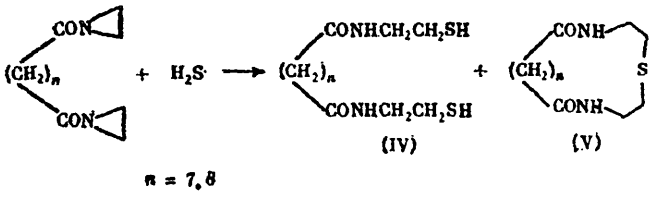
Reaction was carried out at room temperature for 24 h, the yield of macroheterocycle (II) was 20%.

The *N*-(mercaptomethyl)amide of thioglycolic acid reacts with anisaldehyde by a [2 + 2] condensation with the formation of the tetrathiadiaza crown compound (III) (61% yield).[9]

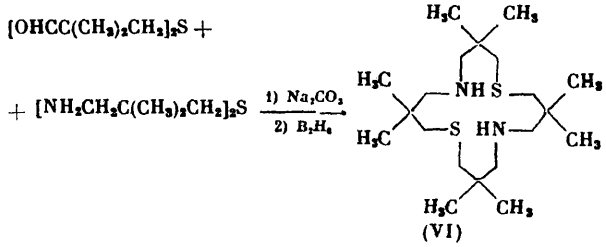


(III)

Fission of the aziridine rings of the bis-*N*-ethylenimides of azelaic and sebacic acids with hydrogen sulphide leads to a mixture of the linear bis(2-mercaptoethyl)diamides of the corresponding acids (IV) and the macrocyclic sulphide (V).[10]

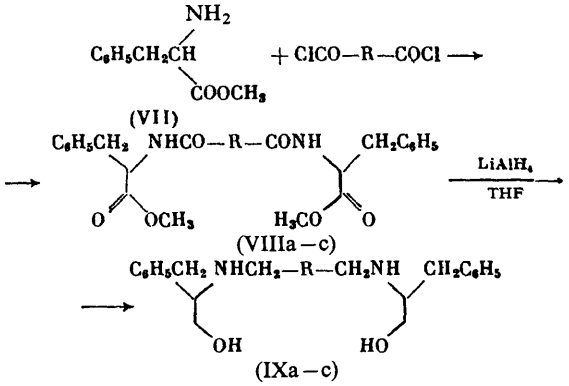


The dithiadiaza crown compound (VI), containing quaternary carbon atoms, is obtained by the reaction of 2,2,6,6-tetramethyl-4-thiaheptane-1,7-dial with 2,2,6,6-tetramethyl-4-thia-1,7-heptanediamine with subsequent treatment with diborane in THF.[11]



(VI)

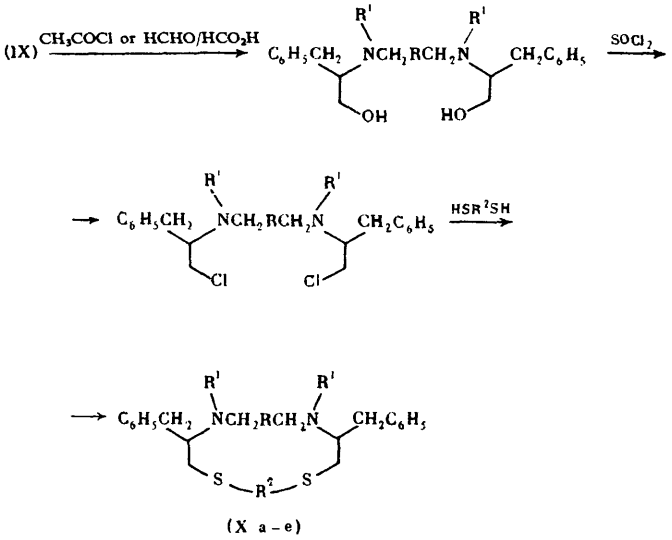
The synthesis of chiral *N,S*-containing macrocycles is effected by the reaction of L-phenylalanine methyl ester (VII) with the diacid chlorides of dicarboxylic acids with several subsequent conversions.[12] On using the diacid chlorides of oxalic, succinic and diglycolic acids, the diamides (VIIIa–c) were obtained in 68–90% yield. Reduction of them with $LiAlH_4$ in THF leads to the diaminoalcohols (IXa–c).



R = a bond (a), $-(CH_2)_2-$ (b), $-CH_2OCH_2-$ (c)

Treatment with CH_3COCl or $HCHO/HCO_2H$ and subsequent reduction gives the alkyl substituted diaminoalcohols. Reaction of the latter with $SOCl_2$ and subsequent cyclisation with α,ω-alkane-

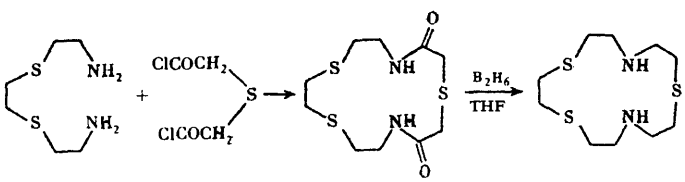
dithiols leads to the chiral *C*- and *N*-substituted *N,S*-containing macrocycles (Xa–f) in 16–26% yield.



(X a–e)

(Xa): R = a bond, $R^1 = C_2H_5$, $R^2 = -(CH_2)_2-$;
(Xb): R = a bond, $R^1 = C_2H_5$, $R^2 = -(CH_2)_3-$;
(Xc): R = a bond, $R^1 = C_2H_5$, $R^2 = -(CH_2)_4-$;
(Xd): $R = -(CH_2)_2-$, $R^1 = C_2H_5$, $R^2 = -(CH_2)_3-$;
(Xe): $R = -(CH_2)_2-$, $R^1 = CH_3$, $R^2 = -(CH_2)_3-$;
(Xf): $R = -CH_2OCH_2-$, $R^1 = CH_3$,
$R^2 = -(CH_2)_2S(CH_2)_2S(CH_2)_2-$

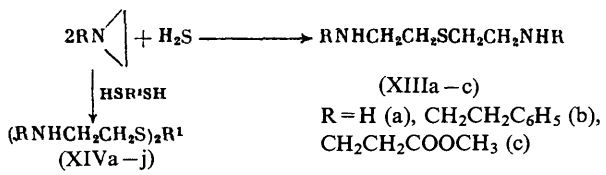
The most accessible method of synthesis of *N,S*-containing macroheterocycles is the acylation of open chain sulphur-containing diamines with diacid chlorides of dicarboxylic acids. On reacting 1,8-diamino-3,6-dithiaoctane with the diacid chloride of thiodiglycolic acid, a cyclocondensation of the [1 + 1] type takes place with the formation of the macroheterocycle (XI).[13]



(XI) (XII)

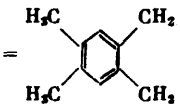
Reduction of the amide groups of the macrocycle (XI) with diborane leads to the crown compound (XII) in 57% yield.

Methods have been developed for obtaining polycarbo-functional *N,S*-containing open chain compounds (XIIIa–c) and (XIVa–j) on the basis of which macroheterocycles with the same various exocyclic functional groups have been synthesised.[14–27]

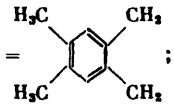


(XIIIa–c)
R = H (a), $CH_2CH_2C_6H_5$ (b), $CH_2CH_2COOCH_3$ (c)

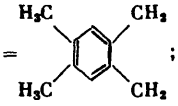
(XIVa): R=H, $R^1=CH_2CH_2$;

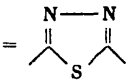
(XIVb): R = H, R^1 =  ,

(XIVc): $R = CH_2CH_2C_6H_5$, $R^1 = CH_2CH_2$;

(XIVd): $R = CH_2CH_2C_6H_5$, R^1 =  ;

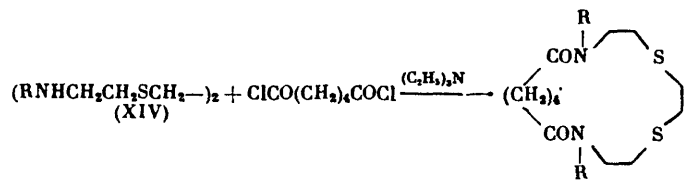
(XIVe): $R = CH_2CH_2COOCH_3$, $R^1 = CH_2CH_2$;

(XIVf): $R = CH_2CH_2COOCH_3$, R^1 =  ;

(XIVg): $R = CH(COOCH_3)CH_2COOCH_3$, $R^1 = CH_2CH_2$;
(XIVh): $R = CH(COOC_2H_5)CH_2COOC_2H_5$, $R^1 = CH_2CH_2$;
(XIVi): $R = CH_2CH_2CN$, $R^1 = CH_2CH_2$;
(XIVj): $R = CH_2CH_2COOCH_3$, R^1 = 

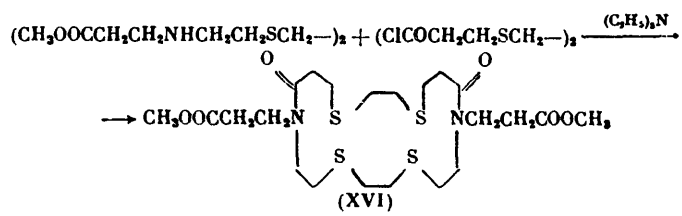
The sulphur-containing diamides are obtained by the reaction of ethylenimine or its *N*-substituted derivatives with hydrogen sulphide or α,ω-aliphatic, aromatic and heterocyclic dithiols.[14–27] The reaction with H_2S proceeds in methanol at room temperature and with α,ω-dithiols at 60 °C. The yields of diamines (XIIIa–c) and (XIVa–j) were 80–90%.

The cyclocondensation of diamines (XIVa), (XIVc), (XIVe) and (XIVi) with the diacid chloride of adipic acid leads to the 16-membered macroheterocycles (XV) in 70% yield.[16]



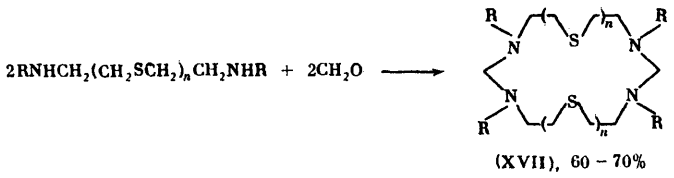
R = H, $CH_2CH_2C_6H_5$, $CH_2CH_2COOCH_3$, CH_2CH_2CN

The 20-membered macrocycle (XVI) containing exocyclic methoxycarbonylethyl groups is obtained by the reaction of diamine (XIVe) with the diacid chloride of dithiaoctane-dicarboxylic acid.[17]



(XVI)

The macroheterocycles (XV) and (XVI) were synthesised in dry benzene under high dilution conditions. The secondary diamines (XIIIb, c) and (XIVc, e, g, i) form a 22-membered polythiaza-crown compound (XVII) with formaldehyde.[25-27]



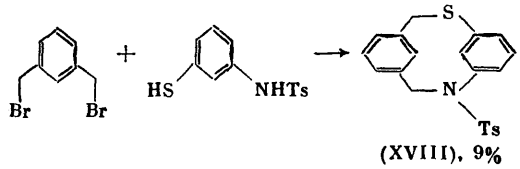
(XVII), 60 – 70%

n=1: R=$CH_2CH_2C_6H_5$, $CH_2CH_2COOCH_3$; n=2: R=$CH_2CH_2C_6H_5$, $CH_2CH_2COOCH_3$, $CH(COOCH_3)CH_2COOCH_3$, CH_2CH_2CN.

The cyclocondensation proceeds in methanol under high dilution conditions according to a [2 + 2] type.

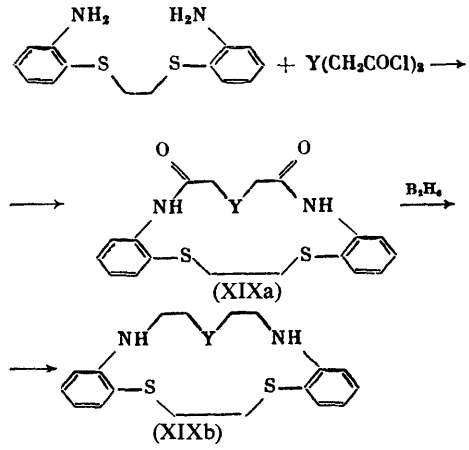
2. *N,S*-containing cyclophanes

Thiazamacrocycles containing a benzene ring in the molecule possess a stable cyclic skeleton which is important on complex-formation with metal ions and organic molecules. For example, the 10-membered cyclophane (XVIII) is obtained by the reaction of 1,3-bis(bromomethyl)benzene with 1-[(*p*-toluenesulphonyl)amino]-3-mercaptobenzene in the presence of caesium hydroxide under high dilution conditions.[28]



(XVIII), 9%

The acylation of 1,4-bis(2-aminophenyl)-1,4-dithiabutane with the diacid chlorides of glutaric and thiodiglycolic acids proceeds more successfully.[29] Reaction is effected under high dilution conditions in benzene, the yield of sulphur-containing diamides (XIXa) was 64–90%.



(XIXa)

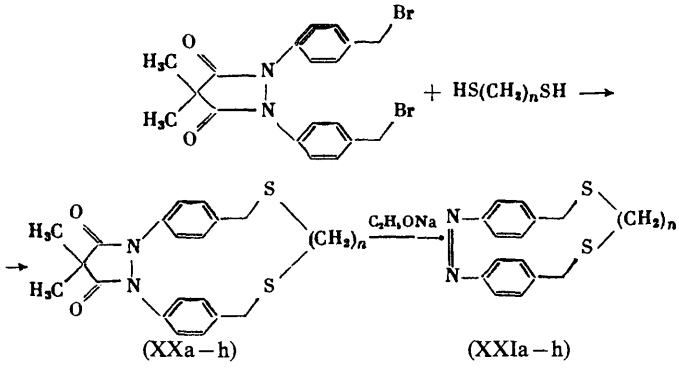
(XIXb)

Y = CH_2, S

Reduction of the amide groups with boron hydride leads to the macroheterocycle (XIXb) in 78–95% yield.

Crown compounds containing chromophoric groups are of interest as new types of macroheterocycle dyestuffs, organic reagents and extracting agents. One of the methods of synthesis of such chromophoric crown compounds is the introduction of an azo group into the molecule. An endocyclic azo group not only does not impair the complex-forming properties of crown compounds but also confers on them new interesting properties such as rigidity of the cyclic skeleton and the possibility of changing their ability towards complex formation under the action of irradiation due to *cis-trans*-isomerisation.

Dithiadiaza[2.n]paracyclophanes (XXa–h) are obtained by the reaction of the appropriate dibromides with α,ω-alkanedithiols. Treatment of them with sodium ethoxide leads to the *N,S*-containing macroheterocycles (XXIa–h) containing an endocyclic azo group.[30]

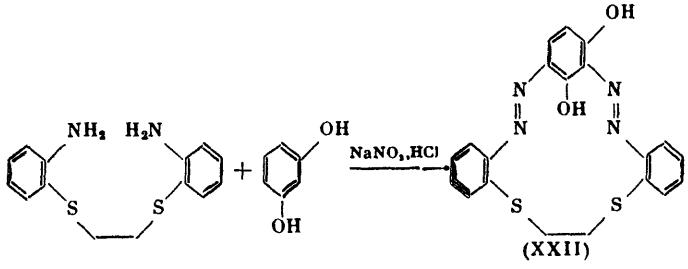


(XXa–h) (XXIa–h)

n=2 (a), 3 (b), 4 (c), 6 (d), 7 (e), 8 (f), 9 (g), 12 (h).

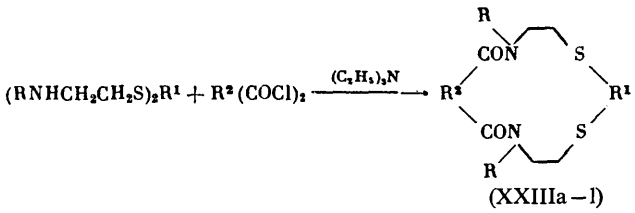
It was found that the macroheterocycles (XXIa–c) have the *cis* geometry while the cyclophanes of larger dimensions (XXIg, h) are more inclined to form *trans* isomers. The macrocycles (XXId–f) have both *cis* and *trans* configurations.

The azo coupling reaction of 1,4-bis(2-aminophenyl)-1,4-dithiabutane with resorcinol has been studied. It leads to a sulphur-containing cyclophane with two azo groups in the macrocycle (XXII).[31]



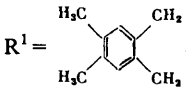
(XXII)

The synthesis of the *N,S*-containing macrocycles (XXIIIa–l) containing aromatic rings and exocyclic functional groups has been effected by the reaction of α,ω-diamines (XIVa–j) with the diacid chlorides of phthalic and terephthalic acids.[14–27,33–37]



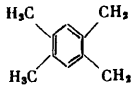
(XXIIIa–l)

(XXIIIa): R = H, $R^1 = CH_2CH_2$, $R^2 = 1,2\text{-}C_6H_4$;
(XXIIIb): $R = CH_2CH_2C_6H_5$, $R^1 = CH_2CH_2$, $R^2 = 1,2\text{-}C_6H_4$;
(XXIIIc): $R = CH_2CH_2COOCH_3$, $R^1 = CH_2CH_2$, $R^2 = 1,2\text{-}C_6H_4$;
(XXIIId): $R = CH(COOCH_3)CH_2COOCH_3$, $R^1 = CH_2CH_2$, $R^2 = 1,2\text{-}C_6H_4$; (XXIIIe): $R = CH(COOC_2H_5)CH_2COOC_2H_5$, $R^1 = CH_2CH_2$; $R^2 = 1,2\text{-}C_6H_4$; (XXIIIf): R = H,



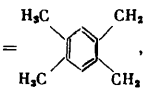
$R^2 = 1,2\text{-}C_6H_4$;

(XXIIIg): $R = CH_2CH_2COOCH_3$, $R^1 =$



$R^2 = 1,2\text{-}C_6H_4$; (XXIIIh): $R = CH_2CH_2COOCH_3$, $R^1 = CH_2CH_2$, $R^2 = 1,4\text{-}C_6H_4$; (XXIIIi): $R = CH_2CH_2C_6H_5$, $R^1 = CH_2CH_2$, $R^2 = 1,4\text{-}C_6H_4$; (XXIIIj): $R = CH(COOCH_3)CH_2COOCH_3$, $R^1 = CH_2CH_2$, $R^2 = 1,4\text{-}C_6H_4$;

(XXIIIk): $R = CH_2CH_2COOCH_3$, $R^1 =$



$R^2 = 1,4\text{-}C_6H_4$;

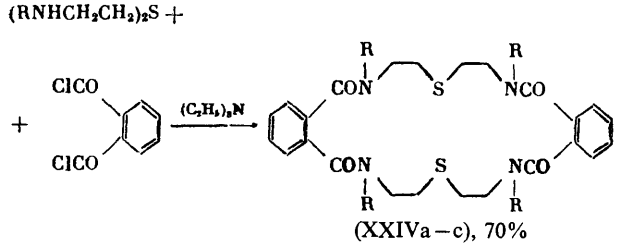
(XXIIIl): $R = CH_2CH_2COOCH_3$ $R^1 =$



$R^2 = 1,2\text{-}C_6H_4$.

Cyclocondensation occurs according to the [1 + 1] type in dry benzene under high dilution conditions. The yields of the *N,S*-containing macroheterocycles (XXIIIa–l) were 70–80%.

Under analogous conditions the reaction of diamines (XIIIa–c) with the phthaloyl chloride was effected according to a [2 + 2] type with the formation of the 22-membered macroheterocycles (XXIVa–c).[32]

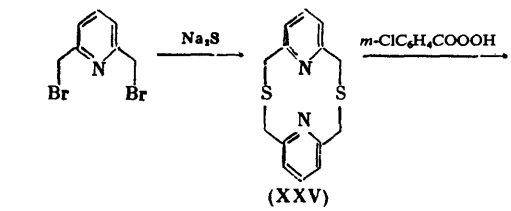


(XXIVa–c), 70%

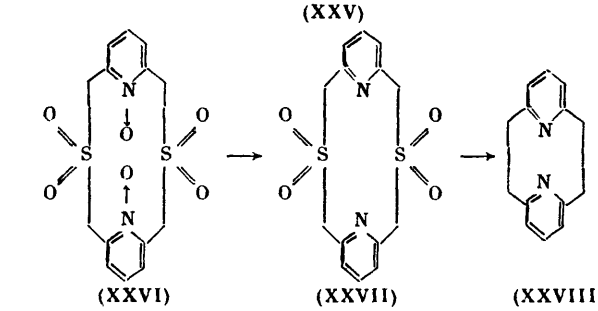
R = H (a), $CH_2CH_2C_6H_5$ (b), $CH_2CH_2COOCH_3$ (c)

3. Sulphur-containing pyridinophans

The synthesis of pyridinophan (XXV) is effected by the reaction of 2,6-bis(bromomethyl)pyridine with sodium sulphide by a [2 + 2] condensation.[38]



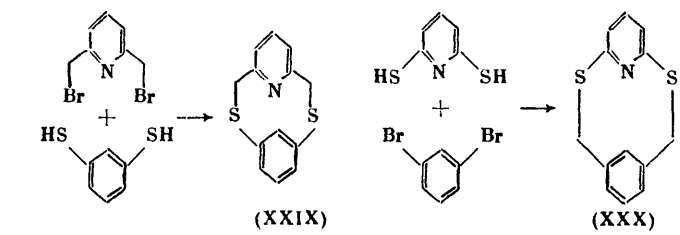
(XXV)



(XXVI) (XXVII) (XXVIII)

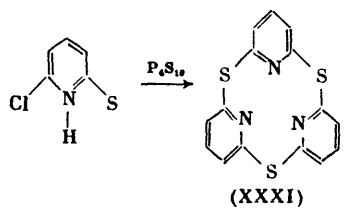
Oxidation of pyridinophan (XXV) leads to its bis-sulphone bis-*N*-oxide (XXVI). The selective reduction of the *N*-oxide groups with iron in trifluoroacetic acid gives the bis-sulphone (XXVII), pyrolysis of which leads to pyridinophan (XXVIII) in 46% yield.[39]

A series of pyridinophans such as (XXIX) or (XXX) containing bridge carbon–sulphur bonds is obtained by the reaction of 2,6-bis(bromomethyl)pyridine with dithioresorcinol[40] and other dithiols,[41–44] and also by the reaction of 2,6-bis(mercaptomethyl)pyridine or 2,6-pyridinedithiol with 1,3-dihaloalkylbenzenes.[45–50] Other methods of synthesis of such pyridinophans have also been described.[51,58]



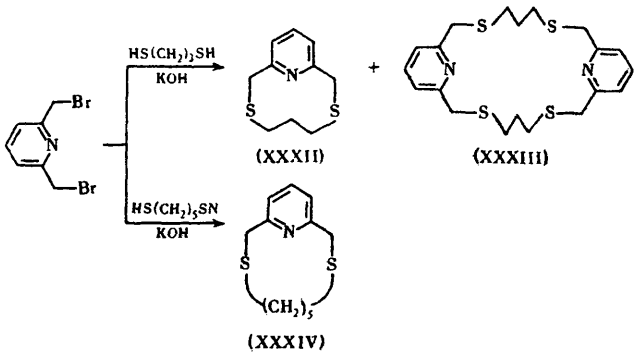
(XXIX) (XXX)

The pyridinophan (XXXI) with bridging sulphur atoms is obtained by intramolecular condensation of 6-chloropyridine-2-thione in the presence of P_4S_{10}.[52]



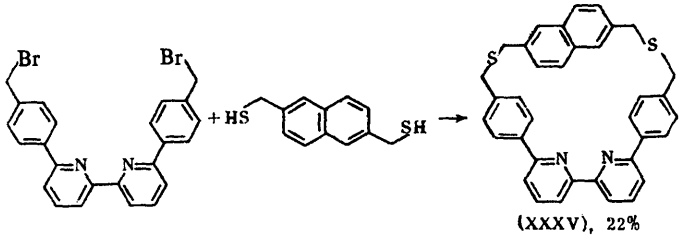
(XXXI)

The reaction of 2,6-bis(bromomethyl)pyridine with 1,3-propanedithiol occurs by a [1 + 1] and a [2 + 2] condensation simultaneously and leads to a mixture of the ten (XXXII) and twenty-membered pyridinophans (XXXIII) respectively.[53]



The analogous reaction with 1,5-pentanedithiol leads exclusively to the twelve-membered macroheterocycle (XXXIV), the formation of the dimeric macrocycle was not observed.

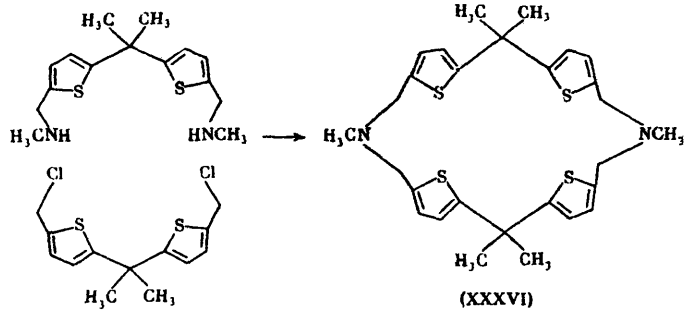
The thiaza crown compound (XXXV) containing a bipyridyl fragment is obtained by the reaction of 6,6′-di-(4-bromomethylphenyl)-2,2′-bipyridyl with 2,6-bis(mercaptomethyl)naphthalene under conditions of high dilution.[54,55]



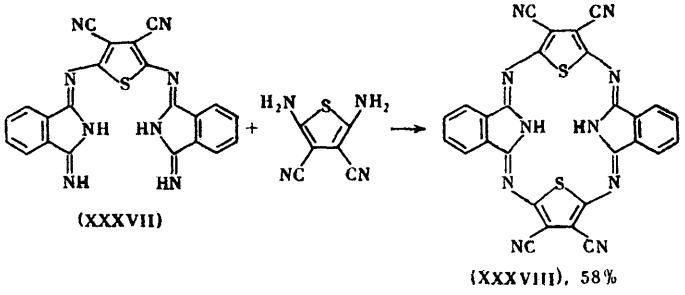
The reaction occurs in the presence of Cs_2CO_3 at 50 °C in DMF.

4. Nitrogen-containing thiophenophans

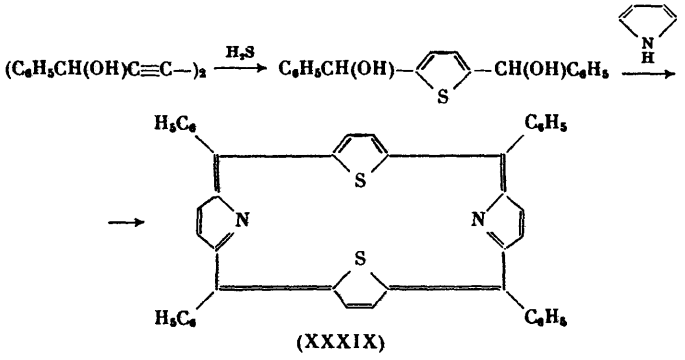
Methods have been developed for the synthesis of macroheterocycles in which thiophene rings are included as structural subunits and chains of C–N–C fragments form bridges. For example, the reaction of 2,2-bis(5′-methylaminomethyl-2′-thienyl)propane with 2,2-bis(5′-chloromethyl-2′-thienyl)propane in benzene at 40 °C leads to the *N,S*-containing macrocycle (XXXVI).[56]



The macroheterocyclic compound (XXXVIII) is formed on treatment of the derivative (XXXVII) with 2,5-diamino-3,4-dicyanothiophene.[57,58]

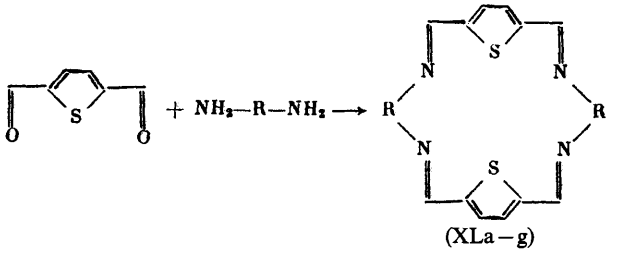


The dithiaporphyrin (XXXIX) is synthesised from 2,5-bis(phenylhydroxymethyl)thiophene and pyrrole.[59]



2,5-Bis(phenylhydroxymethyl)thiophene was obtained by the reaction of the corresponding diacetylene with hydrogen sulphide. Cyclisation was effected in a mixture of chloroacetic acid–benzene, chloroacetic acid–toluene or in propionic acid. The yield of compound (XXXXIX) was 4–10%.

The reaction of thiophene-2,5-dicarbaldehyde with α,ω-alkylenediamines has been studied.[60]



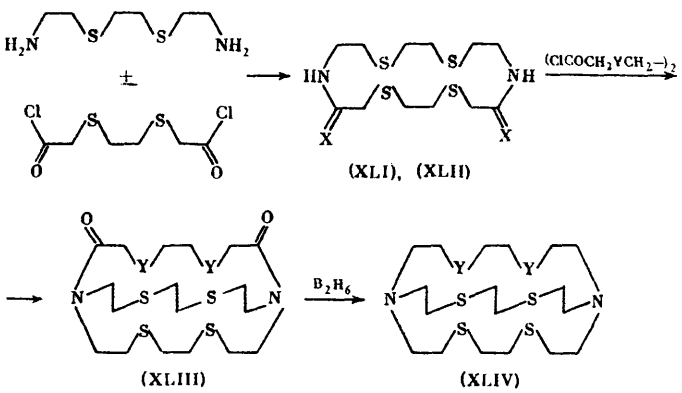
R = $(CH_2)_3$ (a), $(CH_2)_4$ (b), $(CH_2)_5$ (c), $(CH_2)_6$ (d), $(CH_2)_2S(CH_2)_2$ (e), $(CH_2)_2NH(CH_2)_2$ (f), $(CH_2)_3NH(CH_2)_3$ (g).

The reaction occurs in methanol at room temperature in 2.5 h or on heating in 0.5 h with the formation of the dimeric product ([2 + 2] condensation). The yield of *N,S*-containing macrocycles (XLa–g) varied from 50 to 90%.

5. *N,S*-Containing trimeric macroheterocyles

Trimeric macroheterocycles, cryptands, clathrochelants, form exceptionally stable complexes with a wide range of cations. They are capable of completely encapsulating a metal ion. Consequently there is undoubted interest in *N,S*-containing macrobicycles (cryptands) which form stable complexes with transition metals.[61]

The reaction of 1,8-diamino-3,6-dithioctane with the diacid chloride of 3,6-dithioctanedicarboxylic acid leads to the diamide (XLI). The subsequent reduction of diamide (XLI) with diborane gives the *N,S*-containing macrocycle (XLII). The macrobicyclic diamides (XLIII) are obtained by the condensation of the latter with diacid chlorides of dicarboxylic acids. The cryptands (XLIV) are obtained in 30% yield by reduction of the diamides with diborane.

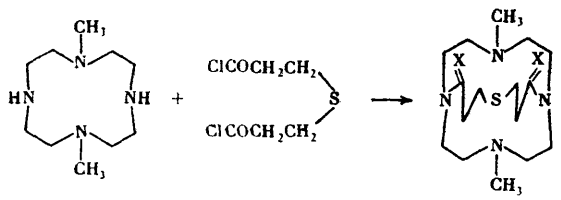


(XLI), (XLII)

(XLIII) (XLIV)

(XLI): X = O; (XLII): X = H_2; (XLIII), (XLIV): Y = S, N—Ts, NH.

The synthesis of cryptand (XLVII), containing four nitrogen atoms and one sulphur atom in the molecule has been carried out.[62]

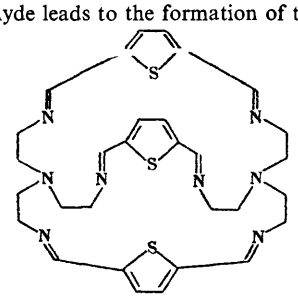


(XLVI), (XLVII)

(XLVI): X = O; (XLVII): X = H_2.

The basis of the preparation of (XLVII) is the reaction of the monomacrocyclic compound 1,7-dimethyl-1,4,7,10-tetraazacyclododecane with the diacid chloride of 3,3'-thiodipropionic acid. The macrobicyclic diamide (XLVI), formed in 75% yield, is reduced in diborane in THF. The cryptand (XLVII) is isolated in 68% yield.

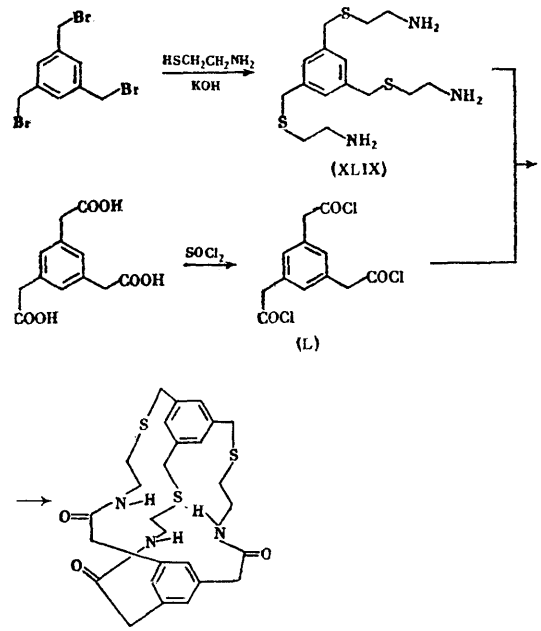
Treatment of tris(2-aminoethyl)amine with thiophene-2,5-dicarbaldehyde leads to the formation of the cage molecule (XLVIII).[63]



(XLVIII)

The reaction occurs at a molar ratio of trisamine and dialdehyde of 2:3 [yield of the macrobicycle (XLVIII) was 56%].

The synthesis of trithiacyclophan (LI) containing three amide groups is effected by the condensation of the triamine (XLIX) with the triacid chloride (L) by the following scheme.[64]



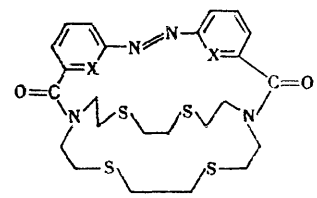
(XLIX)

(L)

(LI)

The triamine (XLIX) is obtained by the reaction of 1,3,5-tris-(bromomethyl)benzene with cysteamine in the presence of KOH in methanol and the triacid chloride of benzene-1,3,5-triacetic acid (L) is synthesised by reaction with thionyl chloride in toluene. Reaction of the triamine (XLIX) with the triacid chloride (L) occurs in dry THF [yield of macrobicycle (LI) is 11%].

The photosensitive *N,S*-containing cryptands (LII) and (LIII) are synthesised by the cyclocondensation of the triaza-crown compound (XLII), with 6,6'-bis(chloroformyl)-2,2'-azopyridine and with 3,3'-bis(chloroformyl)azobenzene respectively under high dilution conditions.[65]



(LII): X = N;
(LIII): X = CH.

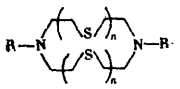
(LII), (LIII)

The yields of *trans*-cryptands (LII) and (LIII) were 33 and 24% respectively.

Polymacrocyclic systems may enclose two or more metal cations in the internal cavity of the molecule. Such cryptates are of interest as models of polynuclear biological complexes or as polynuclear catalysts.

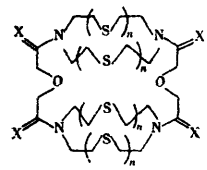
A general method of constructing cylindrical polymacrocyclic systems has been proposed.[66,67] Synthesis of the sulphur-containing trimacrocyclic tetraamide (LVa) is based on the condensation of the

macrocycle (LIVd), containing reactive substituents at the nitrogen atoms, with the macroheterocycle (LIVa). Subsequent reduction of the tetraamide (LVa) with diborane leads to the cylindrical trimacrocyclic tetrathiatetraamine (LVb).

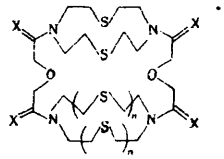


(LIVa–g)

(LIVa): $n=1$, R = H;
(LIVb): $n=1$, R = CH_3;
(LIVc) $n=1$, R = $COCH_2OCH_2COOH$;
(LIVd): $n=1$, R = $COCH_2OCH_2COOC_6H_4NO_2$-*p*;
(LIVe): $n=2$, R = CH_3;
(LIVf): $n=2$, R = $COCH_2OCH_2COOH$;
(LIVg): $n=2$, R = $COCH_2OCH_2COOC_6H_4NO_2$-*p*;



(LVa–d)



(LVIa, b)

(LVa): $n=1$, X = O;
(LVb): $n=1$, X = H_2;
(LVc): $n=2$, X = O;
(LVd): $n=2$, X = H_2;

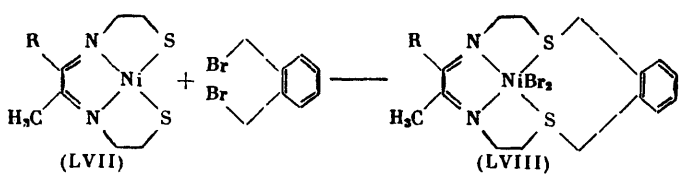
(LVIa): $n=2$, X = O;
(LVIb): $n=2$, X = H_2

The trimacrocycles (LVc) and (LVIb) are obtained in a similar manner.

6. Template synthesis of *N,S*-containing macroheterocycles

The basis of the template method of synthesis is the stereochemical organisation and orientation of reactants by a metal ion or by a metal-containing molecule. This leads to reaction of functional groups which under normal conditions is either difficult or generally impossible.[68]

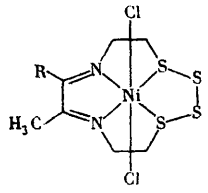
One example of template synthesis is the condensation of α-diketones with mercaptoamines in the presence of nickel salts leading to the complex (LVII) which may in its turn serve as a matrix for the formation of the macrocyclic compounds (LVIII) under the action of α,α′-dibromo-*o*-xylene.[69]



(LVII) (LVIII)

R = CH_3, C_2H_5, C_5H_{11}

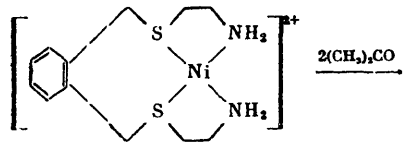
The reaction of the complex compounds (LVII) with sulphur monochloride proceeds in a similar manner and leads to the nickel-containing tetrathiadiazamacrocycle (LIX).[70]



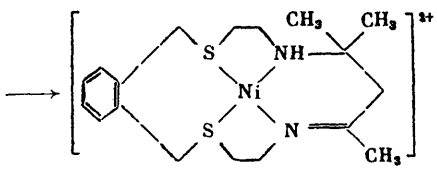
(LIX)

R = CH_3, C_2H_5, C_5H_{11}

The nickel chelate (LX) reacts with two molecules of acetone with the formation of the complex (LXI).[71]

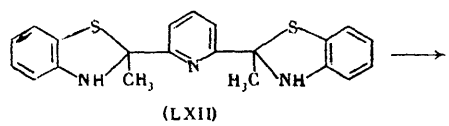


(LX)

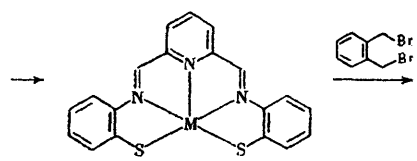


(LXI)

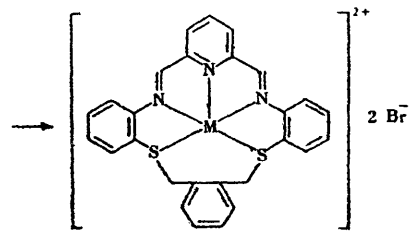
The product (LXII) of the condensation of 2,6-diacetylpyridine with 2-aminothiophenol undergoes an intramolecular rearrangement on reaction with zinc and cadmium acetates being converted into the complex (LXIII). Subsequent template reaction of it with α,α′-dibromo-*o*-xylene in acetone leads to the metal-containing macrocycle (LXIV).[72,73]



(LXII)



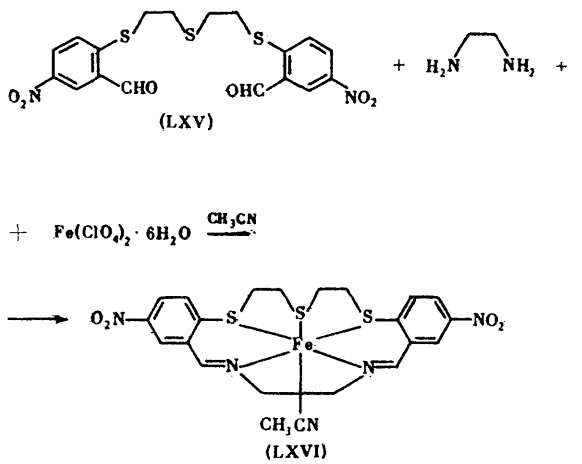
(LXIII)



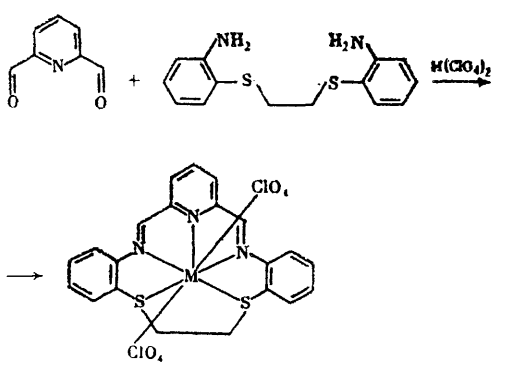
(LXIV)

M = Zn, Cd

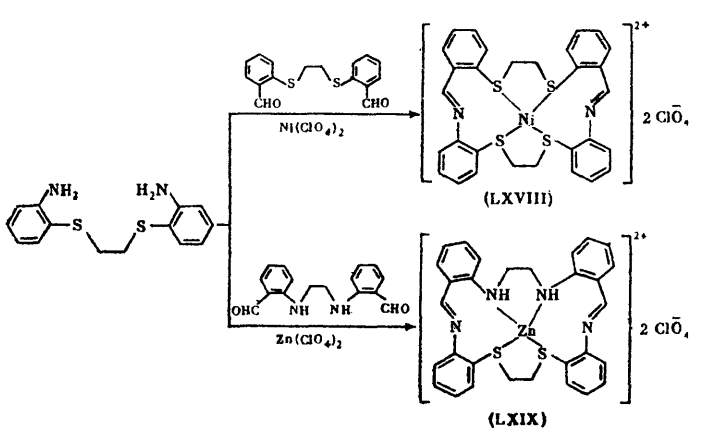
A complex of iron ion with the *N,S*-containing macrocycle (LXVI) is obtained by the condensation of the dialdehyde (LXV) with ethylenediamine in acetonitrile in the presence of $Fe(ClO_4)_2.6H_2O$.[74]



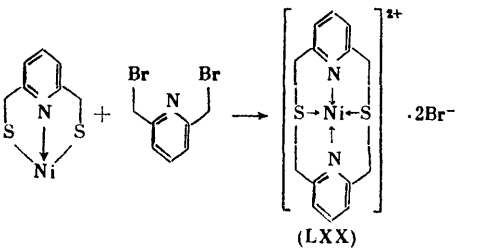
The coordination compound (LXVII) with a pentadentate *N,S*-containing macrocyclic ligand was obtained according to the following scheme.[75]



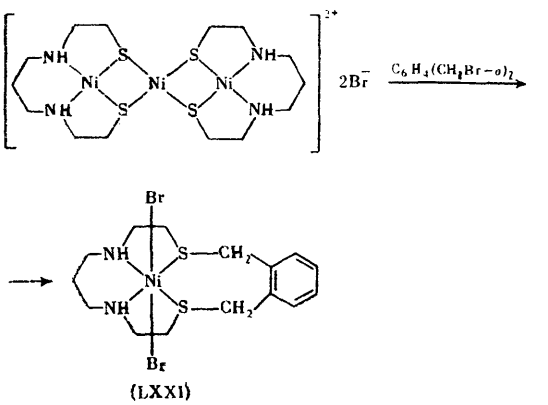
Condensation of 1,2-bis(2-aminophenylthio)ethane with 1,4-bis-(2-formylphenyl)-1,4-dithiabutane or 1,4-bis(2-formylphenyl)-1,4-diazabutane in the presence of nickel or zinc perchlorates leads to the complexes (LXVIII) and (LXIX) respectively.[76–78]



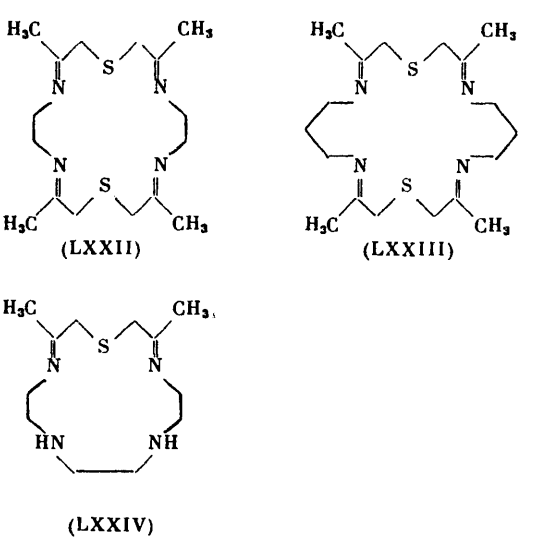
The complex (LXX) of a sulphur-containing pyridinophan with nickel ion is obtained in 86% yield by the reaction of the nickel(II) complex of 2,6-bis(mercaptomethyl)pyridine with 2,6-bis(bromomethyl)pyridine in DMF.[79]



The reaction of α,α′-dibromo-*o*-xylene with bis(3,7-diazanonane-1,4-dithiolate)trinickel(II) bromide leads to the formation of the nickel complex of 3,13-dithia-6,10-diazabicyclo[13.4.0]nonadeca-(15),16,18-triene (LXXI).[80]

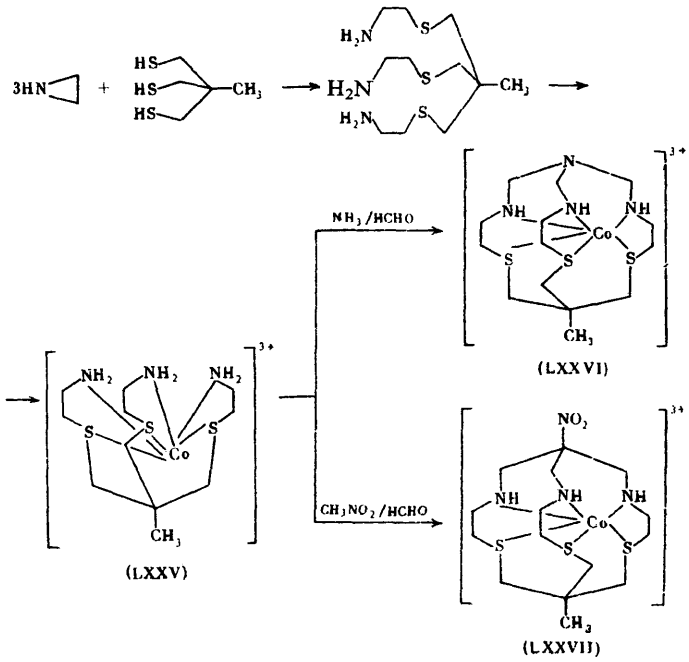


A series of nickel complexes containing macrocyclic Schiff's bases as ligands (LXXII)–(LXXIV) are obtained by the condensation of 1,2-diaminoethane, 1,3-diaminopropane or triethylenetetramine with 4-thiaheptane-2,6-dione in the presence of a nickel(II) salt.[81]



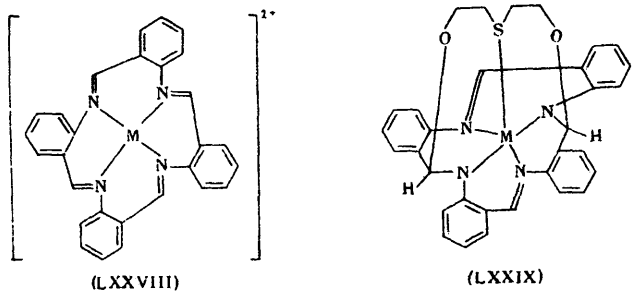
The macrocycles (LXXII)–(LXXIV) are not formed in the absence of nickel(II) ions. The reaction occurs on heating a mixture of diamine, 4-thiaheptane-2,6-dione and the nickel salt in dry ethanol for 0.5–4.0 h. The yield of complexes was 70%.

The template method of synthesising cage-like molecules (sepulchrates, sarcophagins) has been successfully effected in the presence of ions of cobalt(III), rhodium(III), iridium(III) and platinum(IV).[82] The sepulchrate (LXXVI) with an encapsulated cobalt(III) ion is formed on reaction of the hexadentate complex (LXXV) with formaldehyde and ammonia. Reaction of the same complex with nitromethane and formaldehyde leads to the sarcophagin (LXXVII).



(LXXV) (LXXVI) (LXXVII)

The synthesis of "basket-like" complexes with bicyclic ligands (LXXIX) has been effected by the reaction of compounds (LXXVIII) with bis(2-hydroxyethyl) sulphide.[83]



(LXXVIII) (LXXIX)

M = Ni, Cu

In such complexes the central sulphur atom is sterically located so as to occupy an axial position in the coordination sphere of the metal atom, as a result of which the square pyramidal pentacoordination complex (LXXIX) is formed.

III. *N,S*-containing receptors binding cations, anions and neutral organic molecules

1. Cation-binding receptors

N,S-Containing macrocycles form complexes with copper(II) ions which may be considered as low molecular structural models of the active centres of copper-containing "blue" proteins. The copper(II) ion in these proteins is in an environment of donor atoms of nitrogen and sulphur.[84,85] Investigation of the physicochemical characteristics of low molecular complexes showed that they possess the unusual spectral and oxidation–reduction properties characteristic of many copper-containing proteins. The electronic spectra of blue proteins have a strong absorption band in the 600 nm region and a high Cu(II)/Cu(I) oxidation–reduction potential (0.2–0.8 V). The copper-containing proteins, such as plastocyanin, azurin, etc., contain blue copper which is coordination bound with two histidine groups and the sulphur atoms of cysteine and methionine [the coordination polyhedron of copper is a distorted tetrahedron (Fig. 1)].[85,86]

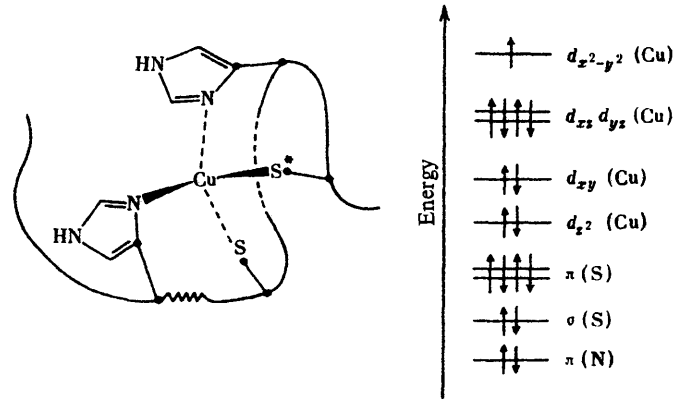


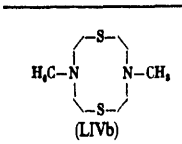
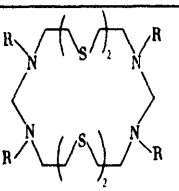
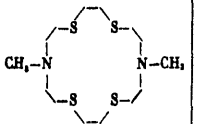
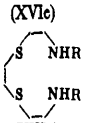
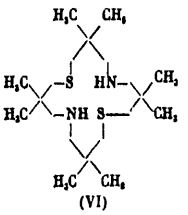
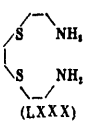
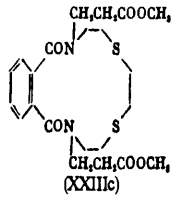
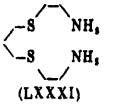
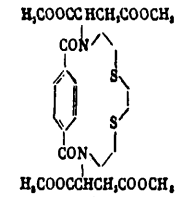
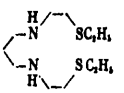
Figure 1. Structural representation of the distorted tetrahedral CuN_2SS^* centre (S is S of Cys; S* is S of Met) in plastocyanin and azurin.[85]

The parameters of the electronic spectra and the oxidation–reduction potentials of the complexes of *N,S*-containing macrocycles and of their open chain analogues and also of plastocyanin and azurin are given in Table 1.

The high intensity absorption bands in the spectra of plastocyanin and azurin with maxima at 752 and 778 nm belong to the charge transfer band (CTB) $\pi(S) \rightarrow d_{x^2-y^2}(Cu)$. The absorption bands at 606 and 552 nm in the spetrum of plastocyanine and at 631 and 567 nm in the spectrum of azurin also belong to CTB $\sigma(S) \rightarrow d_{x^2-y^2}(Cu)$. The absorption bands in the 428–481 nm region are linked with transitions occurring in the highest occupied π-orbitals of the imidazole ring [$\pi(N) \rightarrow d_{x^2-y^2}(Cu)$].[85]

The complexes of the copper(II) ion with *N,S*-containing macrocycles and open chain ligands have absorption bands with a maximum at $\lambda < 300$ nm caused by intraligand transitions, the absorption at 300–400 nm belongs to the CTB $\sigma(S) \rightarrow d(Cu)$ and that in the 650–850 nm region to a $d-d$ transition.[84]

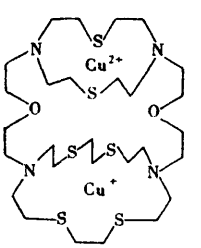
Table 1. Parameters of the electronic absorption spectra and oxidation–reduction potentials of CuL^{2+} at 25 °C.

Ligand L	Solvent	λ_{max}, nm(ε)	$E_{1/2}$, mV	Refs.	Ligand L	Solvent	λ_{max}, nm (ε)	$E_{1/2}$, mV	Refs.
 (LIVb)	80% CH_3OH+ +20% H_2O	370 (5000) 605 (1200)	495	[66]	 (XVIc)	CH_3CN	282 (3840) 333 (2150) 666 (52)	–	[84]
 (LIVe)	80% CH_3OH+ +20% H_2O	415 (2600) 695 (600)	695	[66]	 (XIIIg)	CH_3CN	289 (5200) 333 (3900) 685 (152)	–	[84]
 (VI)	80% CH_3OH+ +20% H_2O	251 (2030) 325 (4150) 390 (5510) 720 (385)	–	[11]	 (LXXX)	80% CH_3OH+ +20% H_2O	–	361	[87]
 (XXIIIc)	CH_3CN	275 sh (2100) 385 sh (1200) 833 (40)	790	[84]	 (LXXXI)	80% CH_3OH+ +20% H_2O	–	312	[87]
 (XXVIj)	CH_3CN	232 (2100) 275 (1200) 787 (45)	940	[84]	 (LXXXII)	80% CH_3OH+ +20% H_2O	–	342	[87]
					Plastocyanin	Thin film	428 (100) 450 (300) 552 (1163) 606 (4364) 752 (1289)	347	[85]
					Azurin	ditto	481 (198) 567 (504) 631 (3798) 779 (686)	330	[85]

The oxidation–reduction potentials of "blue" proteins, *N,S*-containing macrocycles and open chain analogues with the copper(II) ion are 312–940 mV, but for Cu^{2+}(aq) this value is 150 mV (see Table 1).

The copper complexes of the macrotricyclic ligands (LVb, d) and (LVIb) may be considered as binuclear models of copper proteins.[66,67] They have intense absorption near 400 and near 600 nm (375, 565, 430, 590, 375, 563 nm respectively). The oxidation–reduction potential of the copper complex (LVb) is 445 mV.

A mixed complex (LVIc) is formed by the reaction of copper(I) and copper(II) perchlorates (1 : 1) with the unsymmetrical macrotricycle (LVIb).[66] The electronic spectra of the complex indicate that the copper(I) and copper(II) cations are located in the 18- and 12-membered rings of the macrocycle respectively.



(LVIc)

According to the data of X-ray structural analysis the distance between the copper ions in the binuclear complex compounds (LVb, d) and (LVIb) is 5.7–6.0 Å. The macrotricyclic cryptates therefore possess a free space into which a molecule of oxygen or nitrogen may be introduced. Introduction of a molecule of oxygen or nitrogen between the two cations leads to a cascade complex

which may be used in binuclear catalysis or for the fixation of molecules of oxygen or nitrogen. On adding KO_2 or O_2 to the complex of macrotricycles, absorption bands appear at 330 and 370 nm respectively in addition to a wide absorption band at 550–850 nm. These changes in spectra are possible when superoxides or oxygen are included in the binuclear complex. Copper complexes with macrotricyclic ligands are therefore a new type of transition metal polynuclear complex and are potential bioinorganic models of biological processes occurring, for example, with the participation of copper proteins, superoxide dismutase, etc.[66]

N,S-Containing macrocycles also form complexes with cations of silver(I),[88–90] mercury(II),[89–90] nickel(II),[81,88] cobalt(II),[88] palladium(II)[53,88–90] and rhodium(III).[53,88]

2. Anion-binding receptors

Receptor molecules containing positively charged groups, neutral electron-deficient atoms (boron, silicon, tin, etc.), amide or carboxyl groups are capable of binding halide, azide and other anions.[3]

The trithiacyclophan (LI) containing three amide groups is able to form complexes with small-sized anions.[64] According to the data of X-ray structural analysis the size of the cavity of the macrobicycle corresponds to the size of a fluoride or hydroxide anion. In addition the hydrogen atoms of the N–H groups are directed into the ring which aids complex-formation due to the generation of three hydrogen bonds. This type of binding, which was confirmed by ^1H and ^{19}F NMR data, was established in the reaction of tetrabutylammonium fluoride with the macrobicycle (LI).

A cascade type of complex-formation is recorded in the reaction of the macrocyclic receptor (LXXXIII) with copper nitrate and sodium azide.[91] The structure of the complex $Cu_2^{2+}(N_3^-)_4L$ [L is the macrocyclic ligand (LXXXIII)] is shown in Fig. 2.

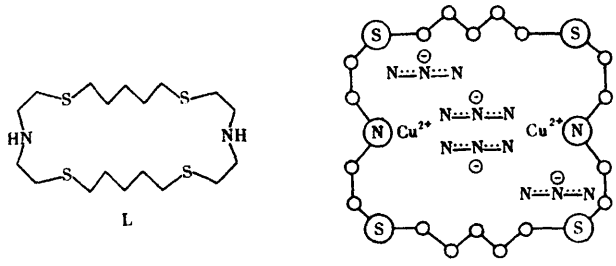


Figure 2. Schematic representation of the $Cu_2^{2+}(N_3^-)_4L$ complex (L is a macrocyclic ligand).[91]

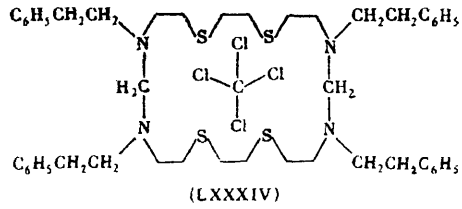
The principle of the cascade complex formation consists of a stepwise reaction. Initially the receptor binds the metal cations which then themselves become centres of association for anions.

3. Receptors forming complexes with neutral molecules

Crown ethers and cryptands form molecular complexes with various neutral molecules. Complex formation has been established with water, molecular bromine, methanol, ethanol, chloroform, urea, acetonitrile, acetylene-dicarboxylic acid dimethyl ester, malonodinitrile, phenylhydrazine, 2,4-dinitrophenylhydrazine, 2,4-dinitroaniline, 3-nitrophenol, etc.[3] Complex formation is effected by all three forms of intermolecular reaction, viz. hydrogen bonds, dipole–dipole interactions, van der Waals forces and hydrophobic binding. Selective binding of the receptor with the substrate leads to a supermolecule, which may consist of an associate of two or more molecular particles. This type of complex formation plays a basic role in such biochemical processes as enzyme–substrate reactions or drug–receptor interactions, etc.

The *N,S*-containing macrocycle (XXXV) forms a molecular complex with CH_3SnCl_3 of composition 1:1 in a mixture of $CDCl_3–CD_3CN$ as solvent. The formation of the complex was established by ^1H NMR spectral data.[54]

The 22-membered macroheterocyclic receptor (XVIIc), containing four exocyclic phenylethyl groups, binds a molecule of chloroform to form the crystalline complex (LXXXIV) which is stable on storage and on heating.[27]



Complex formation with chloroform did not take place on replacing the phenylethyl groups in the macrocycle (XVIIc) by methoxycarbonylethyl or cyanoethyl groups. The main factor in the reaction of this macromolecule with chloroform is therefore of a stereochemical nature created by the bulky phenyl groups.

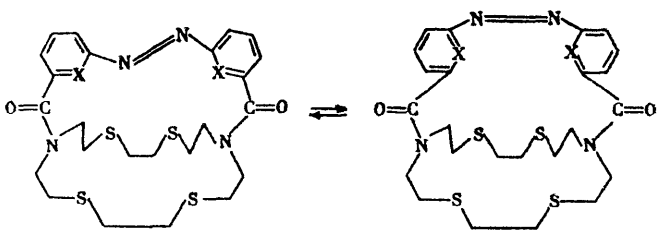
The macrocycle (XVIId), containing exocyclic ester groups, is capable of binding six molecules of urea by a type of complex-formation occurring on the receptor surface.[32] Reaction is effected by the formation of hydrogen bonds of the urea amino groups with the carbonyl oxygen atoms of the ester fragments of the macrocycle.

IV. Transport of metal ions by *N,S*-containing receptors through membranes, catalysis

Crown ethers and cryptands are capable of transferring metal cations through synthetic or natural membranes. It is possible to consider them as simplified models of natural ionophores such as valinomycin, nonactin, etc.[92]

The transport of metal cations through membranes is caused by the extraction of ions from the first aqueous phase due to complex-formation with the carrier and rapid release of them from the complex, which is in the membrane, into the second aqueous phase. The best carriers are therefore ligands forming complexes of average stability. Photoreversible macroheterocycles are attractive for this purpose, as they are capable, under the action of UV irradiation, of reversibly changing the ionophore structure and therefore its stability in complex-formation.[3]

The cryptands (LII) and (LIII), containing azopyridine and azobenzene groups respectively, are such photoreversible carriers.[65]

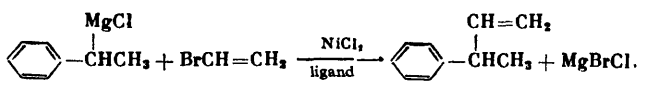


trans-(LII), (LIII) *cis*-(LII), (LIII)

(LII): X = N; (LIII): X = CH

The *cis*—*trans*-isomerisation of these compounds occurs reversibly under photoirradiation. The extraction of the Hg^{2+} ion is effected most efficiently in the presence of the *cis*-isomer of the macrobicycle (LII) compared to the *trans*-isomer, and also by the *cis*- and *trans*-isomers of the cryptand (LIII). The *trans*-isomer of (LIII) does show an appreciable affinity for ions of Cu^{2+}, Co^{2+}, Ni^{2+} and Pb^{2+}. The *trans*-isomer of cryptand (LII) does not react significantly with Cu^{2+} ions while the *cis*-isomer extracts copper(II) ion almost quantitatively. This circumstance enables the transfer of Cu^{2+} ion by the macrobicycle (LII) through a liquid membrane (*o*-dichlorobenzene—n-butanol, 4:1) to be studied. The investigations showed that the rate of transfer of the ion through the membrane was increased significantly by UV irradiation.

The cross-coupling reaction of the Grignard reagent (LXXXV) with vinyl bromide (LXXXVI) proceeds with the formation of (but-1-en-3-yl)benzene (LXXXVII).[12]



(LXXXV) (LXXXVI) (LXXXVII)

The yield of (but-1-en-3-yl)benzene was 10% in the presence of $NiCl_2$. The yield of compound (LXXXVII) was increased to 74—100% on using the complex of $NiCl_2$ with the chiral *N,S*-containing macrocycles (Xa—e) as catalyst.

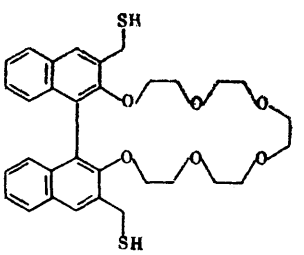
The complexes of copper(II) with the *N,S*-containing macrocycles (XXIII) proved to be efficient catalysts for the oxidation of thiols by oxygen in the air.[93]

V. Conclusion

The design and synthesis of compounds imitating the action of enzymes is one of the most complex and important problems of organic chemistry. Certain successes have been achieved in this direction during the years of development of the chemistry of macroheterocyclic compounds.

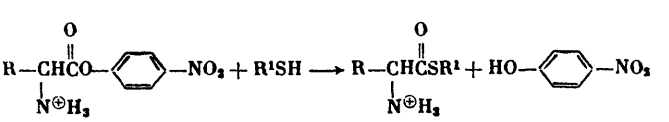
The proteolytic enzymes catalysing the hydrolysis of peptide and ester bonds are the most widely studied among the large number of enzyme systems. The basic conditions for enzymic catalysis are desolvation of the reaction centres of the enzyme—substrate complex[94] and stabilisation of the transition state or reactive form of the substrate.[95] Quantum chemical investigations carried out on the reaction of formamide with the CH_3O^- anion in the active centre of α-chymotrypsin ("the catalytic triad" Ser-195—His-57—Asp-102) confirmed these conclusions. Stabilisation of the transition state of the active centre of α-chymotrypsin may be effected by the formation of hydrogen bonds between the oxygen atom of the substrate carbonyl group and the NH groups of the polypeptide chain amides. Another important factor is the stabilisation of the reactive form of the substrate which leads to significant acceleration of the reaction.

Macroheterocyclic compounds containing donor oxygen atoms in the ring may serve as the cavity in which substrate binding occurs. At present the most studied is the three-point model of binding ammonium ion acting as guest, by a crown ether.[3] The next stage of developing "synzymes" is the synthesis of macrocycles containing a cysteine sulphur atom as active nucleophile. This is used as a model of SH-enzymes of the papain type (LXXXVIII).[3]

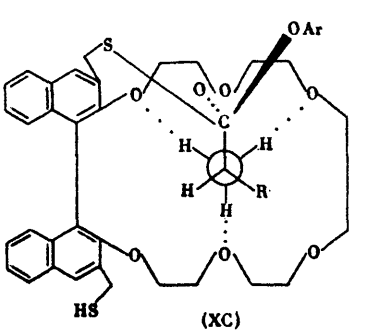


(LXXXVIII)

The crown ether ring serves as the "cavity" and the substrate is the ammonium salt (LXXXIX) which forms a three-point bond with the oxygen atoms of the polyether (XC).



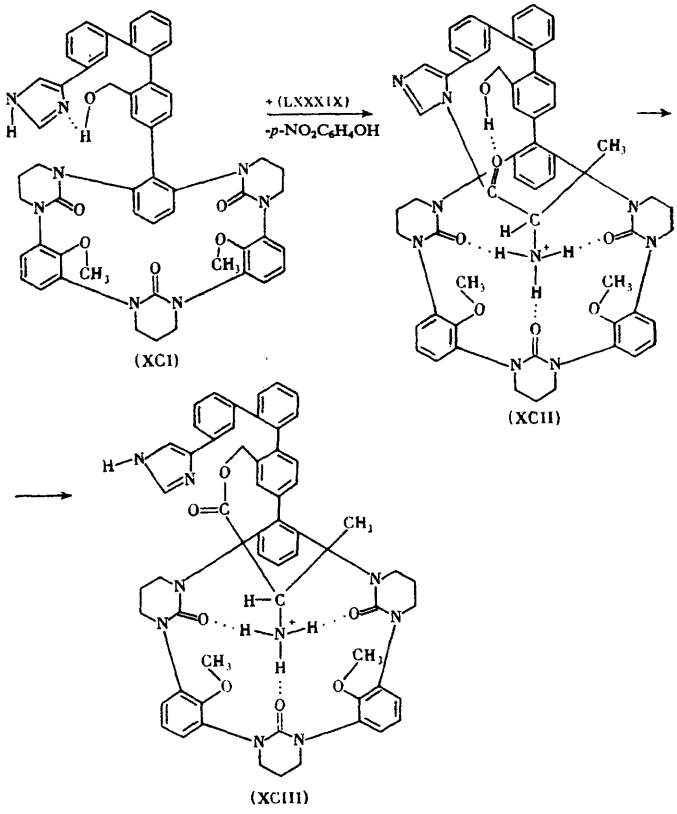
(LXXXIX)



(XC)

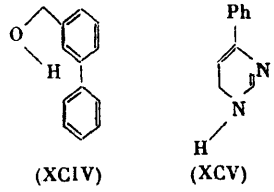
A comparison of the rate constants for the transacylation of the amino acid salts (LXXXIX) showed that the reaction occurs more rapidly with the macrocyclic compound (LXXXVIII) than with its open chain analogue.

A multistage synthesis has been developed for the macrocycle (XCI), which has a complex-forming centre, a nucleophilic hydroxyl and an imidazole proton-transfer agent.[96]



(XCI) (XCII) (XCIII)

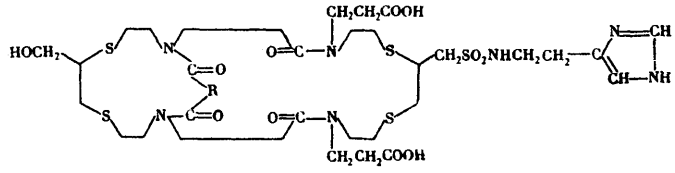
The salt of the amino ester (LXXXIX), which forms a complex with the crown compound (XCI), instantaneously acylates the imidazole group giving the complex (XCII), which is then converted into the more stable complex (XCIII). Acylation has also been studied in the presence of the non-complexing compounds (XCIV) and (XCV).



(XCIV) (XCV)

The rate constant for acylation of the macrocyclic complex is 10^{10} times higher than the rate of acylation with compounds (XCIV) and (XCV). This investigation shows that complex-formation of the receptor with the substrate stabilises the transition state and the reactive form of the substrate, thereby increasing the reaction rate appreciably.[96]

In order to construct new synthetic biomimetic systems as catalysts for the hydrolysis of polypeptides and polyesters, high molecular compounds are required which contain functional groups capable of binding substrates and of catalysing their reactions. We have developed methods of synthesis of the thiazacrown compounds (XCVI). These contain exocyclic hydroxyl, carboxyl and imidazole groups, prearranged for hydrogen bonds, imitating the active centre of the enzyme α-chymotrypsin.[97]



(XCVI)

R = $-(CH_2)_4-$, 1,2-C_6H_4

Further investigations in this region of chemistry will enable, even in the near future, the preparation of the most varied types of "synzymes" based on macroheterocycles and the development of vaccine-like and other biologically important materials.

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Translated from *Uspekhi Khimii* **60** 2528–2542 (1991) U.D.C. 547.732.569.1

Thiophenethiols†

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ABSTRACT. **New data on the chemistry of thiophenethiols have been reviewed systematically. Synthetic routes to these compounds, their reactions with nucleophiles and radicals, and a number of other properties have been examined.**

The bibliography contains 78 references.

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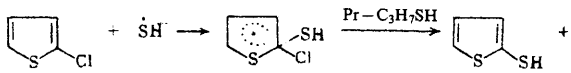
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I. Introduction

Thiophenethiols are highly reactive compounds which are used widely in organic synthesis. Since the publication of an earlier review in this field,[1] the chemistry of this class of compound has developed and a number of new aspects have been brought to light. These include, in particular, new methods of their synthesis, their reactions with radicals, and their recently discovered autothiylation. The reactivity of certain thiophenethiols has also been noted with much interest as new routes to key compounds have been developed. These include drugs and biologically active compounds, scents, polymers and 'organic metals'.

II. Synthesis of thiophenethiols

The primary route to thiophenethiols, notably for industrial syntheses, involves the reaction of halogenothiophenes with H_2S or lower alkyl mercaptans in the gas phase.[2] The reaction proceeds by a radical mechanism. It has been found that the yield of 2- and 3-thiophenethiols is higher with alkyl mercaptans than with H_2S. This would be expected from energetic considerations, since the C–S bond energy is 25–30 kcal/mol less than that of the S–H bond energy in H_2S. Thus, 2-chlorothiophene reacts with isopropyl mercaptan at 540 °C in a quartz tube to give 2-thiophenethiol in 23.6% yield.[3]



+ HCl + CH_2=$CHCH_3$ + $\dot{S}H$.

† This article received the third prize in a competition of reviews on 'Organic and Elementoorganic Synthesis' (Section No. 4), organised by the Inter-departmental Scientific and Technical Council set up to monitor the direction of chemical research and technology.

Dialkyl disulphides, which also produce thiyl radicals on thermolysis, may be used instead of alkyl mercaptans:

$$C_2H_5SSC_2H_5 \longrightarrow 2C_2H_5\dot{S} \xrightarrow{2(C_2H_5)_2S} 2C_2H_5SH + CH_3\dot{C}HSSCH_2CH_3,$$
$$2C_2H_5SH \longrightarrow 2CH_3\dot{C}H_2 + 2SH^{\cdot}.$$

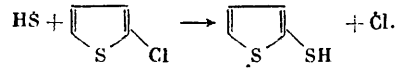
The yield of 2-thiophenethiol by this route is 36.4%.[4]

The low yield of thiophenethiols obtained by the high temperature reaction of halogenothiophenes with H_2S is explained, in part, by their thermal instability and, in part, by the formation of a number of side-products, of which bis(2-thienyl) sulphides predominate. It has been shown that thermolysis of bis(2-thienyl) sulphide, e. g. on hydrothiolysis in the liquid phase at 180 °C in the presence of an excess of sulphur, affords 2- and 3-thiophenethiol in 29.9% and 12.6% yield, respectively.[5,6] A similar yield of thiols is obtained under the same conditions by hydrothiolysis of bis(2-thienyl) disulphides.[7] The added elemental sulphur provides an additional source of thiyl radicals, both by interaction with H_2S and by fission of the S_8 ring.

$$S_8 + H_2S \rightarrow H\dot{S} + H\dot{S}_8 \rightarrow H\dot{S} + S_7.$$

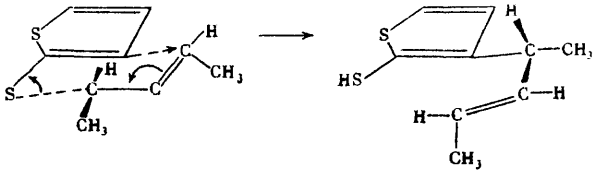
It has been found[8] that the addition of dimethyl selenide, which is readily cleaved into radicals above 300 °C, increases the yield of 2-thiophenethiol on reaction of 2-chlorothiophene with H_2S:

$$(CH_3)_2Se \longrightarrow \dot{C}H_3 + CH_3\dot{S}e \longrightarrow Se + \dot{C}H_3,$$
$$\dot{C}H_3 + H_2S \longrightarrow CH_4 + \dot{S}H,$$



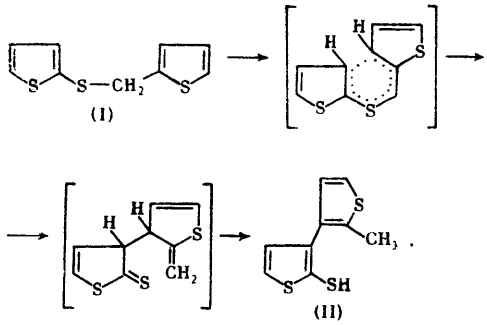
The maximum yield of 2-thiophenethiol is 31.1%.

A V Anisimov et al. have studied the thio-Claisen rearrangement of various thienyl sulphides to give the corresponding substituted thiophenethiols on heating in different solvents.[9,10] (±)-*S*-2-(*trans*-Pent-3-en-2-ylthio)thiophene has been shown to rearrange with retention of optical activity, confirming that reaction proceeds by a concerted [3.3]-sigmatropic shift.[11]



Quantum chemical calculations on the rearrangement of allyl 2-thienyl sulphide have shown that the sulphide and thiol exist in the stable 'open' conformation with a clear separation of the reactive centres.[12] It is thus considered that the rate of the reaction will be determined predominantly by the energetics of the conformational interconversion and by entropy factors.

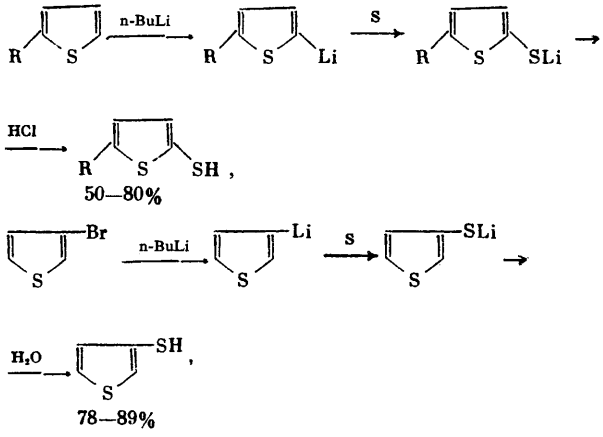
Thio-Claisen rearrangement also provides a convenient route to binuclear heterocyclic thiols.[13] Thus, 2-thienyl 2-thienylmethyl sulphide (I) and 2-benzofurylmethyl 2-thienyl sulphide afford 3-(2-methyl-3-thienyl)-2-thiophenethiol (II) and 3-(2-methyl-3-benzofuryl)-2-thiophenethiol, respectively, in 31% and 30% yield.



(I)

(II)

The commonest laboratory preparations of thiophenethiols are based on the intermediate formation of lithiothiophenes:[10]



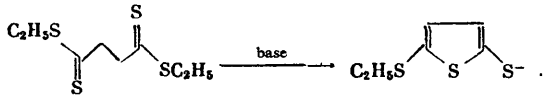
50—80%

78—89%

where R = H, Me, Et, Bu^t, Pr^i, etc. 3,4,5-Trichloro-2-thiophenethiol has also been prepared by this route in 86% yield.[14]

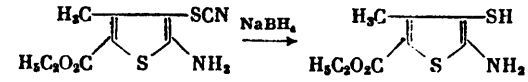
3,4-Thiophenedithiol has recently been obtained in one step by treatment of 3,4-dibromothiophene with two equivalents of butyllithium, followed by addition of flowers of sulphur and water.[15] This contrasts with the former two-step route.[16,17]

Among alternative methods of preparing thiophenethiols, it is worth noting the cyclisation of diethyl tetrathiosuccinate.[18] Cooling is necessary during the reaction, for which a number of tertiary amines or dimethylformamide acetals may serve as catalyst.



60%

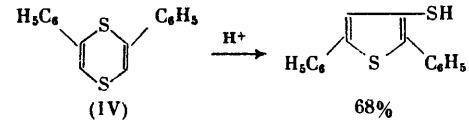
The 2-amino-3-thiophenethiol (III) may be obtained by reduction of the corresponding 3-thienyl thiocyanate with $NaBH_4$ or sodium dithionite:[19]



85%

(III)

A substituted 3-thiophenethiol was also isolated by an unusual acid-catalysed rearrangement of the 1,4-dithiin (IV).[20] The reaction proceeds on heating at 180 °C in σ-dichlorobenzene in a sealed tube.



(IV)

68%

2-Thiophenethiol may also be obtained by reduction of 2-thiophenesulphonic acid with PPh_3.[21]

III. Physical properties

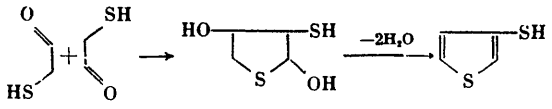
The physical properties of a number of thiophenethiols are given in Table 1. These data were reported after the publication of the previous review.

Table 1. Physical properties of thiophenethiols.

R^2	R^3	R^4	R^5	m.p. °C	b.p. °C/mmHg	^{1}H NMR (ppm)*	Reference
SH	Cl	Cl	Cl	39.0–41.0	56/0.1	3.55 (s) [$CDCl_3$]	[14]
SH	2-Methyl-3-benzofuryl	H	H	–	–	7.5–6.8 (m, 6H, arom.,thiophene); 3.35 (s, 1H, SH); 2.3 (s, 3H, CH_3) [CCl_4]	[13]
SH	2-Methyl-3-thienyl	H	H	–	–	6.5–7.3 (m, 4H, thiophene); 3.15 (s, 1H, SH); 2.27 (s, 3H, CH_3) [CCl_4]	[13]
SH	H	H	SC_2H_5	–	125/0.3	1.26 (t, 3H, CH_3); 2.78 (t, 2H, CH_2); 3.57 (s, 1H, SH); 6.90 (s, 2H, 3-, 4-H) [$CDCl_3$]	[18]
OMe	SH	H	SCH_3	–	123–127/3	2.34, (s, 3H, SCH_3); 3.0 (s, 1H, 4-H); 3.89 (s, OCH_3); 6.68 (s, 1H, 4-H) [CCl_4]	[37]
NH_2	SH	CH_3	CO_2Et	125–128	–	–	[19]

*In parenthesis are given the multiplicity of the signal, its integral intensity (the number of protons) and the position of the protons in the molecule.

Recently much attention has been paid to thermolytically prepared thiophenethiols for their aromatic properties and as starting materials for the synthesis of novel aromatic compounds.[22–34] Chromato-mass spectrometric and gas chromatographic analyses have indicated that 2-thiophenethiol, 3-thiophenethiol and 2-methyl-3-thiophenethiol are responsible for the fleshy odours which have been detected in certain pyrolytic experiments, supporting the view that thiophenethiols play a key role in the formation of sulphur-containing compounds in meat. It is thought that thiophenethiols are formed by condensation of the products derived by thermolysis of cysteine or by reaction with hydrocarbons and hydrogen sulphide. Thus, 3-thiophenethiol may be formed from two molecules of mercaptoacetaldehyde:



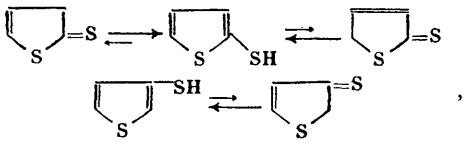
To assist identification and separation of aromatic thiophenethiols in mixtures, mass and IR spectroscopic studies of simple thiophenethiols and the corresponding alkyl thienyl sulphides have been undertaken and retention times on capillary gas chromatography columns determined.[35]

The dipole moments of a number of 3-thiophenethiols and 3-(alkylthio)thiophenes in benzene have also been determined in order to provide conformational information on the structures of the compounds.[36]

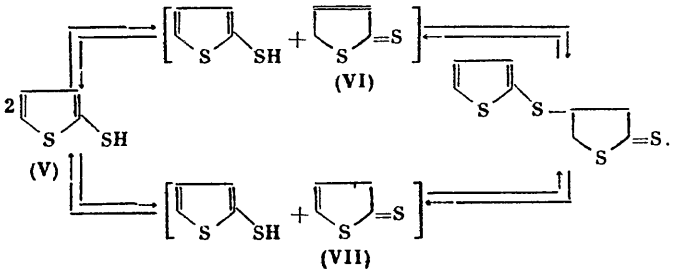
IV. Reactions of thiophenethiols

1. Nucleophilic addition

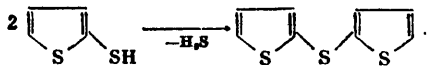
In the tautomeric system:



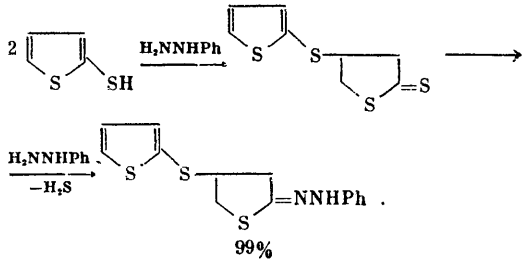
the equilibrium is clearly shifted in favour of the thiol form. This has been established both by quantum chemical calculations[38] and by the fact that proton signals from the thione form are absent in the ^{1}H NMR spectra of thiophenethiols. However, there is evidence that certain reactions of thiophenethiols involve the thione form, such as the recently discovered autothiylation of 2-thiophenethiol to give 4-(2-thienylthio)tetrahydrothiophene-2-thione.[39–42] Reaction takes place on exposing the thiol to air or in the presence of an amine as catalyst. It is most likely that the conversion takes place by a radical mechanism or by the ionic addition of 2-thiophenethiol (V) to the tautomeric thione form (VI) or (VII):



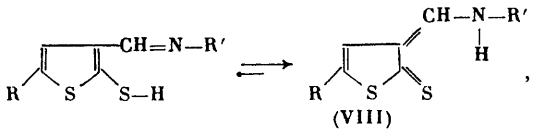
The reaction is reversible, although the equilibrium lies very much to the right. The dimer reverts to the monomer on distillation *in vacuo*. A side-reaction accompanies the autothiylation: the formation of bis(2-thienyl) sulphide with evolution of H_2S, as follows:



If autothiylation takes place in the presence of phenylhydrazine, the hydrazone derivative of the dimer is isolated:[43]

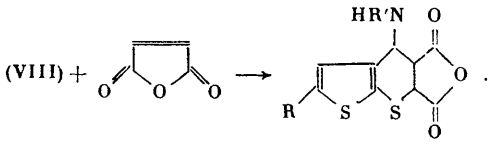


In-depth studies by Ya L Gold'farb et al. of the chemistry of mercaptoaldimines (e.g. Refs. 44 and 45), confirmed the existence of thiol-thione tautomerism in thiophenethiols. In solution, it has been found that mercaptoaldimines (VIII) exist as an equilibriated mixture of tautomers, shifted almost exclusively to the side of the thione form:



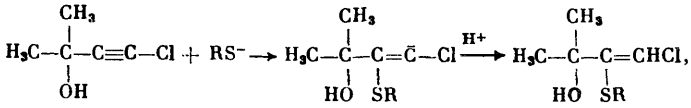
R = Et, OMe; R′ = *cyclo*-C_6H_{11}.

These compounds participate in the Diels–Alder reaction as heterodienes:[46]



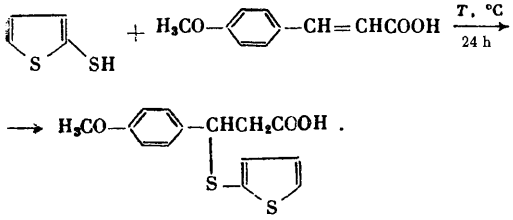
However, from the data available at present, it is clear that thione-type reactions of thiophenethiols are the exception rather than the rule. In fact, all of the reactions outlined below proceed from the thiol form.

The most characteristic and studied reaction of thiophenethiols is their addition to multiple bonds. Thus, treatment of dimethyl(chloroethynyl)carbinol with thienylmercaptide anion leads to the formation of the corresponding chlorovinylcarbinol which may be used subsequently for the preparation of ethynyl sulphides:[47]

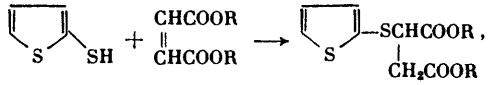


R = thienyl.

There are references to the addition of thiophenethiols to various unsaturated carbonyl compounds.[37,48] Thus, the reaction of 2-thiophenethiol with 4-methoxycinnamic acid yields an adduct which has been used for the preparation of antiglaucoma agents:[49]

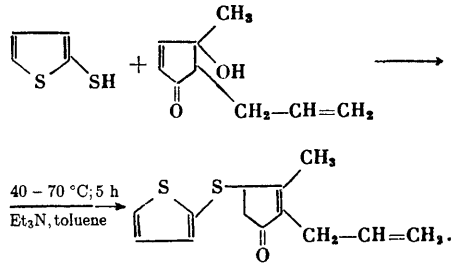


It is interesting that the addition of 2-thiophenethiol to diallyl maleate proceeds exclusively across the double bond of the maleic residue:[50]



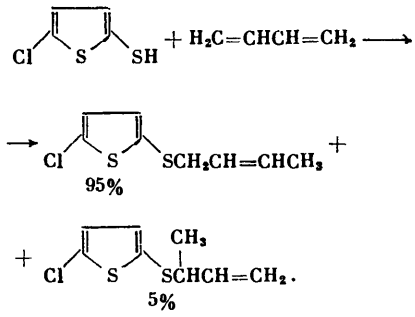
R = $CH_2CH=CH_2$.

A series of cyclopentenones, including 2-allyl-3-methyl-4-(2-thienylthio)-2-cyclopentenone, has been prepared in high yield as follows:[51]

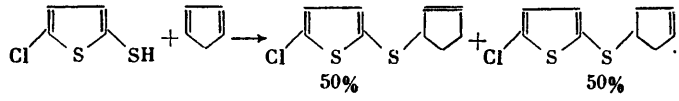


As in the previously described reaction, the allyl group is unaffected.

The addition of 5-chloro-2-thiophenethiol to 1,3-butadiene affords predominantly the 1,4-adduct:[52]

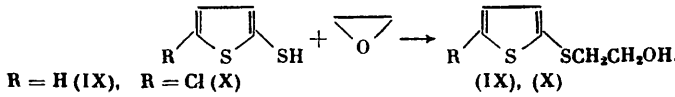


The reaction takes place in the presence of ethanesulphonic acid. In contrast, cyclopentadiene reacts with 5-chloro-2-thiophenethiol to give a 1 : 1 mixture of 1,2- and 1,4-adducts in 79% yield:



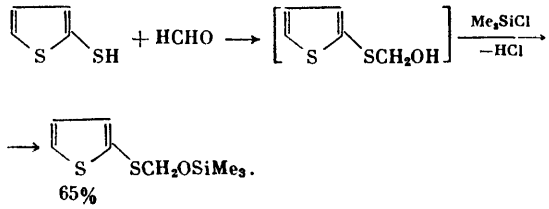
The fact that rate of the addition and the yield of adducts increases in the presence of a protic acid, e. g. ethyl sulphate, confirms the nucleophilic character of the addition of 5-chloro-2-thiophenethiol to such 1,3-dienes.

A study has been made of the interaction of ethylene oxide with heteroaromatic thiols in the liquid phase at 20 °C in the presence of an acid catalyst.[53] It was shown that the yield of the resulting heterocyclic β-hydroxyethyl sulphides increases with increase in the acidity of the thiols. The addition of an acid catalyst, e. g. aluminium oxide or an aluminosilicate, also increases the yield of product. Under optimum conditions, the yield of sulphides (IX) and (X) was 75% and 91%, respectively:

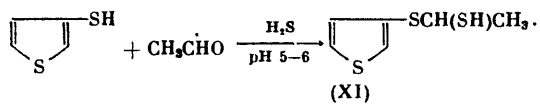


The observed effect of thiol acidity and addition of catalyst confirms that the mechanism of the epoxide ring opening involves protonation of the oxygen atom. The products obtained by addition of thiols to expoxides possess fungicidal and acaricidal activity.[54]

Simple aldehydes react with thiophenethiols to give monothiohemiacetals. Thus, the interaction of 2-thiophenethiol with paraformaldehyde in the presence of an excess of trimethylsilyl chloride affords 2-thienyl trimethylsiloxymethyl sulphide, as follows:[55]

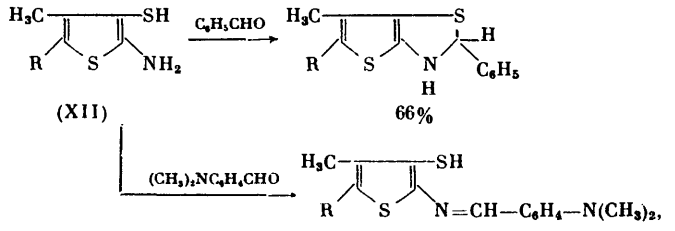


Bis(2-thienylthio)methane is formed as a by-product in 20% yield. The condensation of 3-thiophenethiol with acetaldehyde in the presence of H_2S affords the hemimercaptal (XI):[34]



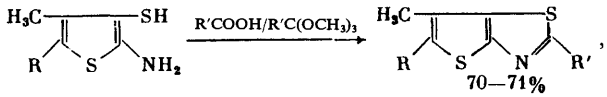
The interaction of 2-amino-3-thiophenethiols (XII) with benzaldehyde leads to substituted thieno[2,3-*d*]thiazolines.[19] It is likely that the reaction involves intramolecular addition of the thiol group across the C=N bond arising by initial condensation of the aldehyde with the amino group. It is interesting that the cyclisation

does not take place with *p*-dimethylaminobenzaldehyde. This has been supported by IR- and ^{1}H NMR spectroscopic data.



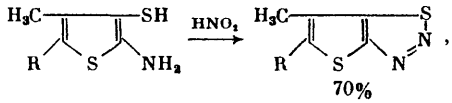
R = $CO_2C_2H_5$.

Substituted thieno[2,3-*d*]thiazoles are obtained by interaction of (XII) with formic or acetic acid and their orthoester derivatives:



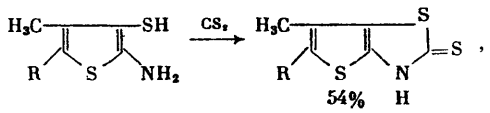
R = CO_2CH_3, $CO_2C_2H_5$; R′ = H, CH_3.

Diazotisation of the amino group in compound (XII) also leads to ring closure:



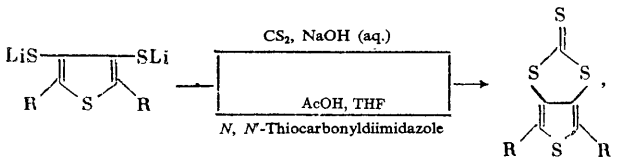
R = $CO_2C_2H_5$.

The reaction of (XII) with carbon disulphide exemplifies nucleophilic addition of a mercaptan across a C=S bond:



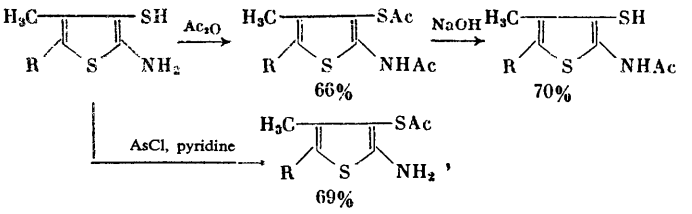
R = $CO_2C_2H_5$.

A similar reaction with thiophenedithiolates leads to $\Delta^{2,2'}$-bithieno-[3,4-*d*][1,3]dithioles, which have been used to prepare "organic metals" in the tetrathiafulvalene series:[56,57]



R = H, Me.

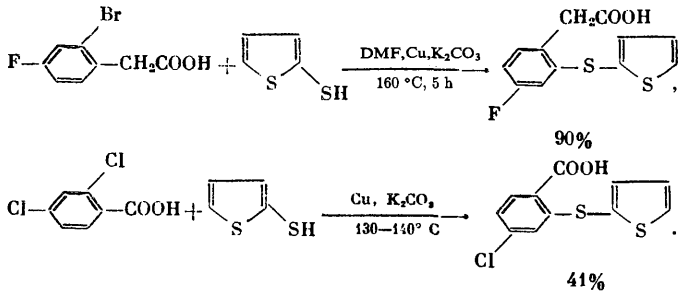
Acylation is also characteristic of thiophenethiols, as exemplified below with acetic anhydride or acetyl chloride as acylating agent:



R = $CO_2C_2H_5$.

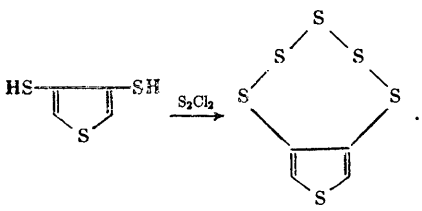
2. Nucleophilic substitution

2-Thiophenethiol participates in nucleophilic substitution of halogen in activated aromatics by heating in the presence of copper as catalyst:

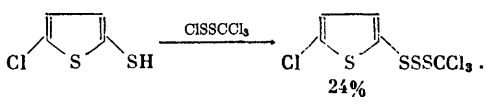


The resulting products have been used as intermediates in the synthesis of neuroleptic compounds.[58–60] The dye, 1-amino-5,8-bis-(2-thienylthio)anthraquinone, has been prepared in a similar way from the corresponding dichloroanthraquinone and 2-thiophenethiol.[61]

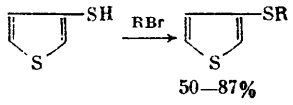
The formation of thieno[3,4-*f*]-1,2,3,4,5-pentathiepin from 3,4-thiophenedithiol and sulphur monochloride in dichloroethane also involves a nucleophilic substitution:[15]



Trichloromethylthiosulfenyl chloride reacts similarly with 5-chloro-2-thiophenethiol to give the corresponding trisulphide:[62]



Thiophenethiols are readily *S*-alkylated to give a wide variety of thienyl sulphides. Thus, *n*-alkyl 3-thienyl sulphides may be obtained by reaction of 3-thiophenethiol with alkyl bromides, RBr, in the presence of potassium tert-butoxide.[63]

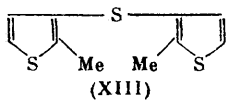


50—87%

R = C_nH_{2n+1}, where $n = 1$—6, 8, 10, 12.

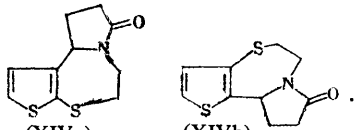
Dimethylformamide acetals may also be used as alkylating agent.[18]

3-Bromo- or 3-tosyloxy-2-methyltetrahydrothiophene has been converted to the bis(thienyl) sulphide (XIII). The latter is a component of certain natural aromas, having a smell of roasted nuts:[33]



(XIII)

The isomeric tricyclic compounds, (XIVa) and (XIVb), are obtained by condensation of 2- and 3-thiophenethiol, respectively, with *N*-(2-chloroethyl)succinimide, followed by partial reduction with sodium borohydride and ring closure of the resulting lactamol in the presence of formic acid.[64]

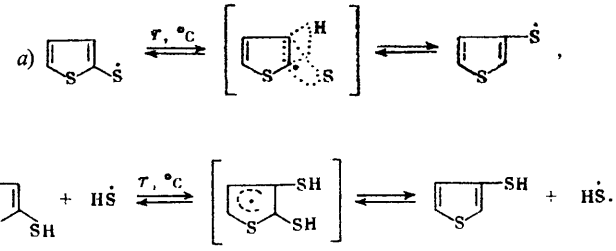


(XIVa) 38% (XIVb) 44%

These products are analogues of biologically active compounds.

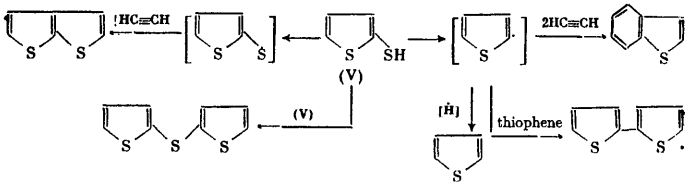
3. Radical reactions

Radical reactions take place on thermolysis or hydrothiolysis of thiophenethiols (at 400—600 °C) to give a mixture of products containing thiophene, dithienyls, and condensed systems.[5] The conversion of 2-thiophenethiol to 3-thiophenethiol also takes place under these conditions and is worthy of note.[5,6,8] Two mechanisms, *a*) and *b*), have been considered:



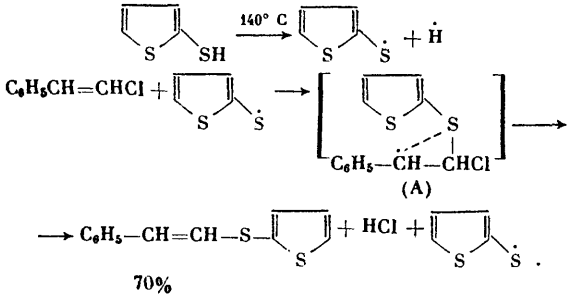
Reaction is favoured by the increased thermal stability of the 3-substituted thiophene, relative to the 2-substituted derivative.

It has been established that 2-thiophenethiol reacts with acetylene at 550—650 °C to give a mixture of thieno[*b*]thiophene, bis(2-thienyl) sulphide, thiophene, and benzo[*b*]thiophene.[65] Dithienyls are also obtained above 530 °C. The yield of each product varies according to the temperature and the proportion of the two reactants. The complexity of the reaction is a result of competing S—H and C—S cleavage in the initial phase of the heterolysis. The acetylene molecule then traps the resulting thiyl and 2-thienyl radicals:



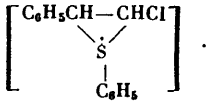
Thiophenol reacts under the same conditions to give benzo[*b*]thiophene as the only product.

The formation of β-styryl 2-thienyl sulphide from 2-thiophenethiol and β-chlorostyrene exemplifies radical substitution of halogen bonded to an unsaturated carbon atom.[66]

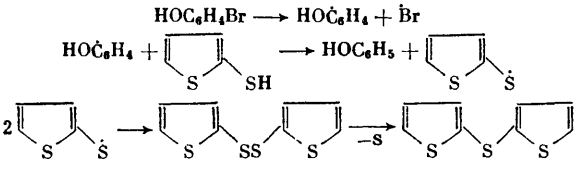


70%

By comparison with substitution by thiphenol, the reaction is much slower and stereo-random as a consequence of steric hindrance in the transition state (A). In the case of thiophenol, there is a clearly defined intermediate (below) which determines the stereospecificity of the reaction.

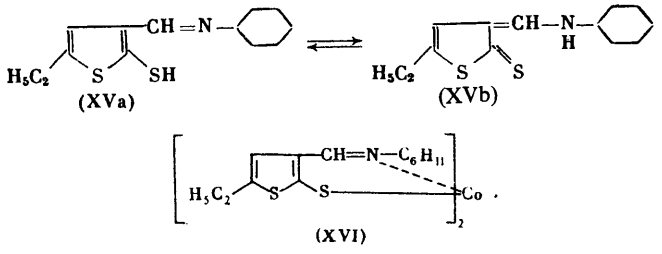


At 180 °C 2-thiophenethiol reduces bromophenols to the corresponding phenols while being oxidised to the disulphide.[67]



The reaction takes palce below the temperature at which the C—Br bond of bromophenols normally dissociates.

2-Mercapto-5-ethyl-3-thienylmethyleneaminocyclohexane and its cobalt(II) chelate complex are used as inhibitors in the oxidation of hydrocarbons.[68,69]



Mechanistically, these inhibitors would appear to function as radical traps interrupting the chain process. In complex (XVI) it is the cobalt(II) atom which is responsible for the deactivation, while in compound (XV) it is either the SH group (of XVa) or the C=S group (of XVb).

$$RO_2^{\cdot} + RSH \rightarrow RO_2H + RS^{\cdot},$$
$$2RS^{\cdot} \rightarrow RSSR.$$

However, the effectiveness of these compounds as inhibitors is less than what might be expected. This is a result of the competing reaction of (XVa) with peroxides, producing both radicals and unreactive products:

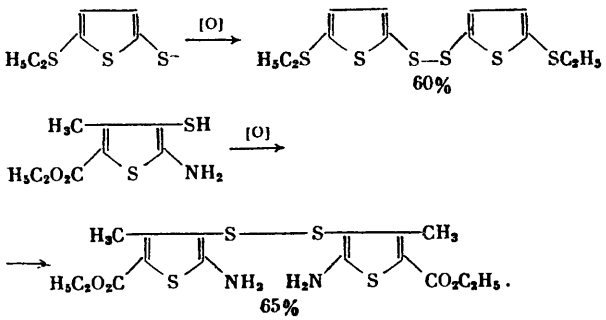
$$RSH + RO_2H \rightarrow RS^{\cdot} + H_2O + RO^{\cdot},$$
$$RSH + RO_2H \rightarrow \text{stable products}.$$

The activity of the inhibitors is thus gradually eroded.

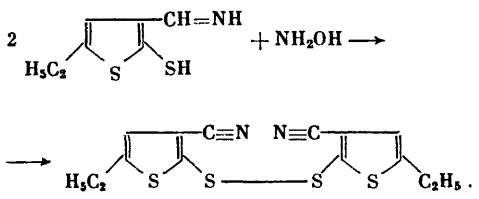
Polymers have been obtained by copolymerisation of 2,5-thiophenedithiol with divinylthiophene or divinylbenzene under UV irradiation or in the presence of radical initiators. These products may be used principally in the manufacture of light-sensitive materials and polaroid films.[70–72]

4. Other properties

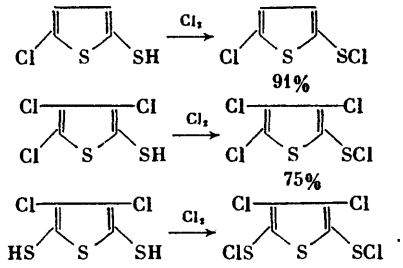
Thiophenethiols are readily converted to the corresponding disulphides in the presence of mild oxidants (air, iodine, iron(III) salts).[73–75] The following conversions are notable:[18,19]



These reactions take place simply on exposing solutions of the mercaptan to air. 2-Mercapto-5-ethyl-3-thienylaldimine is oxidised to bis(3-cyano-5-ethyl-2-thienyl)disulphide in hydroxylic or aqueous alcohol media:[76]

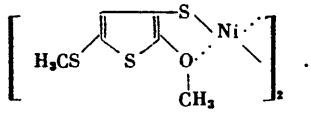


The formation of thienylsulphenyl chlorides from thiophenethiols and chlorine is synthetically very interesting:[14,62]



The reaction takes place in carbon tetrachloride. It is important that the 5-position is blocked. If not, the resulting sulfenyl chlorides react with the starting mercaptans at the unsubstituted 5-position with liberation of HCl. A variety of thienylthio derivatives may be obtained from thienylsulphenyl chlorides, the chlorine atom of which is very labile.

A number of transition metal complexes, e.g. (XVI), may be formed from thiophenethiols and their derivatives. The nickel chelate (below) is formed by heating nickel acetate with a methanolic solution of 2-methoxy-5-methylthio-3-thiophenethiol.[37]



Recently, the synthesis of titanocenethienyl and niobocenethienyl thienylmercaptides was reported,[77,78] and a study made of the stability of the latter towards I_2.

***

Thiophenethiols are an interesting class of heterocyclic compound from both the theoretical and practical viewpoint. From the volume of data published on these compounds in recent years, one can anticipate further developments in this field.

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Translated from *Uspekhi Khimii* **60** 2543–2565 (1991) U.D.C. 547.539.26.32.72.722.78

The synthesis, structure and reactivity of (α-trihalomethyl)carbinols

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Erevan State University

ABSTRACT. Data on the methods of synthesis and chemical properties of (α-trihalomethyl)carbinols are correlated and systematised in the review. Features of the structure are considered and certain effects of the nature of the halogen on their reactivity and physicochemical properties are discussed. An important role has been shown for the (α-trihalomethyl)carbinols as intermediates and synthons.

The bibliography contains 153 references.

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I. Introduction

Interest in the synthesis of (α-trihalomethyl)carbinols has been increasing since the first studies appeared on the preparation of this class of compounds.[1–3] Significant success has been achieved in the synthesis and practical application of these compounds. New degradable organochlorine pesticides have been synthesised, based on (α-trichloromethyl)carbinols, which do not accumulate in vertebrates and are decomposed by enzymic systems.[4–7] It has been established recently that systematic rapid changes in the toxic chemicals used enable the self-purification of the environment from their metabolites and residues to be maintained at a low level. The large number of compounds used for plant protection is increased by a range of (α-trichloromethyl)carbinols.[4]

(α-Trichloromethyl)carbinols are used in medicine as narcotics and analgesics and in recent years effective tranquillisers have been found among the (α-trichloromethyl)carbinols of the acetylenic series,[8,9]

(α-Trichloromethyl)arylcarbinols (ATMC) are converted by a one-stage method, dehydration–rearrangement reaction, into α,β,β-trichlorostyrenes which are co-monomers for heat- and light-stable polymers.[10,11]

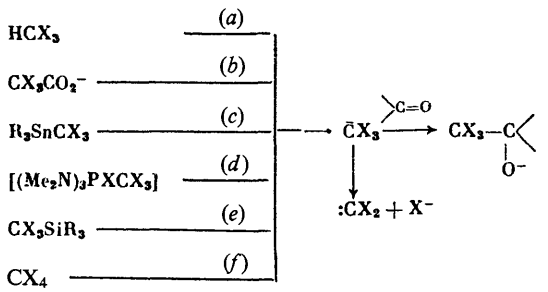
The current review is the first attempt in the Soviet and foreign literature to embrace completely all aspects of the chemistry of the (α-trihalomethyl)carbinols.

II. Methods of synthesising (α-trihalomethyl)-carbinols

1. Condensation of trihalomethyl anions with carbonyl compounds

The most widespread and general method of synthesising (α-trihalomethyl)carbinols is the condensation of trihalomethyl anions with carbonyl compounds. The generation of trihalomethyl anions (THA) is effected by various routes using a wide range of reagents, e. g. from haloforms in basic medium,[12–24] decarboxylation of trihaloacetic acids[25–27] or their salts,[28] from trihalomethyl-organotin compounds[29] and trihalomethylphosphonium salts,[30] from trihalomethylorganosilicon compounds[31] or the electrochemical reduction of carbon tetrachloride.[32–36] The resulting THA tend to dissociate into dihalocarbenes which is an undesirable process in the synthesis of (α-trihalomethyl)carbinols.[37] Experimentally this is readily prevented at relatively low (0 °C and below) temperatures in the presence of carbonyl compounds (Scheme 1).

Scheme 1



X = Cl, Br, combination Cl and Br

It has been shown that THA are formed from the majority of haloforms by a rapid reversible reaction. Many investigators,[12–24] using haloforms as a source of THA, have paid much attention to the choice of basic catalyst and to their proportion in the system of carbonyl compound–haloform–solvent. The generation of THA with almost the same success was effected with potassium and sodium hydroxides,[12,15,16,20,21] alkali metal alkoxides[13,14] and calcium oxide in dimethyl sulphoxide.[17,18] A serious difficulty in the process of simultaneously generating THA from haloforms and condensing them with carbonyl compounds is the inclination of the latter to undergo aldol condensation and Cannizzaro oxidation–reduction processes under the same base catalysis conditions. This hinders appreciably the synthesis of (α-trihalomethyl)carbinols. With the aim of suppressing the competing side reactions mentioned above, many authors have used various solvents, such as aliphatic acetals, ketals, vicinal glycols[38] or, which is particularly important, have tried to reduce the quantity of the basic catalyst to the minimum. In contrast to the early studies[12–19] where the catalyst was used in equimolar ratio to the aldehyde (or ketone), it was shown that the use of liquid ammonia as solvent was extremely convenient and it was possible to reduce the quantity of base (aldehyde : chloroform : potassium hydroxide = 1 : 1 : 0.3–0.5) and simultaneously provide low temperature conditions when the process of dissociative

fission of the THA into dihalocarbene is suppressed. The yield of the desired carbinol was 41–95%.[20] The yield of the desired carbinol was 41–95%.[20] A procedure, competitive at the technological level, has been described[21] in which it was shown that the optimum conditions for synthesising the narcotic chloretone, viz. (α-trichloromethyl)dimethylcarbinol, were a ratio of acetone : chloroform : potassium hydroxide = 10 : 1 : 0.1 without solvent at −5 °C. During the synthesis the excess of acetone was returned into the cycle and yield was 76%.

It was shown, using as example the condensation of benzaldehyde with mixed haloforms (dichlorobromo- and dibromochloromethanes) that under conditions of base catalysis the latter also generate the corresponding THA.[39,40] Condensation has been described with heterogeneous base catalysis (powdered calcium hydroxide) without solvent[39] and with homogeneous catalysis using potassium t-butoxide and t-butanol.[40]

The generation of THA from haloforms is also effected under conditions of phase transfer catalysis.[41,42] This method does not lead to a high yield of product, exceptions being only the higher representatives of aliphatic aldehydes and ketones and also certain aldehydes of the heterocyclic series (2-, 3-, 4-pyridyl-).[43] It must be noted that aromatic ketones do not react at all under phase transfer catalysis conditions.

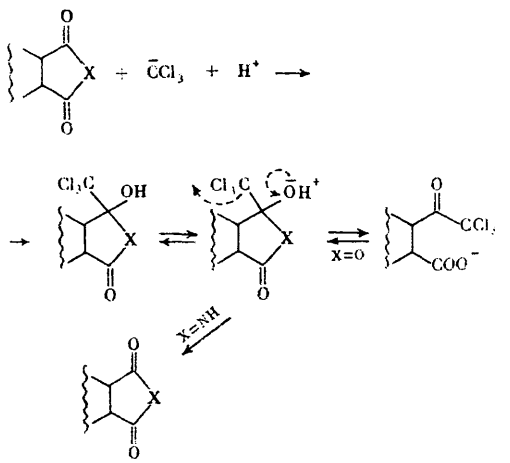
In 1959 Wagner[44] reported the generation of dichlorocarbene by the thermal decomposition of sodium trichloroacetate (TCAA) in 1,2-dimethoxyethane. However Winston and co-workers[28] under the same conditions succeeded in decomposing sodium trichloroacetate in the presence of aldehydes and isolating (α-chloromethyl)carbinols as products of the trichloromethylation of the carbonyl group, albeit in extremely modest yield (29–47%). Decarboxylation of trihaloacetate anions with the formation of trichloro(bromo)methyl anions (Scheme 1, *b*) takes place with comparatively low yields. The reason, in our opinion, is graphically illustrated in recently patented work where it was shown that, when using DMSO, DMF or other related compounds as solvent, spontaneous addition of $\bar{C}X_3$ and CO_2 takes place at the carbonyl group with the formation of the corresponding carbonates. Under specific experimental conditions the reaction may be directed completely to carbonate formation.[45]

$$>C=O + \bar{C}X_3 + CO_2 + Na^+ \longrightarrow >C(CX_3)OCO_2^-Na^+$$

It was shown recently by English scientists[25,27] that THA are readily generated at room temperature by dissolving trichloro- and tribromoacetic acids in DMSO. The use of halogenated acids as sources of THA completely excludes carbonate formation and the desired (α-trihalomethyl)carbinols are isolated in 50–80% yield.[25,27] It is interesting to note that 4-nitrobenzaldehyde does not react with haloforms[46] but 4-nitrophenyl(trichloromethyl)carbinol is formed in 80% yield with trichloro(bromo)acetic acid.[25] This experimentally observed fact is seemingly linked with the use of the highly polar DMSO solvent which in fact reduces the deactivating effect of the 4-nitro group on the α-carbon atom to zero.

This synthetic method enables several pyridinaldehydes to take part in the reaction but not furfural and its homologues, which are rapidly resinified in a TCAA medium. The problem of trichloromethylating these compounds was successfully resolved by the decarboxylation of trichloroacetates (K, Na) in a medium of DMSO or DMF.[47]

The trichloromethylation of cyclic anhydrides and imides in a TCAA–DMSO system is of interest. This reaction leads to a lactone or lactam containing a trichloromethylcarbinol structural unit in the γ-position of the heterocycle. It was shown[48] that either ring–chain isomeric conversions or partial haloform fission occur in this case.



By using various solvents the equilibrium system is successfully displaced in the direction of ring or chain isomers.

It must be noted in regard to the decarboxylation of TCAA into the trichloromethyl anion (TCA) that it is possible to use hexamethylphosphoramide (HMPA) successfully in place of DMSO, which while maintaining the pH of the medium close to neutral has certain advantages over DMSO from the preparative point of view.[49]

Trihalomethylphosphonium salts are also sources of THA. Tris(dimethylamino)trichloromethylphosphonium chloride, on reaction with aliphatic aldehydes and cycloalkanones, forms (α-trichloromethyl)carbinols in preparative yield.[30] Tributyl(trichloromethylstannanes, which are convenient synthons for generating THA, form (α-trihalomethyl)carbinols in 20–69% yield with aliphatic and aromatic aldehydes.[29] The authors excluded any effect of initiators and inhibitors of radical processes from the reaction and demonstrated strictly the heterolytic fission of the $-Sn-CCl_3$ bond with the formation of TCA.

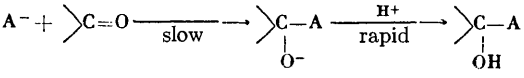
From the preparative point of view it is best to heterolyse the carbon–silicon bond in α-trichloromethylsilanes in a medium of tris(dimethylamino)sulphonium difluorotrimethylsilicate (TASX). This route provides a 75% yield of trichloromethylated carbinols.[31]

The method of generating TCA by the cathodic reduction of carbon tetrachloride in chloroform or DMF is interesting. In the presence of alkyl-, heteryl- or arylaldehydes the corresponding (α-trichloromethyl)carbinols are fomred in 11–92% yield.[32–36]

$$RCHO + CCl_4 \xrightarrow[CHCl_3 \text{ or } DMF]{2\bar{e}} RCH(OH)CCl_3.$$

The synthesis of several previously undescribed (α-trichloromethyl)carbinols has been achieved by this means although the complexity of the experimental conditions places the value of this method in use under some doubt.

The condensation reaction of TCA with aldehydes and ketones proceeds according to the widely known mechanism where the carbanion ($\overline{C}X_3$ in this case) attacks the carbonyl group.



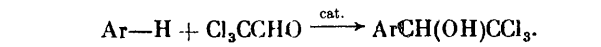
The first stage determines the rate of the reaction which makes it possible to make certain comparisons with the kinetically related Darzens (glycidyl condensation) and Perkin reactions.[50] Because of the absence of sufficient literature data on the kinetic parameters of the Darzens reaction, Reeve and co-workers[51] studied the reactivity of seven aryl aldehydes taking the kinetic data of the Perkin reaction as standard. The results obtained are in good agreement, and in several cases are even identical.

It must be noted that a neighbouring group effect or a secondary steric effect of an *ortho* substituent is observed in the condensation reaction of haloforms with aryl aldehydes. The displacement of the aldehyde group from the plane of the aromatic ring, accompanied by a disturbance of the conjugation, and consequently by the exclusion of the mesomeric effect of the substituent on the reaction centre, is the reason for the acceleration.

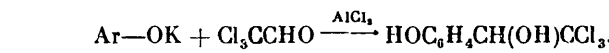
2. Syntheses based on chloral

The method of synthesis of (α-trichloromethyl)carbinols next in significance is based on chloral.

Chloral reacts under conditions of acid–base catalysis with aromatic hydrocarbons with the formation of aryl(trichloromethyl)-carbinols (ATMC) in good yield (70–91%). Both acidic (H_2SO_4, HCl, $AlCl_3$, $AlBr_3$, BF_3, $ZnCl_2$) [52–57] and basic catalysts (potassium hydroxide, pyridine, potassium carbonate) [58–60] are used for the condensation. Until recently it was considered that the method was effective only for benzene and its 1,4-disubstituted derivatives and in the remaining cases (monosubstituted benzenes) a mixture of 2- and 4-isomers is formed. It was shown, however, that this synthetic barrier was readily overcome on using a 10-fold excess of aromatic hydrocarbon relative to chloral.[61]

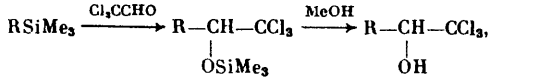


The hydroxybenzaldehydes do not take part in the condensation of haloforms with aryl aldehydes since the hydroxy group is converted into a phenoxide ion under base catalysis conditions, the electronic effect of which reduces significantly the positive charge on the carbon carbon and makes it inactive in relation to TCA. This synthetic gap in obtained 2-, 3-, and 4-hydroxyphenyl(trichloro-methyl)carbinols is eliminated by the reaction of phenoxides of the alkali metals with chloral.[62,63]



Many organometallic compounds also react with chloral with the formation of (α-trichloromethyl)carbinols, however, this method is not used widely due to low yields of the desired carbinols (< 50%) and the poor accessibility of the starting materials.[3,64–66] Furthermore the majority of alkylmagnesium halides react with chloral by an oxidation–reduction reaction forming trichloroethanol and the corresponding olefin (the Grignard reagent is a reducing agent). Exceptions are only the methyl- and benzyl magnesium halides which are not able to undergo such conversions and give adducts in good yield.[67] Vinyl- and substituted vinylmagnesium halides also react satisfactorily with chloral (30% yield) and the vinylcarbinols obtained are readily hydrogenated on palladium–carbon catalyst.[68]

In order to prepare new tranquillisers French scientists[8,9] have effected the synthesis of several(α-trichloromethyl)carbinols by the reaction of silylated hydrocarbons, in which the Si–C bond is activated by vinyl, acetylene and other electron-accepting substituents, with chloral in the presence of Lewis acids.

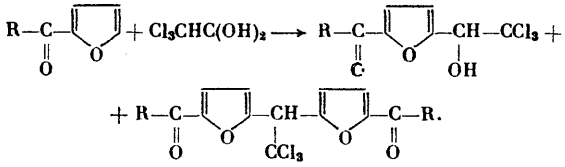


R=BuC≡C, $Me_3SiC{\equiv}C$, $Me_3SiCH_2C{\equiv}C$, PhC≡C, $EtOCOCH_2$, Et_2NCOCH_2,

pyrid-3-ylethynyl, 2-pyridyl, propargyl, allyl, vinyl.

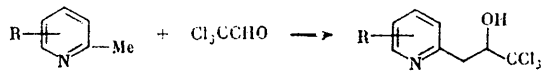
A series of interesting (α-trichloromethyl)carbinols containing α-ester groups has been synthesised by the reaction of chloral with orthoesters in the presence of mineral and Lewis acids.[69]

Studies[70,71] by Spanish scientists merit attention. These are devoted to the synthesis of substituted 2-furyl(trichloromethyl)-carbinols by the reaction of esters and amides of furane-2-carboxylic acid with chloral hydrate. In these studies, carried out for the purpose of obtaining effective pesticides, it was shown that, depending on the temperature and solvent, the reaction may stop at the required ratios of carbinol and the product with the bis structure.



R = NH_2, COOR′.

Chloral readily condenses with CH-acids. The condensation of picolines and lutidines with chloral is important from the applied point of view since the pyridomethyl(trichloromethyl)carbinols display local anaesthetic activity.[72,73]



Seemingly the ease of condensation is explained by the fact that the methyl and methylene substituents at the C(2) and C(4) atoms of the pyridine ring are potential centres for forming carbinols in view of their high CH-activity, which is readily stabilised by delocalisation, particularly if the heteroatom is quaternised. Such an approach is also substantiated by the fact that many authors have effected the condensation of chloral with picolines in the presence of Lewis acids.[74]

III. Conversions of (α-trihalomethyl)carbinols

(α-Trihalomethyl)carbinols are polyfunctional compounds. They react at the hydroxyl and trihalomethyl groups and it is interesting that anything affects one functional group leads to a modification of the other, i.e. there are very few reactions which are selective for one of these groups (exceptions are the partial and complete reduction of the trihalomethyl group and exchange of hydroxyl of halogen and acetoxy groups). Briefly, the numerous studies relate to the two types of conversions of (α-trihalomethyl)carbinols by reaction with basic and acidic reagents or by dehydrohalogenation and dehydration.

1. Reactions with acids

Acid hydrolysis of the isolated trichloromethyl group proceeds with the formation of an intermediate $R\overset{+}{C}Cl_2$ cation which is readily hydrolysed.[75] In sulphuric acid compounds of the type of $RCCl_3$ (R = Alk) at 90–100 °C form the $R\overset{+}{C}Cl_2$ cation,[76] which dissociates according to the scheme.[77]

$$RCCl_3+3H_2SO_4 \rightarrow R-\overset{+}{C}Cl_2+HOSO_2Cl+H_2O^+ +2HSO_4^-.$$

The formation of $R\overset{+}{C}Cl_2$ also occurs as a result of the thermal dissociation of the trichloromethyl group at high temperatures.[78,79]

$$RCCl_3 \rightleftarrows R\overset{+}{C}Cl_2+\overline{Cl}.$$

The hydroxyl group in the α position to the trichloromethyl group in (α-trichloromethyl)carbinols facilitates acidic hydrolysis, however, the reaction goes with complications. Alkyl trichloromethycarbinols form one product and aryl trichloromethylcarbinols form another.

On sulphuric acid hydrolysis of (α-trichloromethyl)carbinols the hydroxyl group is first involved in the reaction,[79,80] and it is possible to form the same $R\overset{+}{C}Cl_2$ cation by fission of hydroxyl and migration of a chlorine atom. Such a route of forming the $R\overset{+}{C}Cl_2$ cation occurs far more easily than through the difficult thermal dissociation of a C–Cl bond of the trichloromethyl group.

The first stage of the reaction of chloretone with 98% sulphuric acid is the protonation of the hydroxyl group with the formation of an oxonium cation, then follows elimination of water, the formation of the carbenium ion $Me_2\overset{+}{C}-CCl_3$, a 1,2-migration of chlorine atom and hydrolysis.[79]

$$Me_2C(OH)CCl_3 + H^+ \longrightarrow Me_2C(\overset{+}{O}H_2)CCl_3 \longrightarrow Me_2\overset{+}{C}CCl_3 \longrightarrow$$

$$\longrightarrow Me_2C\overset{Cl}{\underset{\odot}{\diagup\diagdown}}CCl_2 \longrightarrow Me_2C(Cl)\overset{+}{C}Cl_2 \xrightarrow{HOH}$$

$$\longrightarrow Me_2C(Cl)CCl_2\overset{+}{O}H_2 \longrightarrow Me_2C(Cl)COCl + HCl + H^+$$

With insufficient water the reaction stops at the stage of forming the acid chloride.

It is interesting that aryl[di(tri)chloromethyl]carbinols (ADMC, ATMC) do not give similar products on solvolysis with sulphuric acid.[81] In this case compounds of two types are formed, viz. a product of replacement of the hydroxyl group and a product of elimination of the HOCl fragment.[81]

$$ArCHCCl_2X \xrightarrow{H_2SO_4} ArCH(Cl)CCl_2 + ArCH=CCl_2,$$

$$\begin{matrix} | \\ OH \end{matrix} \qquad\qquad \begin{matrix} | \\ X \end{matrix}$$

X = H, Cl; Ar = *o*-, *p*-ClPh.

The reasons for the toxicity of diphenyldichloromethylmethane (DDD) have appeared in recent investigations and are a drawback for these medicinal preparations which have been approved for the treatment of adrenal neoplasia. It is proposed[81] that the increase toxicity of DDD and its analogues is linked with the formation of side products in their preparation by the condensation of the corresponding ADMC with chlorobenzene catalysed by acids.[82,83]

$$ArCH(OH)CCl_2X + PhCl \xrightarrow{H^+} Ar_2CHCCl_2X,$$

X = H, Cl; Ar = *o*-, *m*-, *p*-Cl, Alk-, AlkOPh.

Non-persistent analogues of DDD and DDT are obtained on an industrial scale by this reaction from readily available carbinols. Nevertheless yields are mainly low at 30–50% [82,83] and this already indicates the presence of side reactions. The products have been identified[81] and are formed by the action of concentrated H_2SO_4 on ADMC, ATMC and phenyltrichloropropanols. In contrast to ADMC and ATMC, 2,2-dichloro-1-(2-chlorophenyl)propanol forms only 1-(2-chlorophenyl)-1-chloropropanone with concentrated H_2SO_4. It is proposed that the reaction proceeds through an intermediate chloronium ion.

$$ArCH(OH)CCl_2Me \xrightarrow[-H_2O]{H^+} Ar-CH\overset{Cl}{\underset{\odot}{\diagup\diagdown}}CClCH_3 \xrightarrow[H^+]{H_2O}$$

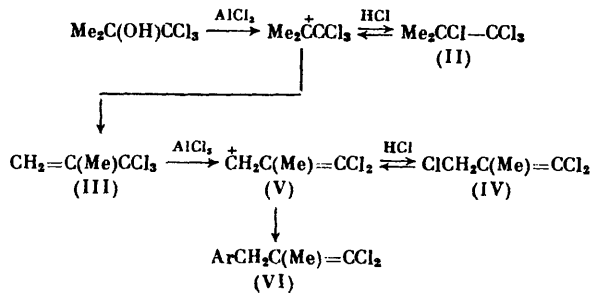
$$\longrightarrow ArCHClC(OH)ClCH_3 \xrightarrow[-HCl]{} \underset{(I)}{ArCHClCOMe}$$

It was shown by ^1H NMR using an acidified sample of carbinol that the quantity of water formed in the first stage of the reaction was sufficient for the transition into ketone (I). In fact the rearrangement occurs far more rapidly, condensations with chlorobenzene do not occur and ketone (I) is formed completely. On the other hand esterification in a sulphuric acid–acetic acid mixture occurs without anomaly with the formation of the acetoxy derivative of the starting carbinol.[81]

The use of Lewis acids for the dehydration of (α-trichloromethyl)-carbinols leads to a complex mixture of trichloroalkanes and tetrachloroalkanes.[84]

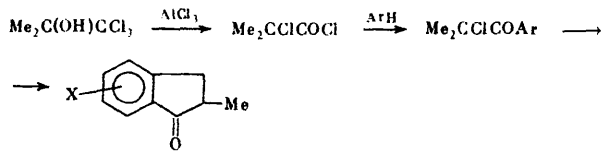
Even in the last century Willgerodt and Genieser[1] reported that on condensing chloretone with benzene, toluene and *o*-xylene in the presence of anhydrous $AlCl_3$ products of the replacement of a chlorine atom and the hydroxyl group were isolated in low yield. Kundiger and collaborators[84] repeated this reaction with toluene, chlorobenzene and anisole. The conclusions of the original authors[1] were not confirmed, alkylation of aromatic compounds by (α-tri-carbinols)carbinols by the direct replacement of chlorine atoms did not occur and neither did replacement of the hydroxyl. It was shown,[84] using chloretone as example, that dehydration occurs initially and the resulting 3,3,3-trichloro-2-methylpropene (III) is isomerised into 1,1,3-trichloro-2-methylpropene (IV). Compound

(IV) alkylates the aromatic nucleus via the allylic chlorine with the formation of 1,1-dichloro-2-methyl-3-arylpropenes (VI).



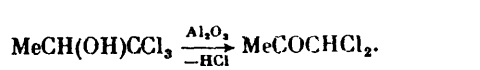
This scheme was confirmed by direct alkylation with individual (II)–(IV). Each of the intermediate products may give a carbonium ion of the type of (V) which forms the above-mentioned products in the course of the reaction.

On using chloretone under the conditions of the Friedel-Craft reaction the acid chloride of α-chloroisobutyric acid is formed together with the 1,1-dichloro-2-methyl-3-arylpropene.[84] If the experiment is carried out with small quantities of $AlCl_3$ it is possible to isolate the acid chloride mentioned above which condenses with aromatic hydrocarbons with an excess of $AlCl_3$ and gives 2-methyl-indanones.[84]



X = H, Cl

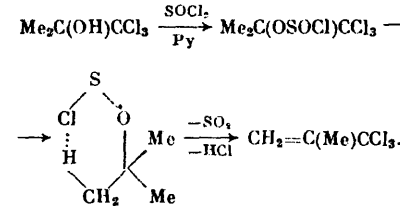
Primary and secondary trichloromethylated alcohols readily form alkoxy chlorides of the $ROAlCl_2$ type with $AlCl_3$,[85] which are comparatively stable. In this case alkylation by these carbinols proceeds not at the carbon linked with the hydroxyl but at the trichloromethyl group.[86] Seemingly the above-mentioned carbinols form mainly dehydrochlorination and not dehydration products under the action of zinc chloride and for the same reason. For example, it was shown[87] that 1,1,1-trichloropropan-2-ol forms 1,1-dichloroacetone on reaction with zinc chloride in hydrochloric acid solution. The same result was obtained on passing the same carbinol over a heated layer of aluminium oxide at 200–250 °C.[87]



Analysis of the available experimental data shows that under the influence of a trichloromethyl group all types of aliphatic α-carbinols should lose the ability to alkylate at a carbon atom linked with a hydroxyl group. Under the condensation conditions trichlorinated alcohols are either dehydrated with the formation of reactive compounds which lead to alkylation,[84] or the reaction proceeds at the expense of chlorine atoms of the trichloromethyl group.[85]

From the preparative point of view the dehydration reactions of (α-trihalomethyl)carbinols are attractive since interesting halogenated alkenes of various structures are generally obtained.

A mixture of thionyl chloride with various amines is used successfully for the dehydration of t-(α-trichloromethyl)carbinols.[88] The success of the dehydration depends critically on the molar ratio of thionyl chloride to amine. It was shown[89] that an increase in the quantity of amine leads to the formation of sulphates and chlorosulphonate esters. When using a catalytic quantity of amine (pyridine, aniline hydrochloride, t-butylamine, di-n-butylamine, *N,N*-dimethylaniline, triethylamine) 3,3,3-trichloro-2-methylpropene was obtained from chloretone in good yield.



On the other hand the use of a catalytic quantity of tetramethylammonium iodide leads to the allyl isomer due to the catalytic action of the resulting molecular iodine causing isomerisation.[88]

The introduction of a phenyl group into the α-position reduces the possibilities of dehydration. The absence of α-hydrogen atoms in phenyl(trichloromethyl)carbinol leads to the formation of α,β,β,β-tetrachloroethylbenzene (88%).[90] The latter was also obtained in 87% yield on using phosphorus pentachloride as dehydrating agent.[91] Replacement of the benzene ring by an aliphatic group leads to complications. In the case of ethyl-(trichloromethyl)carbinol Reeve[92] isolated the product of replacing the hydroxyl by chlorine in only 18% yield, the product of further dehydrohalogenation, viz. 1,1,2-trichlorobut-1-ene, in 13% yield and a high boiling mixture of phosphate and α-chloro-carboxylic acid ester.

$$EtCH(OH)CCl_3 + PCl_5 \longrightarrow \underset{18\%}{EtCH(Cl)CCl_3} + \underset{13\%}{EtC(Cl)=CCl_2} +$$
$$+ MeCH=CH-CCl_3 + \underset{4\%}{MeCH(Cl)-CH=CCl_2} + EtCH(Cl)COOEt$$

In the case of vinyl(trichloromethyl) carbinol the reaction is accompanied by a double allylic isomerisation.

$$CH_2=CH-CH(OH)CCl_3 + PCl_5 \longrightarrow CH_2=CH(Cl)CCl_3 \longrightarrow$$
$$\longrightarrow ClCH_2-CH=CH-CCl_3 \xrightarrow{Cu,\ 220^\circ C} ClCH_2-CHCl-CH=CCl_2$$

The products obtained by the reaction of alkynyl(trichloromethyl)carbinols with phosphorus pentachloride indicate the trivial course of the reaction. In this case the authors also identified the crystalline phosphate ester of the initial carbinols.[92]

$$RC\equiv C-CH(OH)CCl_3 + PCl_5 \longrightarrow RC\equiv C-CH(Cl)CCl_3 +$$
$$+ RCCl=C=CH-CCl_3 + (RC\equiv C-\underset{\displaystyle Me}{\underset{|}{CH}})_3PO_4$$

R = H, n-C_5H_{11}

It is interesting that replacement of the hydroxyl group in phenyl(trichloromethyl)carbinol by chlorine by the action of hydrochloric acid in the presence of 20% (by weight) zinc chloride was unsuccessful, while in phenyl(methyl)carbinol exchange occurs by the action of gaseous hydrogen chloride.[91] Bis(trichloromethyl)carbinol also does not react with hydrochloric acid.[93] This phenomenon may be explained by the presence of the electron-accepting trichloromethyl group, the effect of which on the reaction of the hydroxyl group is extremely significant.

Acid dehydrating agents such as phosphorus pentachloride are used for the dehydration of alkyl(trichloromethyl)carbinols. It was shown[94] that chloretone is dehydrated with difficulty. Mainly, resinification occurs and the dehydration product, 3,3,3-trichloro-2-methylprop-1-ene is obtained in very low yield (8%), the isomeric 1,1,3-trichloro-2-methylprop-2-ene is formed in somewhat larger amounts (15%).

The dehydration of 1,1,1-trichloropropan-2-ol has been studied by many authors. Here the literature data are fairly contradictory. Only in one case do the data agree. Pierce and collaborators[87] and Kirrmann and collaborators[95] assigned the structure of 1,1,2-trichloroprop-1-ene to the dehydration product of 1,1,1-trichloroisopropanol, both studies giving the yield as very small (8–10%). The dehydration products, which distilled over a wide temperature range (11°), were divided into four fractions of which only one was identified as 1,1,2-trichloroprop-1-ene.[87]

$$MeCH(OH)CCl_3 \xrightarrow{P_2O_5} MeCCl{=}CCl_2.$$

While carrying out the dehydration under the same conditions Henne and co-workers[96] reported that mainly 3,3,3-trichloroprop-1-ene was obtained with very little of the isomerised 1,1,3-trichloroprop-1-ene.

$$MeCH(OH)CCl_3 \xrightarrow{P_2O_5} \underset{85\%}{CH_2{=}CH{-}CCl_3} + ClCH_2{-}CH{=}CCl_2.$$

Using the same reaction as an example Kharasch and collaborators[97] considered that they had a 1,1,1-trichloro-containing compound. Fractions were separated during the dehydration which were distillable over a wide temperature range. On a second distillation two products were separated. The first was assigned the structure 3,3,3-trichloroprop-1-ene and the second 1,3-dichloroallene (based on IR spectroscopy).

$$MeCH(OH)CCl_3 \xrightarrow{P_2O_5} CH_2{=}CH{-}CCl_3 + ClCH{=}C{=}CHCl.$$

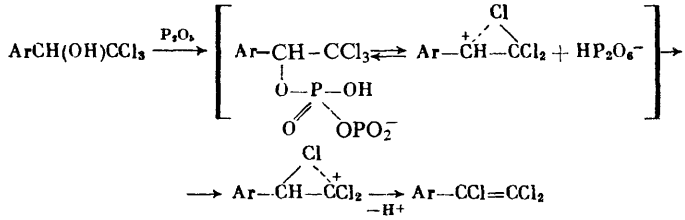
The constants for the first product agree with the data for the product obtained by Henry[98] but do not agree with the constants of Vitoria.[99] The authors[97] explain this by the fact that Vitoria most probably had a mixture of a propene and an allene and not the individual 3,3,3-trichloroprop-1-ene.

When generalising the results of all the studies in which phosphoric anhydride is used as the dehydrating agent in the reaction with alkyl(trichloro)carbinols (chloroetone, isopral), it may be concluded that dehydration occurs in this case by a mechanism leading to a complex mixture of isomeric chloroalkanes and allenes. It is quite probable that some products of the same dehydration process were successfully identified by one author and others by another. The low selectivity of this dehydration process is linked with the stabilisation of the intermediate carbenium ion simultaneously by several sources independently leading to one or other product, fission of the α-proton, shift of a double bond or skeletal rearrangement.

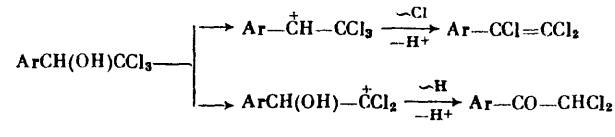
From the point of view of selectivity the considered reactions are only of theoretical interest, including the dehydration of aryltrihalo(chloro, bromo) methylcarbinols which leads to α,β,β-trihalo(chloro, bromo)styene in high yield (61–93%) by dehydration rearrangement with phosphorus pentoxide or oxychloride[10] and also on industrial aluminosilicates.[11]

$$ArCH(OH)CHal_3 \xrightarrow[Hal = Cl,\ Br.]{\text{dehydration}} Ar - CHal = CHal_2,$$

The dehydration of aryl(trihalomethyl)carbinols proceeds highly selectively compared with their aliphatic analogues because in this case the other means of stabilisation of the intermediate carbenium ion, which predominate in the aliphatic analogues, are suppressed. The relative reactivity of ATMC towards phosphorus pentoxide in cyclohexane was determined by the method of competing reactions.[100] The combination of the values for the ratio of the rate constants of substituted and unsubstituted carbinols (k/k_0) and the reaction constant ρ enabled the reaction mechanism to be established.



Industrial aluminosilicate (NBNZ) was also used as a dehydrating agent. Depending on its previous heat treatment this leads the process either towards dehydrochlorination with the formation of dichloromethyl aryl ketones[11] or towards a dehydration isomerisation reaction.



Evidently the previous heat treatment has a strong effect on the acid–base properties of the catalyst surface which also leads to a product of dehydration and dehydrochlorination.

The dehydration isomerisation reaction was used for a comparison of the migration properties of certain functional groups (halogens, alkyls) which form the series Br > Cl ≫ Alk in migrating ability under structurally identical conditions. Various α,β,β-trisubstituted styrenes, which are difficultly accessible by other methods of synthesis, were synthesised by the dehydration isomerisation one-stage method while of solving the theoretical problems.[101]

2. Reduction of the trichloromethyl group

The selectivity of the reduction of the trichloromethyl group in compounds of the $RCCl_3$ type depends on the nature of the initiator of the reduction reaction.

Carbon tetrachloride is selectively reduced by isopropanol to $CHCl_3$ on initiation by various peroxides,[102,103] by complexes of transition metal hydrides[104,105] or iron carbonyl $[Fe(CO)_5]$,[106] and further reduction of the resulting $CHCl_3$ to CH_2Cl_2 does not occur in practice. In the presence of $Mn_2(CO)_{10}$ and $Mo(CO)_6$ reduction occurs selectively with the formation of a mixture of $CHCl_3$ and CH_2Cl_2.

The reduction of the trichloromethyl group in compounds of the DDT type was the subject of several investigations with the aim of discovering new biologically active preparations.

The trichloromethyl group in DDT is exceptionaly inert towards the action of weak reducing agents. It is reduced by zinc in concentrated hydrochloric acid.[107] However it must be noted that the reduction proceeds non-selectively, the trichloromethyl group is reduced both to a dichloromethyl and to a methyl group with the formation of a mixture of 1,1-dichloro-2,2-di-(4-chlorophenyl)ethane, 1,1-di-(4-chlorophenyl)ethane and 4,4′-dichlorostilbene as the side product of the main reaction.

The selectivity of the reduction is significantly greater for the precursors of DDT, the (α-trichloromethyl)carbinols, however it also depends strongly on the character of the reduction initiator used and the substituent in the aromatic ring. Under the action of aluminium amalgam in alcohols, ATMC form the corresponding (dichloromethyl)carbinols in preparative yield.[108,109] Metallic aluminium (modified Meerwein-Pondorf method),[110,111] complexes of polystyrene with Ru, Rh and Ir containing organophosphorus ligands[112] and $Fe(CO)_5$ [106] in isopropyl alcohol have also been successfully applied for the same purpose.

$$ArCH(OH)CCl_3 \xrightarrow[iso-PrOH]{\text{reduction}} ArCH(OH)CHCl_2.$$

When reducing ATMC with zinc dust in acids or with lithium in liquid ammonia the selectivity of the process falls sharply.[113] The reduction of phenyl(trichloromethyl)carbinol with zinc dust in neutral or acid medium leads to a mixture of β,β-dichlorostyrene and β-chlorostyrene and in acetic acid to the methyl ether of phenyl(dichloromethyl)carbinol. Lithium in liquid ammonia gives α-phenylethanol in low yield and acetophenone and 2-phenylethan-1-ol as byproducts.

$$PhCH(OH)CCl_3 \begin{cases} \xrightarrow{Zn/H^+} PhCH{=}CCl_2 + PhCH{=}CHCl \\ \xrightarrow{Zn/AcOH} PhCH(OH)Me + CHCl_2 \\ \xrightarrow{Li/NH_3} PhCH(OH)Me + PhCOMe + PhCH_2CH_2OH \end{cases}$$

The introduction of a methoxy group into the 4-position of the aromatic nucleus in phenyl(trichloromethyl)carbinol increases the lability of the hydroxyl hydrogen. Reduction of the carbinol in isopropyl alcohol in the presence of $Fe(CO)_5$, $Mo(CO)_6$ or $Mn_2(CO)_{10}$ leads to a mixture of 4-methoxyphenyl(dichloromethyl)carbinol and 4-methoxyphenylisopropoxycarbinol in a ratio dependent on the nature of the carbinol and metal.[106] β,β-Dichlorostyrene is obtained as the main reaction on electrochemical reduction of the same carbinol.[114]

$$4\text{-}MeOC_6H_4CH(OH)CCl_3 \rightarrow 4\text{-}MeOC_6H_4CH{=}CCl_2.$$

There is even less selectivity on reducing the trichloromethyl group in alkyl(trichloromethyl)carbinols and in trichloromethylethanol. According to the data of Favorskii[115] a mixture of 1,1-dichloro-2-methylprop-1-ene and 1-chloro-2-methylprop-1-ene and isobutene, which are products of further reduction, is obtained from chloretone by reduction with zinc dust in ethanol.

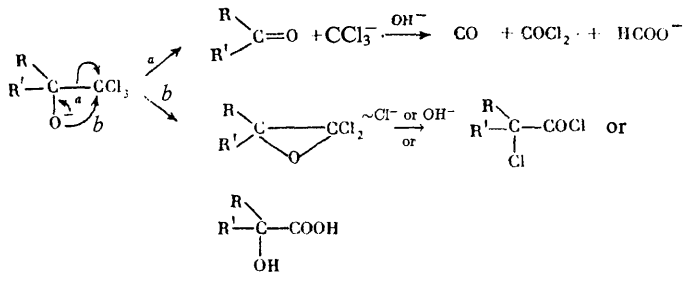
A dichlorocarbinol is obtained in 32% overall yield by the reduction of trichloroethanol in isopropyl alcohol in the presence of $RuCl_2(PPh_3)_3$.[116] The same dichloromethylcarbinol was obtained as a byproduct by electrochemical reduction when the main product was dichloroethylene.[117]

$$HOCH_2CCl_3 \longrightarrow CH_2{=}CCl_2 + \underset{\text{(byproduct)}}{HOCH_2CHCl_2}.$$

3. Reactions with bases

The isolated trichloromethyl group is inert to the action of nucleophilic reagents in general and of OH^- ions in particular.[118] The first studies devoted to the reaction of (α-trichloromethyl)carbinols with bases were carried out using as example dimethyl(trichloromethyl)carbinol (chloretone), however it turned out that in the course of the reaction chloretone is subject to alkaline decomposition with the formation of acetone, chloroform, carbon monoxide, phosgene and formic acid,[119] i.e. a reaction is observed which is the reverse of the chloretone synthesis with subsequent alkaline hydrolysis of chloroform. A similar decomposition was even observed by Iotsich in the reaction of phenyl(trichloromethyl)-carbinol with aqueous KOH.[2] In parallel, Willgerodt and collaborators[120] successfully isolated a small quantity of α-hydroxy-, and Ostropyatov[121] α-chloroisobutyric and methacrylic acids from the products of the reaction of chloretone with aqueous KOH. Seemingly both the decomposition and the formation of the acids mentioned proceeds through the same alkoxide ion of the (α-trichloromethyl)carbinol (Scheme 2).

Scheme 2



In numerous studies devoted to this reaction the molar ratios of carbinols and bases were selected which provide the maximum yields of α-chloro- and α-hydroxyacids, i.e. experimental conditions directed to the suppression of route *a*. This is successfully carried out at the expense of hydrolysis of the carbinols in aqueous dioxan in the presence of ion exchange resin[122] or by replacement of the aqueous by alcohol alkali, the use of which leads to α-alkoxyacids in preparative yields. The observed phenomenon is seemingly linked with the basicity of the RO^- formed from the initial carbinol, which further attacks selectively the electrophilic centre in the trichloromethyl group to a greater extent than is regulated by haloform decomposition.

It was shown that chloretone forms α-ethoxyisobutyric acid in 72% yield on reaction with three equivalents of sodium ethoxide in ethanol.[123] The mechanism by which this conversion occurs passes, "indisputably" according to Jacob,[124] through the intermediate dichloroepoxide which then undergoes alcoholysis. The author arrived at this conclusion from the reaction of chloretone with dimethylaniline and comparison of these results with data on the alcoholysis of the epoxide ring.[125]

$$Me_2C(OH)CCl_3 \xrightarrow[EtOH]{EtONa} Me_2C(O)CCl_2 \xrightarrow[EtOH]{EtONa} Me_2C(OEt)COOEt$$

The formation of α-alkoxyacids may be considered probable from the intermediate acid chloride of the α-chloroacid, the rearrangement product of the dichloroepoxide. However the high yields of the final products make this alternative variant less probable. The absence of the formation of unsaturated acid and of chlorine-containing products excludes the rearrangement of the dichloroepoxide before its alcoholysis.

α-Butoxyisobutyric acid is isolated on reaction with 4 M KOH in alcoholic medium or with potassium butoxide in butanol at 0 °C.[126]

$$Me_2C(OH)CCl_3 + KOH \longrightarrow Me_2C(O)CCl_2 + KCl + H_2O,$$

$$Me_2C(O)CCl_2 + 2KOH \longrightarrow Me_2C(O)C{=}O + 2KCl + H_2O,$$

$$Me_2C(O)C{=}O + ROH \longrightarrow Me_2C(OR)COOH.$$

At the same time the preparation of an alkoxyacid ester may take place without the participation of an α-lactone.

$$Me_2C(O)CCl_2 + ROH + 2KOH \longrightarrow Me_2C(OH)(OR)C + KCl + H_2O,$$

$$Me_2C(OH)(OR)C + ROH \longrightarrow Me_2C(OR)COOR + H_2O.$$

Reeve and collaborators,[127] while studying the reaction of ATMC with bases as though resuming their investigations on the study of the mechanism of the conversion in question, published stereochemical data on the reaction of (*S*)-(+)- and (*R*)-(−)-phenyl(trichloromethyl)carbinols with MeONa/MeOH at 40 °C leading to (*S*)-(+)- and (*R*)-(−)-α-methoxyphenylacetic acids respectively. It was shown that the conversion proceeds with 9% inversion of configuration and 91% racemisation of the initial carbinol. The mechanism considered does not differ appreciably from the mechanisms discussed by Bergman and Jacob. According to Reeve's mechanism HCl is eliminated from the initial carbinol by the action of methoxide ion with the formation of the dichloroepoxide, which then is subjected to methanolysis and hydrolysis with the formation of α-methoxyphenylacetic acids. The inversion of configuration occurs during methanolysis of the dichloroepoxide.

$$PhCH(OH)CCl_3 \xrightarrow[-HCl]{} PhCH(O)CCl_2 \xrightarrow{MeO^-} PhCH(OMe)COCl \xrightarrow{hydrolysis} PhCH(OMe)COOH$$

According to an alternative mechanism the dichloroepoxide is rearranged with migration of a chlorine atom to the acid chloride of α-chlorophenylacetic acid with inversion of configuration due to attack by the migrating chlorine atom at the α-carbon atom from the side opposite the epoxide oxygen. After hydrolysis of the acid chloride, replacement of chlorine by a methoxy group occurs.

$$PhCH(O)CCl_2 \xrightarrow{-Cl} PhCH(Cl)COCl \xrightarrow{hydrolysis} PhCH(Cl)COO^- \xrightarrow{MeO^-}$$

(inversion of configuration)

$$\longrightarrow PhCH(OMe)COO^- \xrightarrow{H^+} PhCH(OMe)COOH$$

It was shown experimentally[127] that under the reaction conditions the (*R*)-(−)-acid chloride of α-chlorophenylacetic acid is 96% racemised by the action of methoxide ion and the racemisation of the (*R*)-(−) configuration occurs more rapidly than that of the (*S*)-(+).

It is proposed that methanolysis leading to the α-methoxy ester also occurs through the intermediate gem-dichloroepoxide.[128]

The deacetoxychlorination of chloretone acetate leading to α-ethoxyisobutyric acid ethyl ester in 55% yield has been carried out[129] by boiling with an ethanolic solution of sodium ethoxide. The authors postulate the formation of this ester through the same intemediate dichloroepoxide.

α-Alkoxyarylacetic acids, obtained by the reaction of ATMC with alcoholic bases, have a high practical value (in analytical chemistry, agriculture).[130–134] Proceeding from this, a broad investigation was undertaken to optimise the synthesis of these acids.[130,135] The synthesis of aryl[trichloro(bromo)methyl]carbinols, their subsequent dehydrohalogenation and alcoholysis of the intermediate dihaloepoxide have been successfully combined in one stage.

$$ArCHO + CHHal_3 \xrightarrow[MeOH]{KOH} [ArCH(OH)CHal_3] \xrightarrow{KOH} ArCH(O)CHal_2 \xrightarrow{MeO^-}$$

(without isolation)

$$\longrightarrow ArCH(OMe)COHal \longrightarrow ArCH(OMe)COOMe,$$

Hal = Cl, Br.

It is interesting that the synthesis of phenyl(tribromomethyl)carbinol from an aldehyde and bromoform occurs with difficulty and in low yield (10–40%) but under the conditions of the reaction being considered (without isolation of the carbinol) the yield of the final α-methoxyarylacetic acids was 75% of theoretical. The condensation of 3-chlorobenzaldehyde with chloroform also proceeds with difficulty and the yield of the desired 3-chlorophenyl(trichloromethyl)carbinol was 12% overall.[15] Under the conditions of the given reaction α-methoxy-(3-chlorophenyl)acetic acid was isolated in 70% yield.

Replacement of methanol by liquid ammonia in the system aldehyde–haloform–potassium hydroxide–methanol leads to the formation of α-amino acids in low yield (29–48%) as a result of fission of the epoxide ring by amide ion.[14]

$$RCHO + CHCl_3 \xrightarrow[-33^\circ C]{KOH,\ NH_3} RCH(OH)CCl_2 \xrightarrow[-HCl]{} RCH(O)CCl_2 \xrightarrow{NH_3}$$

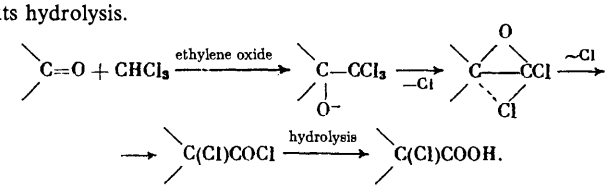
(isolation not obligatory)

$$\longrightarrow RCH(NH_2)COOH.$$

Although this method contradicts somewhat the synthesis of (α-trichloromethyl)carbinols under the same conditions,[20] it has been confirmed by recent work by Chinese authors,[136] in which a similar synthesis of amino acids was effected by the condensation of aliphatic aldehydes, ketones and cyclic ketones with chloroform and ammonia by phase transfer catalysis (dichloromethane–water, the catalyst was diethylbenzylamine ethochloride).

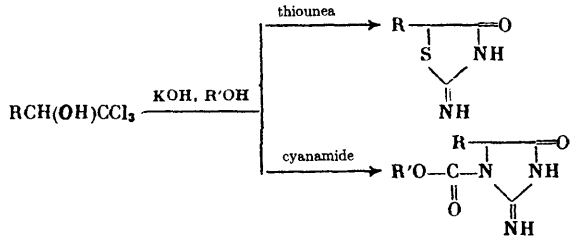
It should be mentioned that an analogous single-reactor method was used for the first time by Link.[137]

By a method similar to that of Link and Reeve, Buddrus and collaborators[138,139] carried out the condensation of isobutyraldehyde, acetone and cyclohexanone with chloroform taking ethylene oxide as base. The corresponding α-chlorocarboxylic acids were isolated in this case and are products of the rearrangement of the intermediate dichloroepoxide into the acid chloride of the α-chlorocarboxylic acid and its hydrolysis.

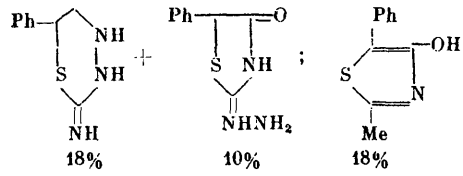


The high preparative value of α-haloacids and their acid chlorides in synthetic organic chemistry, particularly as synthons of α-amino acids and other functionalised α-carboxylic acids, was the reason for the in-depth study of the dehydrochlorination of (α-trihalomethyl)-carbinols. As was mentioned above the haloform fission of (α-trihalomethyl)carbinols (Scheme 2, route *a*) is the main obstacle to the dehydrochlorination process. It was established that the process depends strongly on temperature, reaction time and also on the alkali used.[140] Optimum conditions for obtaining α-chloroaryl-acetic acids were 0 °C, 10% aqueous KOH (10% aqueous NaOH forms a gel and the yield of product is reduced), the carbinol : KOH = 1 : 4 (yield 60–70%) and the reaction time was several days. The use of (tribromomethyl)- or mixed (chloro, bromo)carbinols leads to a significant reduction in the quantity of alkali, in the reaction time and to an increase in the yield of the desired α-haloacetic acids (17–100%).[141] Since the limiting stage of the process is the formation of the gem-dihaloepoxide, it is evident that the replacement of chlorine by bromine facilitates the intramolecular S_N2' substitution of halogen in the trihalomethyl grouping (Scheme 2, route *b*) with the formation of the epoxide ring and also rearrangement into α-haloacetic acids.

The single reactor method of Link and Reeve has limited application since the majority of the nucleophiles enter into direct condensation with carbonyl compounds with an incommensurably higher rate than does THA. For this reason the reaction of certain nucleophiles was studied directly on (α-trichloromethyl)carbinols. Cyanamide and thiourea[142–144] were tested with ATMC in various alcohols (methanol, ethanol, ethyleneglycol) and cycloadducts were isolated, viz. functionally substituted 1-imidazolinecarboxy imidates and thiazolidinones in low yields.

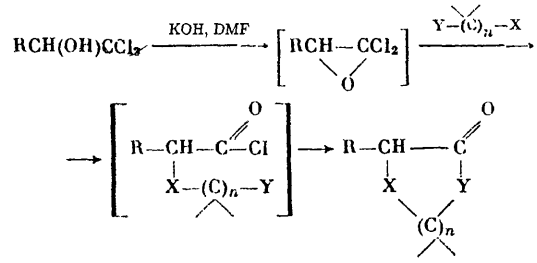


R was varied in (α-trichloromethyl)carbinols (alkyl, aryl, vinyl, ethinyl), but the yield of cycloadduct was not increased successfully. Replacement of nucleophiles (thiosemicarbazide, thioacetamide) also did not lead to the expected result. A mixture of dihydro-2-imino-6-phenyl-2H-1,3,4-thiadiazin-5-(6H)-one and 5-phenyl-2,4-thiazoldinedione-2-hydrazone in yields of 18 and 10% respectively was isolated from phenyl(trichloromethyl)carbinol by reaction with thiosemicarbazide. With thioacetamide by 4-hydroxy-2-methyl-5-phenylthiazole was isolated in 18% yield.[145]



The yield of cycloadduct was sharply increased on replacing a protic solvent by the dipolar aprotic solvent DMF. 2,5-Disubstituted thiazolidin-4-ones (a) were isolated from ATMC by reaction with thioacet(benz)amides in 40–85% yield,[146] tetrahydro-2-hydroxy-3-aryl-1,4H-quinoxalines (b) in 70–80% yield with *o*-phenylenediamine, 2-hydroxy-3-arylpiperazines (c) in 57–60% yield with ethylenediamine, 2-hydroxy-3-aryl-1,4-benzodioxans (d) in 63–84% yield from pyrocatechol and 2-aryl-3-hydroxy3,4-dihydro-2H-1,4-benzoxazines (e) from 2-aminophenol in 70–85% yield (Scheme 3).[147]

Scheme 3



R = Ar, Het;
X = S, Y = N, n = 1(a), X = Y = N, n = 2(b); X = Y = N, n = 2(c); X = Y = O, n = 2(d); X = P, Y = N, n = 2(e).

Since all the addition reactions considered above proceed through the intermediate gem-dihaloepoxide, the favourable influence of the dipolar solvent DMF on the dehydrochlorination of (α-trichloro-methyl)carbinols[146,147] is explained by the fact that the oxygen atom in DMF, being a centre of increased electron density, strongly coordinates potassium ions but the less effective positive portion weakly solvates the alkoxide ion. The weakly solvated anion possesses greater energy consequently the energy of activation of the intramolecular epoxidation is appreciably reduced in comparison with the use of protonated solvents.

The available literature data obtained by spectral methods in combination with quantum chemical calculations of the distribution of electron density in epoxides show that the epoxide carbon atoms, independent of the nature of the substituent, are extremely electron deficient. The value of the electron density on these atoms differs little.[148] This explains why the nucleophilic fission reaction of

epoxides occurs at both the α- and at the β-carbon atoms. However analysis of the total literature data on the fission of gem-dichloroepoxides by mono- and dinucleophiles shows that only the α-carbon atom is subject to nucleophilic attack. The reason for the observed regioselective fission of the ring may be attributed to shielding of the β-carbon atom by the bulky chlorine atoms. However the data on the X-ray structural analysis of the only stable gem-dichloroepoxide, 1,1,3,3,3-pentachloropropylenepoxide† gave a complete answer. According to X-ray structural analytical data the unfavourable conditions for the approach of a nucleophile to the β-carbon atom created both by the steric screening of the chlorine atoms, and by the strengthening of the C–O bond with the participation of the β-carbon atom which creates additional blocking from the side of the "adjacent" oxygen atom. On the other hand the O(1)–C(3) bond involving the α-carbon atom is longer than the O(1)–C(2) bond and is therefore weaker to a considerable extent (Fig. 1).[150]

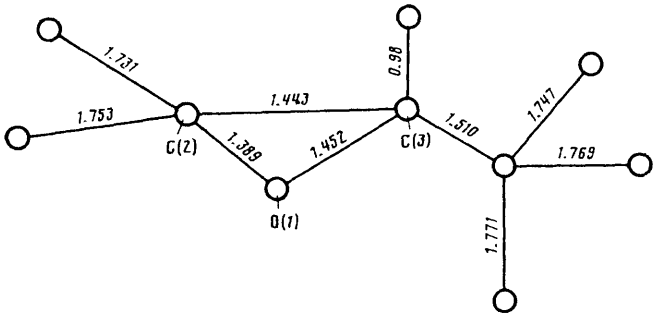


Figure 1. The structure of the 1,1,3,3,3-pentachloropropylene oxide molecule; σ = 0.003–0.004 Å.[150]

The reaction of aromatic and heterocyclic (α-trichloromethyl)-carbinols with mono-*C*-nucleophiles, viz. malonic, acetoacetic[151] and cyanoacetic[152] esters, has been studied with a view to clarifying the synthetic possibilities of gem-dichloroepoxides. It was established that adducts of vicinal structure are formed by the reaction and are the diethyl esters of substituted adipic acids which thermally, catalytically or spontaneously cyclise into substituted hetero- and carbocyclic ketones (Scheme 4).

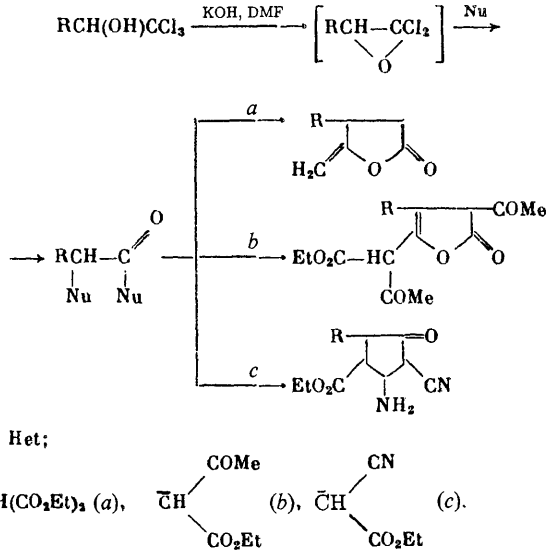
† 1,1,3,3-Pentachloropropylene oxide is the sole stable representative of the gem-dichloroepoxides. It is obtained by the reaction of bis-trichloromethylcarbinol with 2 N NaOH at 20 °C.[93]

$$Cl_3C{-}CH(OH){-}CCl_3 \xrightarrow{NaOH} Cl_3CCH{-}CCl_2$$

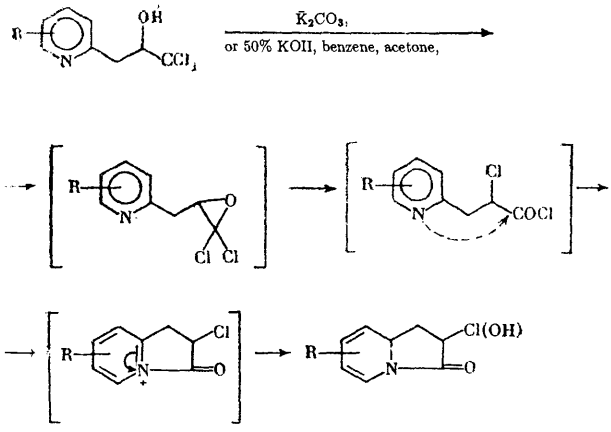
It is appropriate to mention that this dichloroepoxide was also obtained by Seyferth and collaborators[149] by the reaction of the carbenoid $PhHgCCl_3$ with chloral in boiling benzene and the physicochemical constants given agree exactly[93] although the author describes this compound as being synthesised for the first time.

In the studies considered the direction of the reaction of (α-trichloromethyl)carbinols of the aromatic and heterocyclic series with mono-*C*- and 1,3,1,4-dinucleophiles is the same and the difference consists only in the yield of the cycloadduct.

Scheme 4



It is interesting that the 2-pyridomethyl(trichloromethyl)carbinols are converted by base phase transfer catalysis (PTC) in the absence of external nucleophiles into [2,3H]-indolizines as a result of a rearrangement–heterocyclisation of the gem-dichloroepoxides generated as intermediates.



Depending on the type of PTC (liquid–solid, liquid–liquid) the product of heterocyclisation, the [2,3H]-indolizine, has either an α-chloro- or an α-hydroxyketone grouping. Since the indolizine structure forms part of the composition of the veratrum alkaloids, which are obtained by the multistage syntheses of Barret, Chichibabin and Shol'ts, the observed conversion acquires value in applied chemistry.[153]

In general the chemistry of [α-trihalo(chloro, bromo)-methyl]-carbinols is at the stage of promising development. The universal nature of these compounds for the solution of a whole series of problems of theoretical and practical chemistry has been demonstrated. The facile generation from them of highly reactive, little-studied gem-dihaloepoxides, which are synthons for a whole range of compounds with various properties, is just one factor indicating that the development of this field extends knowledge and creates new areas for using (α-trihalomethyl)carbinols.

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Translated from *Uspekhi Khimii* **60** 2566–2592 (1991) U.D.C. 547.1:541.1

Methods of replacing halogen in aromatic compounds by RS-functions

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ABSTRACT. This review is devoted to methods of replacing aromatic halogen by RS-groups. The essential mechanisms of these reactions have been examined, and the advantages and limitations of each method noted.

The bibliography contains 124 references.

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I. Introduction

Nucleophilic replacement of halogen in the aromatic nucleus has always been a focus of attention in view of the enormous synthetic implications. The large volume of experimental and theoretical data published in this field has been reviewed several times.[1–6] The replacement of aromatic halogen by RS-groups has been covered in part, but interest in this particular substitution has noticeably increased during the last ten years. This is partly because the theoretical aspects of this conversion have been under scrutiny, and partly because of the development of new practical routes to sulphur-containing compounds of potential use as antioxidants, polymer stabilisers, pesticides and drugs, and in the oil and petroleum industry.[7]

The replacement of aromatic halogen by organothio groups is by no means straightforward, and several key routes have been developed: 1) purely ionic processes, notably involving activation by strong bases and/or specific solvents; 2) catalytic processes, involving both metal complexes and phase transfer catalysts; 3) high-temperature, free-radical processes; and 4) photo- and electro-chemical processes, principally of an ion-radical nature.

A number of publications on the thiylation of aromatic halides prior to 1972 has been examined in a monograph.[8] However, there have been no recent surveys covering this theme in its entirety. This is a systematic review of data published in this field during the last 10–15 years.

II. Nucleophilic thiylation of aryl halides without the use of specific catalysts

In the initial attempts to replace aromatic halogen by mercaptide (RS^-) or thiyl (HS^-) anions, sodium sulphide and polysulphide were used as reagent. Unactivated aromatic halides were inert under these conditions. Thus, chlorobenzene reacts with Na_2S only at 350–360 °C under a pressure of 180–190 atm.[9] In an aqueous ethanolic solution of Na_2S, activated aromatic halides, e.g. *o*- and *p*-nitrochlorobenzene, afford a mixture of products. Here, intermediate thiophenoxide anions react with the starting halide to give the corresponding symmetrical diaryl sulphide, while, at the same time, being oxidised to the corresponding disulphide.[9] Heating *p*-nitrochlorobenzene with an excess of Na_2S_2 in an alcoholic medium for a short period of time leads to the formation of *p*-nitrothiophenol in 65% yield:[1]

$$6\,p\text{-}ClC_6H_4NO_2 + 4Na_2S_2 + 6NaOH \rightarrow 6\,p\text{-}NO_2C_6H_4SNa + 6NaCl + 3H_2O + Na_2S_2O_3.$$

2,4-Dinitrochlorobenzene has a reactivity similar to alkyl chlorides: on heating in an aqueous alcoholic medium with Na_2S it is converted to the tetranitrodiphenyl sulphide in 79% yield.[9] Treatment of activated nitroaryl halides with Na_2S results in both substitution and reduction of the nitro group to give azoxy compounds and aniline derivatives.[1]

The majority of the early syntheses of unsymmetrical thioesters were based on the reactions of halogenonitrobenzenes with methanethiol and *o*- or *p*-nitrothiophenol in the presence of alcoholic base.[1] Data published before 1970 on the reactions of halogenonitrobenzenes with MeS^- and PhS^- in alcoholic media have been surveyed in a monograph.[10]

By measuring the rate of the reaction of PhS^- with 1-halogeno-2,4-dinitrobenzenes in methanol between 0–15 °C, Bunnett and Merritt verified that the kinetic data were in accord with an S_N2 mechanism.[11] The reactivity of aryl halogen followed the order $F \gg Br > I > Cl$. The rate of replacement of Br, I and Cl was approximately the same, but that of F was approximately twice as great.

Unactivated aromatic halides interact more smoothly with mercaptide anion in the presence of a strong base. Thus, bromobenzene reacts with PhS^- in liquid ammonia in the presence of alkali metal amide.[12,13] However, as ammonia itself is weakly nucleophilic, the formation of diphenyl sulphide is accompanied by amination products:

$$PhBr + PhS^- \xrightarrow{NH_3} \underset{10\%}{PhNH_2} + \underset{12\%}{Ph_2NH} + \underset{52\%}{Ph_2S}.$$

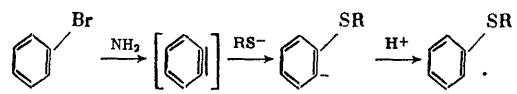
As the reaction of 1-bromonaphthalene with PhSNa yields a mixture of 1- and 2-naphthyl phenyl sulphide, it is assumed that under these conditions an elimination-addition (benzyne-type) mechanism prevails.[12]

The substitution of bromobenzene can be extended to other mercaptans if an aprotic solvent (a mixture of hexamethylphosphoramide and THF) is used in the presence of sodium amide at 35–40 °C.[14,15]

$$\mathrm{PhBr + RSH \xrightarrow[12-66\%]{HMPA+THF} PhSr,}$$

R = Et, *n*-Bu, $PhCH_2$, Ph.

Here too, it is considered that reaction involves intermediate formation of benzyne, which undergoes subsequent nucleophilic attack by RS^-:

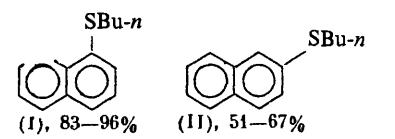


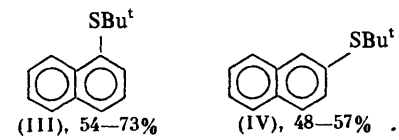
Judging by the products formed by interaction of *o*-toluyl iodide with thiophenol in DMSO containing tert-BuOK, it would appear that benzynes are also involved in the reaction of aryl iodides with aryl mercaptans:

$$\mathrm{PhSH + PhI \rightarrow \underset{100\%}{PhSPh}}$$

$$\mathrm{PhSH + \textit{o}\text{-}MeC_6H_4I \rightarrow \underset{50\%}{\textit{o}\text{-}MeC_6H_4SPh} + \underset{50\%}{\textit{m}\text{-}MeC_6H_4SPh}.}$$

1-Fluoro- and 2-fluoro-naphthalene, as well as the bromine analogues, react with n-butyl and tert-butyl mercaptan on heating in DMSO (110 °C) in the presence of MeONa to give the corresponding naphthyl thioethers (I)–(IV):[17,18]





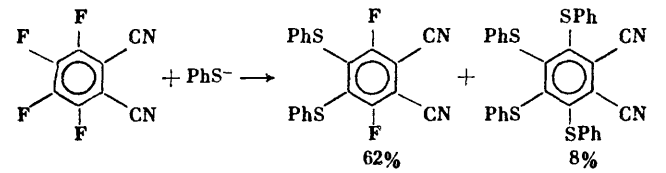
Under these conditions, butyl 2-naphthyl sulphide is not formed from 1-bromo- or 1-fluoro-naphthalene, so that the intermediate formation of the corresponding benzyne (1,2-dehydronaphthalene) can be excluded.

From a synthetic point of view, it is interesting that hexahalogenobenzenes—C_6F_6, C_6Cl_6 and C_6Br_6—react smoothly and rapidly with mercaptides on heating in a mixture of ethylene glycol and an organic base, e. g. pyridine. In the reaction of C_6Br_6 with RS^-, there is the possibility of both substitution and protodebromination, according to the following proposed scheme:[19]

$$\mathrm{C_6Br_6 + MeS^- \rightarrow C_6Br_5SMe,\ C_6Br_4(SMe)_2,\ C_6Br_2(SMe)_4,}$$
$$\mathrm{C_6Br_5H,\ C_6Br_2H(SMe)_3,\ C_6H_2Br_3(SMe),}$$
$$\mathrm{C_6Br_6 + EtS^- \rightarrow C_6Br_4H(SEt),\ C_6Br_5H,\ C_6Br_4H_2.}$$

Products such as C_6Br_4HSEt and $C_6Br_2(SMe)_4$ have never previously been prepared. However, the reaction of C_6F_6 and C_6Cl_6 with RS^- (R = Me, Et, Ph, C_6F_5, CH_2CH_2SH) proceeds only by substitution (up to 4 atoms of halogen being replaced by an organothio group); there is no protodehalogenation.[20–22]

The interaction of tetrafluorophthalonitrile with PhS^- in methanol proceeds primarily by replacement of two atoms of fluorine:[23]



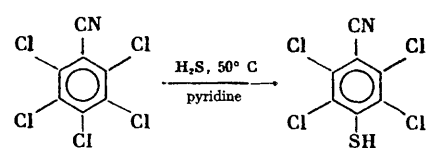
Hexafluoro- and hexachloro-benzene react with NaSH on heating in a mixture of ethylene glycol and pyridine to give the corresponding pentahalogenothiophenol:[24,26]

$$\mathrm{C_6Cl_6 + NaSH \rightarrow \underset{95\%}{C_6Cl_5SH} + NaCl,}$$

$$\mathrm{C_6F_6 + NaSH \rightarrow \underset{59\%}{C_6F_5SH} + NaF.}$$

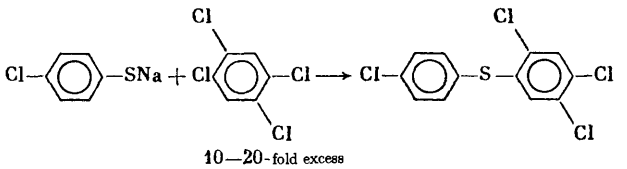
However, no such reaction takes place with hexabromobenzene.[19]

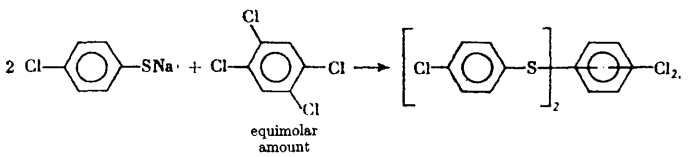
Pentachlorothiophenol can also be obtained by treatment of C_6Cl_6 with alkali metal hydrogen sulphide under 1 atm in DMF [2] or methanol.[27] Polychlorocyanobenzenes react with H_2S in pyridine in the presence of triethylamine to give the corresponding *p*-cyanothiophenol,[28] e. g.



In the 1960s it was discovered that aprotic solvents significantly enhance nucleophilic processes involving alkali metal salts by solvating the cation. Aromatic thiylation is no exception. Thus, both symmetrical and unsymmetrical diaryl sulphides have been prepared by prolonged heating of aryl mercaptides with aromatic halides in DMF—a solvent with weak dipolarophility.[29] The following thiylating agents were used: PhSNa, *p*-MeC_6H_4SNa,

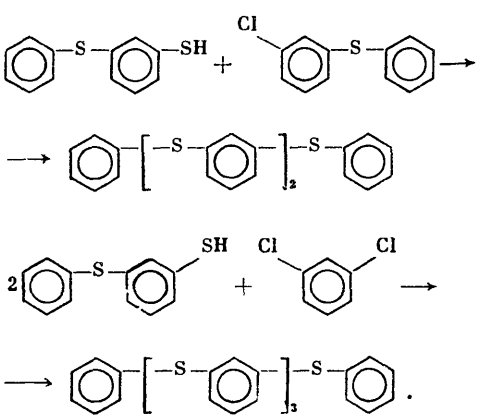
p-ClC_6H_4SNa. The reactivity of aromatic halides towards these thiophenoxides was in the following order: PhBr < bromonaphthalene < $C_6H_4Cl_2$ < $C_6H_3Cl_3$ < $C_6H_2Cl_4$. With polychlorobenzenes, the degree of substitution depends on the molar proportion of the starting materials:





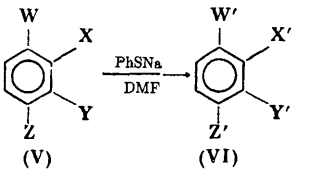
In order to extend the reaction as a preparative route to diaryl sulphides from unactivated aromatic halides, while at the same time improving the overall yield without complicating the procedure, Campbell et al. proposed the use of various amide or amine solvents: dimethylacetamide (DMA) at 170–175 °C; diethylaniline at 210–216 °C; and *N*-methyl-2-pyrrolidone at 185–190 °C.[30–32]

A thermal route is recommended for the preparation of aryl mono-, bis-, tris-, and poly-thioethers, alkyl aryl thioethers, and phenylthiobiphenyls. Thus, the conversion of bromobenzene at high temperature affords diphenyl diphenyl sulphide in ~65% yield, contrasting with 13% by the conventional route.[29] Polyphenyl thioethers with four or five aromatic nuclei were obtained for the first time as follows:[32]



It is suggested that the mechanism of the reaction is of a bimolecular, S_NAr, type,

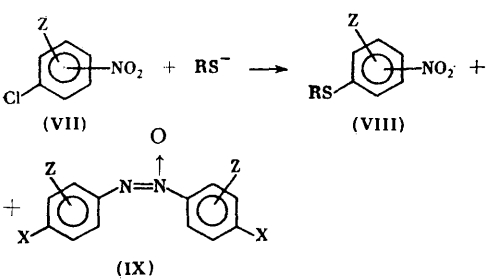
The thiylation of activated aromatic halides can be conducted at a much lower temperature by using an aprotic solvent, e.g. DMF. Thus, bis(phenylthio)benzenes (VI) were obtained from dihalogenonitrobenzenes (V) at 0 °C.[33]



(V) (VI)

(Va) W = NO_2, X = Cl, Y = H, Z = Cl; (VIa) W′ = NO_2, X′ = SPh, Y′ = H, Z′ = SPh (72%)
(Vb) W = Cl, X = NO_2, Y = H, Z = Cl; (VIb) W′ = SPh, X′ = NO_2 Y′ = H, Z′ = SPh (27%)
(Vc) W = NO_2, X = H, Y = Cl, Z = Cl; (VIc) W′ = NO_2, X′ = H, Y′ = SPh, Z′ = SPh (31%).

Another advantage of using DMF for thiylation of halogenonitrobenzenes is that side-reactions are reduced. The reaction of halogenonitrobenzenes with RS^- in alcoholic base[1] is complicated by competitive reduction of the nitro group. However, the preparation of thioethers (VIII) is significantly improved by using DMF as solvent, in which the formation of azoxybenzenes as by-product is suppressed.[34] Adjusting the order of addition of the reactants also has a beneficial effect:

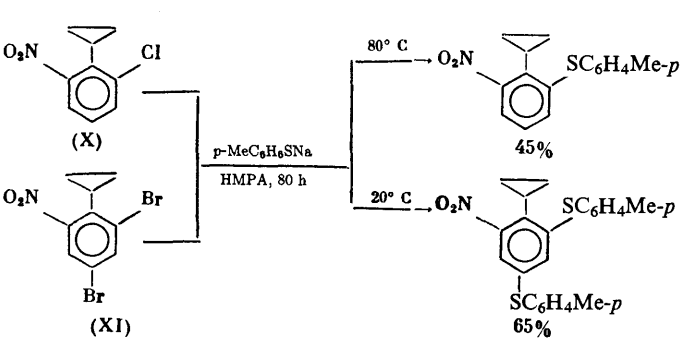


(VII) (VIII) (IX)

Z = H (a); CF_3 (b); R = Me, Pr^i, CH_2Ph, Ph; X = Cl, SPh.

As an example, the yield of (VIIIb, R = Me) and azoxybenzene (IXb) is 18% and 81%, respectively, by the conventional route.[1] However, in DMF [34] the yield of (VIIIb, R = Me) is 95%.

Replacement of halogen in (nitrohalogenophenyl)cyclopropanes (X, XI) by *p*-tolylthio groups with sodium *p*-thiocresolate can be carried out in *N*-methyl-2-pyrrolidone or hexamethylphosphoramide.[35]



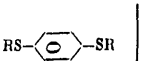
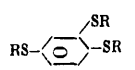
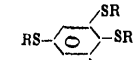
(X) (XI)

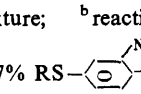
On the other hand, heating the chloride (X) with sodium *p*-thiocresolate in ethanol results in reduction of the nitro group to give 3,3′-dichloro-2,2′-dicyclopropylazobenzene.

The method described above is essentially limited to the reaction of aromatic halides with arylmercaptides (ArS^-). The same reaction with alkylmercaptides (RS^-) can be achieved in hexamethylphosphoramide, as reported by Italian chemists in a series of publications.[36–40]

Activated aryl halides, such as *o*- and *p*-nitrochlorobenzene (XIII), 1-chloro-2,4-dinitrobenzene (XIII) and picryl chloride (XIV) react at room temperature with excess of RSNa (where R = Me, Et, iso-Pr, tert-Bu) in hexamethylphosphoramide by replacement of both halogen and nitro groups (Table 1).[36] The highest yield of poly(alkylthio)benzene is obtained with sodium isopropylmercaptide in hexamethylphosphoramide. It should be noted than an alkylthio group in the *ortho*- or *para*-position activates replacement of the nitro group by RS^-.

Table 1. Reaction of *p*-nitrochlorobenzene (XII) 2,4-dinitrochlorobenzene (XIII) and picryl chloride (XIV) with RSNa in HMPA at room temperature.[36]

Substrate, *R*	Yield of product %		
	 from (XII)	 from (XIII)	 from (XIV)
Me	7 [a]	–	6 [a]
Et	14 [a]	15 [a]	68
Me_2CH	65	50	69
Me_3C	44 [b]	44 [c]	33

[a] RSSR is present in the reaction mixture; [b] reaction mixture contains unreacted (XII); [c] also isolated 17% 

Competitive reduction of the nitro group depends on the structure of the nitroaryl halide and the nature of the mercaptide. If the nitro group is not activated by an isopropylthio group in the *ortho*- or *para*-position, it is possible that a mechanism other than the S_NAr type is involved. In such instances, reaction may be initiated by a single electron transfer from RS^- to the substrate to give a nitroaryl radical anion:

$$ArNO_2 + RS^- \xrightarrow{\bar{e}} ArNO_2^{\cdot -} + RS^{\cdot},$$

$$2RS^{\cdot} \rightarrow RSSR,$$

$$ArNO_2^{\cdot -} \rightarrow \text{products of reduction}.$$

Unactivated aryl halides (PhF, PhCl, PhBr, PhI) react with sodium isopropylmercaptide in hexamethylphosphoramide at a higher temperature (80 °C) to give isopropyl phenyl sulphide in 57–81% yield.[37] By measuring the relative rates of replacement of each halogen by the isopropylthio group, the relative lability of halogen was found to decrease in the order: I > F > Br > Cl. This sequence is not that which would be anticipated for substitution of an activated aryl halide according to a S_NAr mechanism.[11] Nonetheless, the authors of this work still propose such a mechanism by taking into account the differing rates of the addition and elimination steps and their dependence on the nature of the halogen atoms.[37]

The same authors also studied the reaction of iso-PrSNa with dihalogenobenzenes in hexamethylphosphoramide.[37] Thus, *o*-, *m*- and *p*-dichlorobenzene afford mono- or bis(isopropylthio)benzenes, depending on the relative proportion of the mercaptide. Other *m*- and *p*-dihalogenobenzenes (except *p*-difluorobenzene) under these conditions are converted exclusively into the corresponding isopropyl *p*-halogenophenyl sulphides. The reaction of tri-, tetra-, penta- and hexa-chlorobenzenes with excess of iso-PrSNa (or EtSNa) proceeds readily in hexamethylphosphoramide with substitution of all the chlorine atoms in 80–95% yield.[38] Both hexachlorobenzene and hexafluorobenzene afford the corresponding hexakis(alkylthio)-benzene in hexamethylphosphoramide, while partial replacement of halogen takes place in other solvents, as indicated above.[20–22]

1,3-Dimethyl-2-imidazolidone may be used as solvent in place of hexamethylphosphoramide for the preparation of hexakis(alkylthio)-naphthalenes[41] and hexakis(arylthio)benzenes[42] in high yield. The relatively inaccessible hexakis(*p*-tert-butylphenylthio)benzene (76%) and hexakis(β-naphthylthio)benzene (72%) were also obtained under these conditions.

The reactions of polychlorobenzenes with MeSNa are complicated in certain instances by partial cleavage of the resulting methylthio groups by nucleophilic attack of mercaptide anion.[38] This leads to the formation of poly(methylthio)thiophenols,† as exemplified below:

$$C_6Cl_6 \xrightarrow{MeSNa} C_6(SMe)_6 \longrightarrow C_6(SMe)_5SH.$$

Aromatic mercaptans may also be prepared from unactivated aryl halides under the same conditions.[39] Reaction proceeeds in two steps: nucleophilic replacement of the halide according to an S_NAr mechanism, followed by dealkylation according to the more familiar S_N2 displacement at a saturated carbon:

$$ArX + MeSNa \rightarrow ArSMe + NaX,$$

$$ArSMe + MeSNa \rightarrow ArSNa + Me_2S.$$

Table 2. Reaction of aryl halides with MeSNa in HMPA at 100 °C.[39]

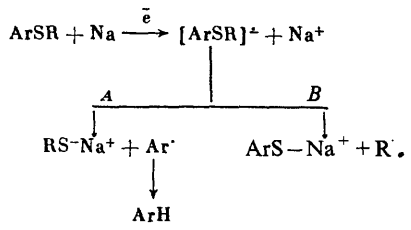
Thiol	Time, h	Yield, %	X in ArX
Thiophenol	5	90	Cl
α-Mercaptonaphthalene	3.5	90	Br
β-Mercaptonaphthalene	5	97	Br
p-Mercaptobiphenyl	2	96	Br

Some examples of this conversion are given in Table 2.

† Data on the cleavage of alkylthiobenzenes to give the corresponding thiophenols by alkali metals in liquid ammonia, ether or methylamine have been given previously.[40,43,44]

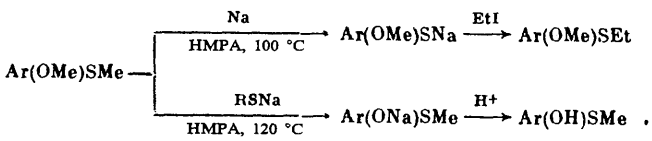
Dealkylation of alkyl aryl sulphides to give the corresponding monomercaptoarenes can be achieved with both MeSNa and EtSNa.[39] Polymercaptobenzenes may be obtained from the corresponding polychlorobenzenes via treatment of the intermediate isopropylthiobenzenes with sodium in hexamethylphosphoramide at 100 °C.[45] Alternatively, the polychlorobenzenes may be treated with NaSMe in 1,3-dimethyl-2-imidazolidone, followed by demethylation with sodium in liquid ammonia.[46] By comparison with the reaction with MeSNa, cleavage with sodium in hexamethylphosphoramide is not selective and proceeds with total dealkylation of all RS groups.

It is considered that the interaction of isopropylthiobenzenes with sodium in hexamethylphosphoramide involves an electron transfer,[45] as a result of which a thioether anion radical is formed:

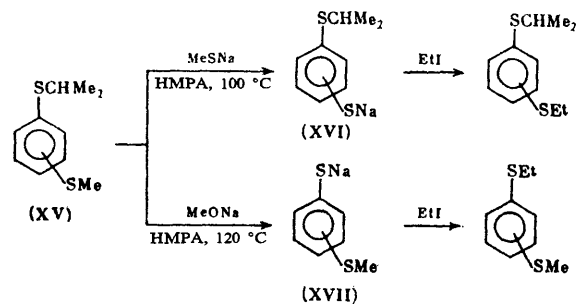


Pathway *B*, i.e. cleavage of the R–S bond, is preferred under these conditions and can only be suppressed sterically if the RS group is in an *ortho* position.

By choosing a suitable dealkylating agent (Na, MeSNa, MeONa) in hexamethylphosphoramide, selective dealkylation may be achieved. Alkoxyaryl alkyl sulphides, for example, may be selectively cleaved to give alkoxythiophenols, mercaptophenols or (alkylthio)-phenols:[47–49]

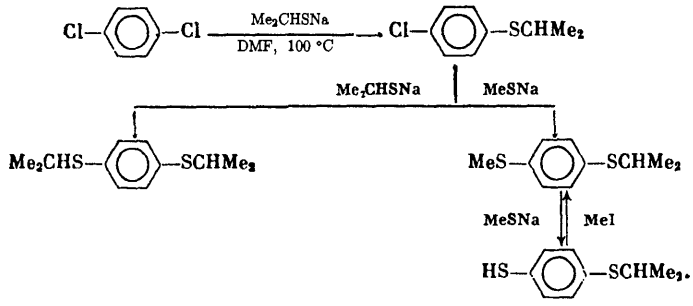


Preferential dealkylation of bis(alkylthio)benzenes having different RS-groups may also be carried out, as exemplified below.[50]



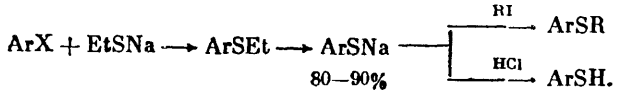
As seen above, the reaction of compound (XV) with sodium methylmercaptide involves nucleophilic aliphatic substitution by an S_N2 mechanism, which explains the selectivity towards the methyl group to give product (XVI). In contrast, sodium alkoxides in aprotic media function as strong bases, inducing elimination of the isopropyl group as propene with the formation of mercaptide (XVII).[50]

In view of the carcinogenic properties of hexamethylphosphoramide, the above-described substitution of aryl halides and the dealkylation of the resulting thioethers have been studied in DMF and dimethylacetamide.[51] Thus, nucleophilic aromatic substitution of unactivated aromatic halides by mercaptide anion proceeds smoothly in DMF at 100 °C:

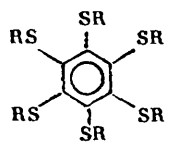


Selective monodealkylation with excess of MeSNa can be achieved at 160 °C in DMF by nucleophilic aromatic substitution. In this respect, tert-BuOK is better than MeONa for selective dealkylation in DMF. Dealkylation by electron transfer with sodium is more effective in dimethylacetamide than in DMF.

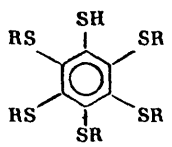
Reference has also been made[51] to the one-step synthesis of thiophenols by heating unactivated aryl halides with excess of EtSNa in DMF:



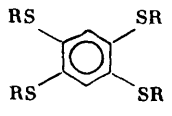
Recently, polyglymes have been used as solvents for the substitution of activated[52,53] and unactivated[54,55] aryl halides by mercaptide anion. The effectiveness of polyglymes is in the order: tetraglyme > triglyme > diglyme > monoglyme. The following products have been obtained by heating aromatic halides with RSNa at 130–200 °C in tetraglyme:



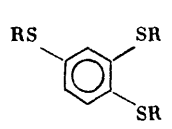
R = Ph (23%)
R = *n*-$C_{12}H_{25}$ **(95%)**
R = Et (30%)



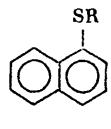
R = Et (25%)



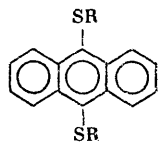
R = Et (63%)
R = *n*-C_8H_{17} (87%)
R = *n*-$C_{12}H_{25}$ (86%)
R = Ph (56%)



R = Ph (16%)
R = *n*-$C_{12}H_{25}$ (96%)



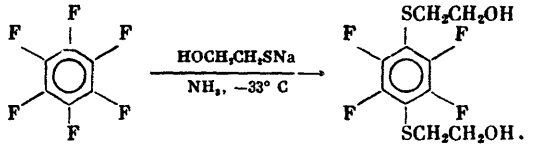
R = *n*-C_8H_{17} (67%)
R = *n*-$C_{12}H_{25}$ (81%)
R = Ph (62%)



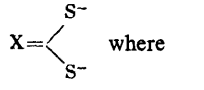
R = *n*-$C_{12}H_{25}$ (95%).

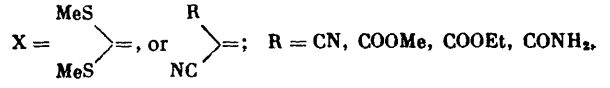
Tetraglyme is recommended as an alternative to hexamethylphosphoramide, DMF and dimethylacetamide as a solvent for the thiylation of aromatic halides.

Liquid ammonia also serves as a useful solvent, selectively solvating the cation of alkali metal mercaptides. Under these conditions it is possible to achieve thiylation of polyfluoro- and nitrohalogeno-aromatic compounds without side reactions.[56,57] This is exemplified below:

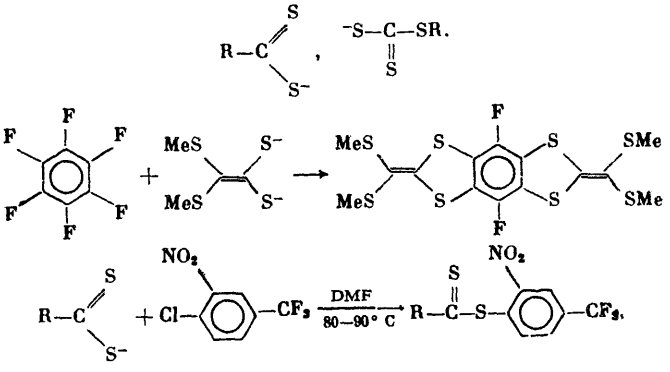


It should also be noted that activated aromatic halides react with ambident *S*-nucleophiles, such as dithiolates[58,59] of the type:





The sodium salts of dithiocarboxylic and trithiocarbonic acids, i.e. RC(S)SNa and RSC(S)SNa, are also effective nucleophiles.[60,61] The following two reactions exemplify the displacement of aromatic halogen by such *S*-nucleophiles:



where R = dimethylamino, diethylamino, and morpholino.

From the information set out in this part of the review, it is clear that the inertness of unactivated aromatic halides can only be effectively overcome by using a strong base in an aprotic, bipolar solvent. Such conditions are often used for the reactions of activated aromatic halides, and have been recommended for preparative purposes.

III. Thiylation of aryl halides in the presence of catalysts

Aromatic nucleophilic substitution is promoted by transition metals and their salts, those of copper being the most prominent.[62–64] Such catalysed thiylation of aromatic halides can be regarded as the sulphur equivalent of the classical Ullman reaction.

Copper may be used for thiylation in two ways: a) on the one hand by an exchange mechanism of the type

$$ArX + CuY \rightarrow ArY + CuX,$$

where X = halogen, and Y may be SAlk or SAr; and b) on the other hand by a nucleophilic displacement of aromatic halogen with Cu, Cu_2O, or a copper salt as catalyst:

$$ArX + Y^- (\text{or } HY) \xrightarrow{Cu} ArY + X^- (\text{or } HX).$$

As an example of method a), 1-bromonaphthalene reacts with cuprous phenylmercaptide in a polar organic solvent.[65] Thus, on heating the reactants in pyridine for 24 h, 1-naphthyl phenyl sulphide is obtained in 26% yield, while the same product is formed in 21% yield by heating in DMSO for 4 h at 144 °C, and in 31% yield in DMF.

As an example of method b) thioethers are obtained in preparatively useful yield by thiylation of aromatic halides in an aprotic solvent in the presence of a catalytic amount of suspended Cu_2O.[66] Thus, heating 1-bromonaphthalene with PhSNa or EtSNa for 24 h in the presence of Cu_2O affords 1-naphthyl phenyl sulphide and ethyl 1-naphthyl sulphide in 99% and 95% yield, respectively.

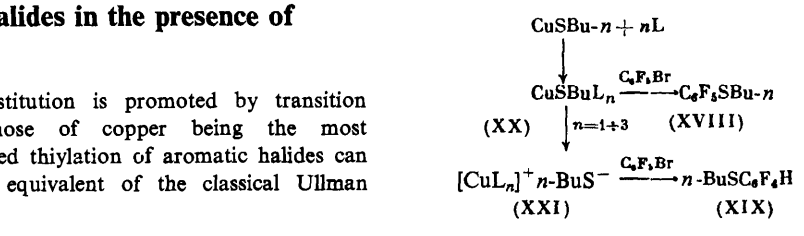
Where mercaptans (RSH) are used as substrate, reaction involves initial formation of CuSR, which then reacts with the aromatic halide. The mercaptide anion, RS^- (PhS^- or EtS^-), is more effective than the corresponding neutral mercaptan (RSH). Thus, diaryl sulphides are obtained in low yield (21%) in the system $ArBr/Cu_2O/PhSH$, but in high yield (99%) in the system $ArBr/Cu_2O/PhSNa$.

A variety of aromatic halides (ArX) may be used in the reaction with cuprous mercaptides: Ar = $C_6H_4NH_2$, C_6H_4OMe, C_6H_4Me, C_6H_4OH, C_6H_4Br, C_6H_4Cl with CuSR (R = Ph, Et, n-Bu).[67–69] The reactants are heated at 200 °C for 1–5 h in a mixture of quinoline and pyridine until the medium becomes homogeneous. It should be noted that unactivated aromatic chlorides react under these conditions with PhSCu but not AlkSCu, while both of these mercaptides react with aryl bromides and activated aryl chlorides (e.g. *o*-$ClC_6H_4NO_2$) to give the corresponding thioethers in 50–90% yield.

The replacement of bromine in bromoperfluoroaryl derivatives may be achieved with mercaptides RSCu (R = C_6F_5, Me, n-Bu):[70–72]

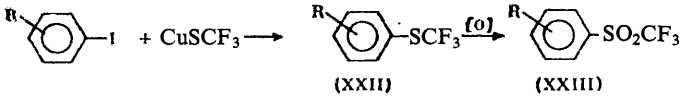
$$C_6F_5Br + CuSBu\text{-}n \rightarrow \underset{\text{(XVIII)}}{C_6F_5SBu\text{-}n} + \underset{\text{(XIX)}}{n\text{-}BuSC_6F_4H}.$$

The proportion of (XVIII) and (XIX) in the product depends on the nature of the solvent. The former predominates in DMF while the partially reduced product, (XIX), predominates in pyridine. It is thought that the reaction involves the intermediate formation of complex (XX) derived from the cuprous mercaptide and solvent:



n-Butylmercaptide anion coordinates with copper in the weakly ligating DMF to give (XVIII). However, in the strongly ligating pyridine, an ionic complex (XXI) is formed prior to reaction with C_6F_5Br to give (XIX).

Aryl trifluoromethyl sulphides (XXII) are obtained in high yield of reaction of CF_3SCu with aromatic iodides in DMF at 150 °C.[73] The products are oxidised to the corresponding sulfones (XXIII) possessing the strongly electron-withdrawing SO_2CF_3 group:



(XXII) (XXIII)

R = H, 4-Me, 2-NO_2, 4-NO_2.

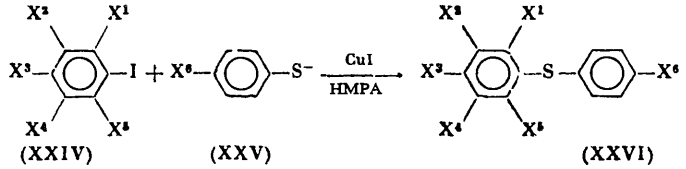
Aryl trifluoromethyl sulphides are also obtained by interaction of aromatic bromides with $HgSCF_3$ and Cu.[64]

The preliminary isolation of cuprous mercaptide, CuSr, and its insolubility are the main limitations of the above-described method. However, these may be avoided in the direct conversion of aromatic halides to alkyl aryl sulphides or diaryl sulphides with dialkyl or diaryl disulphides in dimethylacetamide containing copper at 160–170 °C:[74]

$$RSSR + PhBr \xrightarrow{Cu} PhSR,$$
$$RSSR + BrC_6H_4Br \rightarrow RSC_6H_4SR,$$
$$R = n\text{-Bu, Ph, } m\text{-}MeC_6H_4 .$$

The reaction involves copper-induced cleavage of the disulphide bond to give the corresponding cuprous mercaptide, which then reacts with the aromatic halide. Disulphides may also be reduced by other metals (Zn, Na, Al), normally in the presence of an acid, to give the corresponding mercaptan. Certain cuprous mercaptides prepared by method[67] are unstable. Thus, cuprous benzylmercaptide is converted to the corresponding benzyl sulphide and stilbene on reaction with aromatic halides. *m*-Bis(benzylthio)benzene is obtained from *m*-dibromobenzene in 46% yield via *in situ* formation of Cu(I)-benzylmercaptide from dibenzyl disulphide.[74]

The *in situ* formation of cuprous arylmercaptides from CuI and ArS^- (XXV) is considered likely during the formation of diaryl sulphides from unactivated aromatic iodides (XXIV):[75]

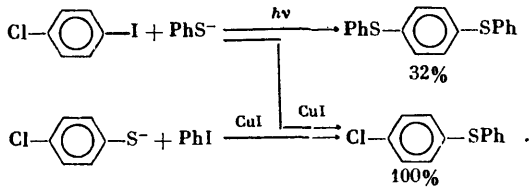


(XXIV) (XXV) (XXVI)

X^1 = Me, NO_2; X^{2-5} = H, Me; X^6 = H, Cl.

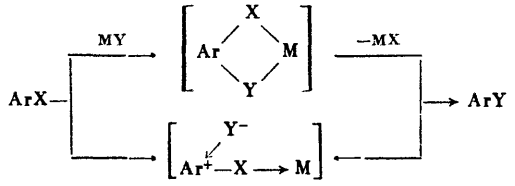
Thus, diaryl sulphides (XXVI) are obtained in 60–75% yield by heating a mixture of the appropriate aryl iodide (XXIV), alkali metal mercaptide (XXV) and CuI in hexamethylphosphoramide at 70–80 °C for 1–2 h.

Catalysis by copper(I) is recommended where processes involving an $S_{RN}1$ mechanism do not give the desired result.[76] Thus, whereas photo-initiated $S_{RN}1$ thiylation of certain dihalogenobenzenes leads exclusively to disubstitution (see also Section V), only monosubstitution takes place under Cu(I) catalysis:



Copper complexes containing P-, As- or Sb-ligands may also be used as catalyst for the thiylation of aromatic halides.[77]

The mechanism of copper-catalysed substitution of aromatic halides is thought to involve initial coordination of copper to the displaced halogen with the intermediate formation of a σ-complex:[64]

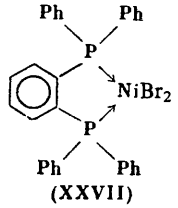


X = halogen; Y = nucleophile .

For nucleophilic substitution in the presence of copper salts, the facility of the initial addition of catalyst across the carbon-halogen bond increases with decrease in the electronegativity of the halogen and with increase in its polarisability (F < Cl < Br < I), reflecting the lability of halogen. This order is the reverse of that found for non-catalytic substitution.[1]

Copper-catalysed nucleophilic substitution may also involve coordination of the copper salt as a π-complex, in which Cu^+ serves as an acceptor.[62,63] A radical mechanism, involving a single electron transfer, has also been proposed for copper-catalysed substitution of halides.[62]

Other transition metals are reported to catalyse thiylation of aryl halides. For example, diaryl sulphides may be prepared in the presence of *o*-bis(diphenylphosphino)benzenenickel(II) bromide (XXVII).[78]



(XXVII)

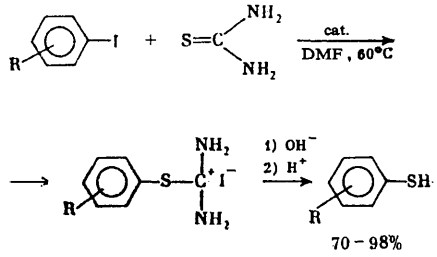
Table 3. Reaction of aryl bromides, ArBr, with NaSPh by method (200 °C, 24 h, ethylene glycol).[78]

Ar	Ph	*p*-MeC_6H_4	*o*-MeC_6H_4	*m*-MeC_6H_4	anthracene	*p*-CNC_6H_4
Yield of sulphide, %	100[a]	94	90	98	90	80

[a] In the absence of catalyst the yield of Ph_2S was 3%.

The reaction conditions and yields for this latter conversion are given in Table 3. The method is regioselective, and reaction is not suppressed by electron-donating groups in the benzene ring of the aryl bromide.

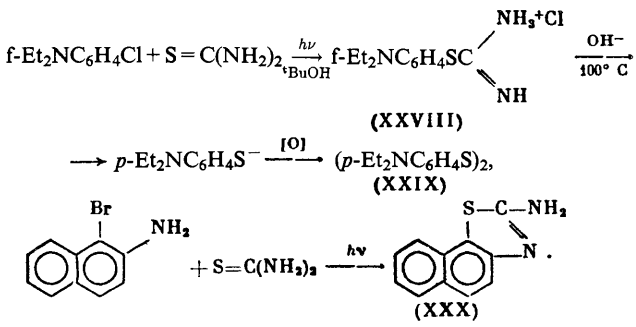
Catalysis by Ni(II) complexes has also been applied successfully to the synthesis of aromatic mercaptans from unactivated aromatic iodides and thiourea. The method is mild and involves the intermediate formation of *S*-arylisothiouronium salts.[79] It is known that unactivated aromatic halides do not form isothiouronium salts with thiourea under normal conditions.[80]



R = H, *p*-Me, *o*-Me, *p*-MeO, *p*-NH_2, *p*-Cl, *p*-Br.

In this reaction, the Ni(II) complex is formed *in situ* from bis(triethylphosphine)nickel(II) chloride and sodium trihydridocyanoborate.

S-Arylisothiouronium salts are also formed on irradiation of thiourea (or thiosemicarbazide) with *o*- or *p*-substituted aryl halides having electron-donating substituents in the benzene ring.[81] However, the mechanism of the reaction is quite different from the $S_{RN}1$ process proposed for photo-substitution of aromatic halogen by mercaptide anion, RS^- (see also Section V). Reaction ceases on formation of the arylisothiouronium salt (XXVIII). *p*-Substituted derivatives may be converted to the corresponding diaryl disulphides by basic hydrolysis at 100 °C, followed by oxidation of the resulting arylmercaptides. *o*-Substituted derivatives, however, are partially cyclised to give thiazoles, e. g. (XXX):

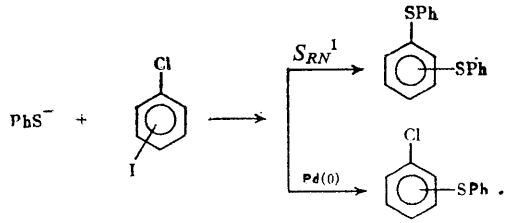


Palladium(0) complexes e.g. tetrakis(triphenylphosphine)-palladium(0), may also be used as catalyst for the reaction of unactivated aromatic halides with mercaptide anion.[82,83] Thus, phenyl and tolyl iodides or bromides react with mercaptans, RSH (R = Ph, Et, tert-Bu, *n*-Bu), in the presence of tert-BuONa as base and $Pd(PPh_3)_4$ as catalyst on heating in DMSO [82] or in alcoholic media.[83] It has been found that PhBr interacts with mercaptans more slowly than PhI. Thus Pd-catalysed reaction of PhSH with PhBr and PhI in refluxing ethanol affords diphenyl sulphide in 19% and 100% yield, respectively. There was no formation of sulphide in the absence of catalyst. Chlorobenzene is noticeably less reactive under these conditions, affording only a trace of diphenyl sulphide on heating in DMSO. Iodobenzene reacts nine times more rapidly with tert-BuS^- than with PhS^-.

It is thought that the mechanism of the substitution involves the formation of an anion radical, $ArX^{\cdot-}$. However, an $S_{RN}1$ process may be excluded for the following reasons:

1) palladium(0)-catalysed substitution is not inhibited by *p*-dinitrobenzene — a good electron acceptor, conventionally used to suppress $S_{RN}1$ reactions. Thus, there is no electron transfer initiation;

2) mono-substitution of iodochlorobenzene by PhS^- predominates under Pd(0) catalysis:



The authors propose that Pd-catalysed thiylation takes place by the following mechanism:

a) oxidative addition of the aryl halide, ArX, to Pd(0) with formation of an adduct:

$$ArX + Pd(0) \rightarrow Ar-Pd(II)-X;$$

b) nucleophilic substitution of the adduct:

$$Ar-Pd(II)-X + RS^- \rightarrow Ar-Pd-SR + X^-;$$

c) reductive elimination:

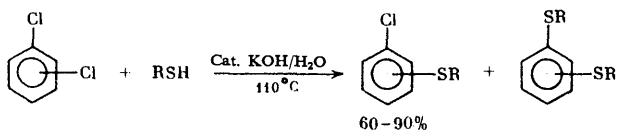
$$Ar-Pd-SR \rightarrow ArSR + Pd(0).$$

As indicated previously, the thiylation of weakly activated aryl halides requires forcing conditions: high temperatures, strong base, and a transition metal complex as catalyst. In the last five years, phase transfer catalysis, which often enhances anionic substitution, has been applied to the thiylation of aromatic halides under mild conditions.[84]

The phase-transfer catalysed thiylation of strongly activated aryl halides (by the nitro group) is worth noting.[85,86] Here, both thiophenols[85] and thiophenoxides (obtained *in situ* by reduction of the corresponding diaryl disulphide with aminoiminomethanesulphinic acid[86]) have been used as the nucleophile. Thus, diaryl sulphides have been prepared in 80–97% yield at room temperature by using a quaternary ammonium salt as phase transfer catalyst in a two-phase medium comprising aqueous base and an organic solvent (THF or toluene).

It has been reported that the rate of reaction depends on the leaving group (deceasing in the order: F > Cl > Br > I), and on the degree of activation of the aromatic ring (decreasing in the order: di-2,4-$(NO_2)_2$ > *o*-NO_2 > *p*-NO_2 > *m*-NO_2).[85] Thioethers are not formed, however, from mononitroaryl halides in the absence of catalyst; with dinitro compounds, the rate of reaction is increased 4 times in the presence of catalyst. Less activated aryl halides, e.g. *m*-BrC_6H_4Cl, are unreactive.[86]

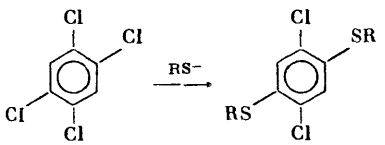
It has been found that the S_NAr reaction of dichlorobenzenes with alkylmercaptide anion is noticeably more facile under liquid-liquid phase transfer catalysis.[87] The synthesis of alkyl aryl sulphides can be carried out at 110 °C by stirring a heterogeneous mixture of the halide, catalyst and mercaptan in 60% aqueous alkali under an inert atmosphere mixture. Dicyclohexano-18-crown-6 is a suitable catalyst for this conversion:



R = Pr^i, Bu^t, *n*-Bu.

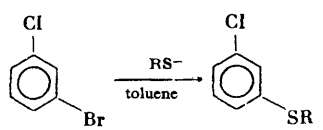
There was no reaction in the absence of catalyst. It has been shown that the rate of displacement of the first chlorine atom in dichlorobenzenes decreases in the order 1,2- > 1,3- > 1,4-dichlorobenzene. This would indicate that the inductive effect is primarily responsible for activation of the leaving group. The order of reactivity of the mercaptide anion is: n-alkyl > sec-alkyl > tert-alkyl ≫ aryl.

A wide range of chlorobenzenes has been submitted to displacement by alkylmercaptide anion.[88] Reaction proceeds in toluene at 25 °C in the presence of a phase transfer catalyst (n-Bu_4NBr, n-Bu_4PBr, 18-crown-6):



R = *n*-C_7H_{15}, *n*-C_8H_{17}, *n*-$C_{12}H_{25}$.

Substitution of halogen in 1,2,4-trichlorobenzene proceeds more slowly than the reaction with tetrachlorobenzene, and takes place exclusively at the 2 position. All three isomeric dichlorobenzenes are less reactive still, and require heating in toluene. Aromatic bromides are substituted more rapidly than chlorides,[88] as confirmed by the following reaction:



R = *n*-C_7H_{15} (86%).

Quaternised 4-dialkylaminopyridinium salts are also effective phase transfer catalysts.[89] They are stable up to 300 °C and increase the rate of thiylation in non-polar solvents (or without solvent) at temperatures below 200 °C.

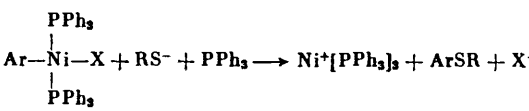
It is also reported that transition metal complexes are effective under phase transfer catalysis.[90] Thus, unactivated aryl halides interact with mercaptides in a mixture of aqueous alkali and toluene in the presence of σ-arylbis(triphenylphosphine)-nickel or -palladium complexes and triphenylphosphine (see Table 4).

Table 4. Reaction of bromobenzenes and chlorobenzene with thiophenol under conditions.[90]

PhX	Catalyst	Time, h	Temperature °C	Yield, %
Br	A	7.5	100	97
Br	A (without PPh_3)	5	100	94
Br	B	23	55	95
Cl	B (without PPh_3)	20	55	70

Key: σ-arylbis(triphenylphosphine)nickel complex (a) or palladium analogue (B).

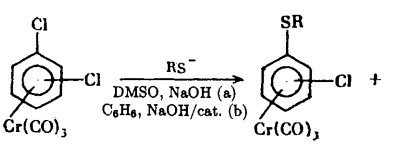
Even chlorobenzene reacts with mercaptide anion in high yield under these conditions. It is thought that the displacement involves a catalytic cycle,[90] the overall process being represented as follows:

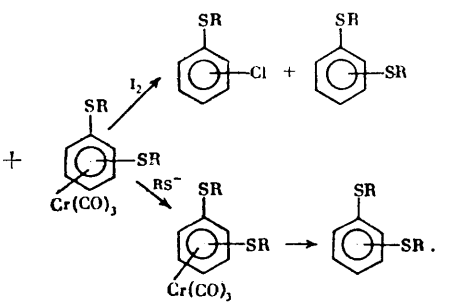


Nucleophilic substitution of halogen in aryl halides may also be activated by π-coordination with transition metal carbonyl or cyclopentadienyl complexes.[91] Reactivity increases in the order:

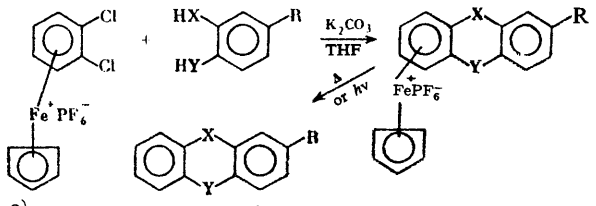
$$Cr(CO)_3 < Mo(CO)_3 \ll (\eta^5\text{–}C_5H_5)Fe^+ < Mn^+(CO)_3.$$

Particular reference has been made to S_NAr substitution of tricarbonyl(halogenobenzene)chromium complexes with alkylmercaptides ($AlkS^-$, where Alk = Me, iso-Pr, tert-Bu, n-Bu) in aprotic media either under a) phase transfer catalysis or b) solid-liquid conditions.[92,93] The following halogenobenzenes participate in this conversion: PhF, PhCl, *m*-MeC_6H_4Cl, *p*-MeC_6H_4Cl, and dichlorobenzenes, e.g.





The reaction of π-coordinated *o*-dihalogenobenzenes with binucleophiles is of potential for the synthesis of heterocyclics,[94,95] as exemplified below.



a) X = S, Y = O, R = H (76%)
b) X = Y = S, R = Me (82%)
c) X = NH, Y = S, R = H (23%).

These results confirm that activation of aryl halides by π-coordination with metals is equivalent to activation by strongly electron-accepting substituents in the aromatic ring, which facilitate thiylation under mild conditions either in aprotic solvents or under phase transfer catalysis.

Thus, specific catalysts may be used for thiylation, notably in combination with phase transfer catalysts. The only limitation of this method is the relative inaccessibility of the catalysts themselves.

IV. High-temperature thiylation

High temperature thiylation of aryl halides has been conducted at 500–700 °C with H_2S, thiophenol, alkyl mercaptans, dialkyl sulphides and disulphides. Studies in this area have been carried out systematically by M G Voronkov et al. at the Institute of Organic Chemistry of the Siberian Section of the Academy of Sciences of the USSR.

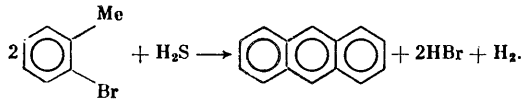
Thiophenol, diphenyl sulphide and benzene are the main products obtained by reaction of chloro-, bromo-, and iodo-benzene with H_2S.[96,98] In the high temperature conversion of halogenobenzenes with H_2S, thiophenol is formed initially and diphenyl sulphide is an intermediate, arising in the second stage:

$$PhX+H_2S\rightarrow PhSH+HX,$$
$$PhX+PhSH\rightarrow PhSPh+HX,$$
$$PhX+H_2S\rightarrow C_6H_6+HX+S.$$

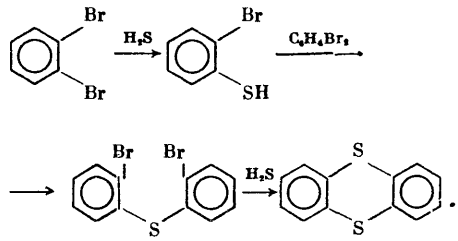
Fluorobenzene does not react with H_2S in the gas phase up to 700 °C. At this temperature and above, thermolysis takes place with cleavage of a C–H bond.

The proportion of thiol : sulphide in the reaction of PhX with H_2S increases in the following order of X; I < Br < Cl. The principal products from the reaction of iodobenzene with H_2S are benzene and diphenyl sulphide, formed also by oxidation of thiophenol with liberated iodine.[98] In comparative experiments, the reaction of bromobenzene with H_2S is more selective for the formation of diphenyl sulphide, while the reaction with chlorobenzene is more selective for the formation of thiophenol. At a fairly low ratio of H_2S : PhBr (1.25), the yield of diphenyl sulphide increases to 72% at 60% conversion.

Both electron-accepting and -donating substituents in the *para*-position (relative to halogen) accelerate the reaction with H_2S and increase the overall conversion. The distribution of electron density in the intermediate thiophenol has a pronounced effect on the ultimate thiol : sulphide ratio and is largely responsible for the rate of the reaction.[99] Thus, electron-donating groups (Me, OMe) favour formation of thiol. However, *o*-methyl groups induce side reactions by virtue of their steric effect, e.g.

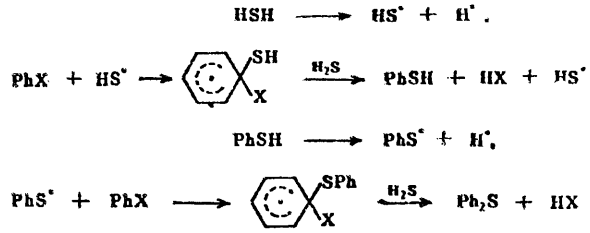


The reaction of *o*-dihalides with H_2S leads to the formation of heterocycles, e. g.



The reactions of fused halogenobenzenoid systems with H_2S have also been studied.[100] Thus, 1-chloronaphthalene reacts in the gas phase at 600 °C to give 1-thionaphthol, bis(1-naphthyl) sulphide, and naphthalene. 1-Bromonaphthalene and brominated derivatives of anthracene and phenanthrene react with H_2S in the liquid phase at 180–250 °C with the formation of symmetrical diaryl sulphides.

The authors have classified the high temperature reaction of aromatic chlorides and bromides with H_2S as a homolytic bimolecular substitution of halogen by thiyl radicals.[101] The following radical chain mechanism has been proposed:

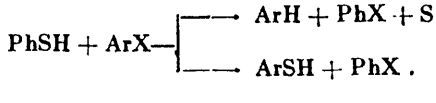


Thiophenol interacts with aryl halides at 400–600 °C primarily with the formation of unsymmetrical sulphides:[102]

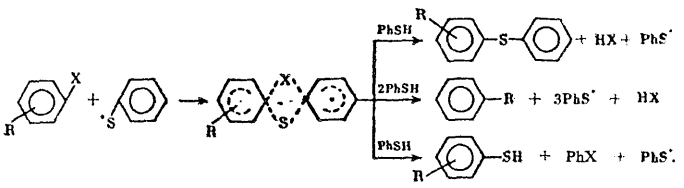
$$PhSH + ArX \rightarrow PhSAr + HX,$$

X = Cl, Br; Ar = *o*-, *p*-, *m*-MeC_6H_4, 3,4-$Me_2C_5H_3$, *o*-, *p*-OHC_6H_4, *o*-, *p*-$MeOC_6H_4$, *o*-, *p*-XC_6H_4.

The reaction is more selective at low temperature and with an excess of halide. An increase in the temperature favours reduced and exchange reactions:



The mechanism of the reaction of thiophenol with aryl halides is evidently a bimolecular homolytic process involving substitution by thiyl radicals. This takes place synchronously via a transition state which reacts with the mercaptan by one of three routes depending on the temperature:



For such high temperature conversions of aryl halides, the requisite thiyl radicals may also be generated from aryl mercaptans, dialkyl sulphides or disulphides.[103,104] Alkyl mercaptans react with chlorobenzene at 600–660 °C with the formation of thiophenol, diphenyl sulphide, and benzene as side-product. Lower (C_1–C_3) mercaptans are more reactive than higher ones. By comparing reactions with H_2S and alkyl mercaptans, treatment with the latter is less facile but the thiol : sulphide proportion is greater. Co-pyrolysis of chlorobenzene with dialkyl sulphides $[Me(CH_2)_n]_2S$ (n = 0, 1, 3, 6) and disulphides affords, primarily, benzene, thiophenol, and diphenyl sulphide, together with thiophene, benzothiophene and toluene.

The high temperature thiylation of aryl halides is synthetically attractive as a one-step route to important aromatic organosulphur compounds, namely aromatic and heteroaromatic thiols and sulphides. However, such methods require much energy and are complicated by side-reactions which reduce selectivity and the yield of desired product. This clearly limits the usefulness of these routes for practical purposes.

V. Photo- and electro-chemical thiylation

As indicated above, the thiylation of unactivated aromatic halides requires relatively harsh conditions (high temperatures, aprotic solvents) to secure high yields of the desired thioether, or may be conducted in strongly basic media or under transition metal catalysis. These reactions usually take place by an anionic mechanism, involving the formation of a σ-complex (S_NAr) or aryne-type intermediates, or by a free-radical pathway.

Substitution of unactivated aromatic halides can be effected under mild conditions by photo- or electro-chemical activation. Reaction proceeds by a 'radical, nucleophilic, monomolecular' ($S_{RN}1$) mechanism, as originally proposed and reviewed by Bunnett[105,106] (recent review, see Ref. 6). The key steps of such $S_{RN}1$ substitutions are as follows:

initiation $ArX + \bar{e} \rightarrow (ArX)^{\cdot-}$,

chain propagation $(ArX)^{\cdot-} \rightarrow Ar^{\cdot} + X^-$,

$Ar^{\cdot} + Nu^- \rightarrow (ArNu)^{\cdot-}$,

$(ArNu)^{\cdot-} + ArX \rightarrow ArNu + (ArX)^{\cdot-}$.

The length of the chain depends on the reaction conditions.

The photo-induced (λ_{max} = 350 nm) reaction of aryl iodides with thiophenoxide anion in liquid ammonia is quite facile (1–3 h), affording aryl phenyl sulphides in 70–95% yield:[107]

$$ArI + PhS^- \xrightarrow{h\nu} ArSPh + I^-,$$

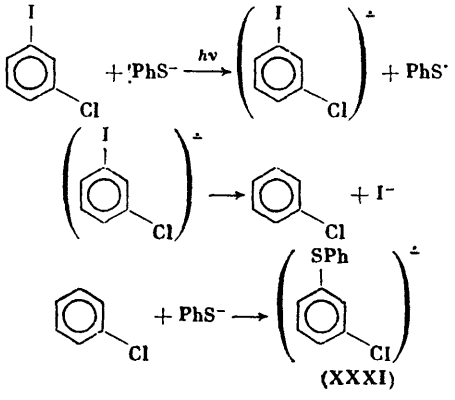
Ar = Ph, 1-naphthyl, *o*-, *p*-, *m*-MeC_4H_4,

o-, *p*-, *m*-$MeOC_6H_4$.

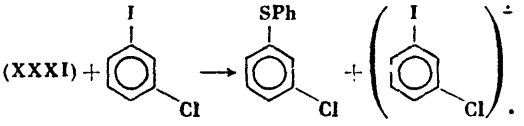
Aryl bromides also participate in this reaction, but more slowly than aryl iodides. Thus, irradiation of a mixture of PhI and PhS^- affords diphenyl sulphide in 94% yield after 70 min, but the yield from PhBr is 23% after 120 min.

The substitution is more effective in the presence of an organic base as catalyst.[108,109] Thus, the conversion of unactivated aryl bromides to diaryl sulphides can be achieved in higher yield (e.g. PhBr affording Ph_2S in 65–70% yield) by photo-initiation in the presence of tetra-n-butylammonium hydroxide or triethylamine; even chlorobenzene reacts under these conditions, Ph_2S being formed in 30% yield.[108] It is likely that such catalysts accelerate the single electron transfer in the initial formation of anion radical by the $S_{RN}1$ mechanism outlined above. The effect of tetra-n-butylammonium hydroxide on the photo-initiated reaction of aryl halides with pyridylthio anion (PyS^-) is less pronounced than its effect on the same reaction by PhS^-.[109] 2-(Phenylthio)pyridine is obtained from PhI in 68% yield, from PhBr in 19% yield, and from PhCl in 3% yield. The relatively inaccessible 3-(nitrophenylthio)pyridines may be prepared by this route under fairly mild conditions.

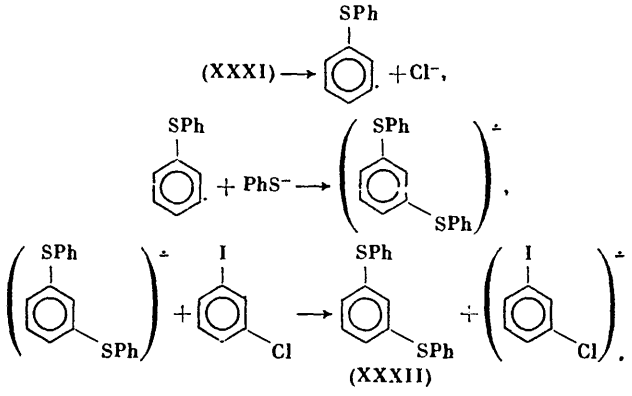
Irradiation of dihalogenobenzenes in liquid ammonia results in disubstitution.[110] Usually, the yield of mono-substitution product is poor or negligible. An $S_{RN}1$ mechanism has been proposed, the initial steps being the following:



The resulting anion radical (XXXI) may react further by two independent pathways. One involves an electron transfer:



The other is a fragmentation, leading ultimately to the disubstituted product (XXXII):



With the majority of dihalogenobenzenes (except fluorides), the formation of monosubstituted product by electron transfer from (XXXI) to the substrate is not significant, and fragmentation is the predominant process. With aromatic halogenofluorides, however, only monosubstitution takes place, i.e. electron transfer is more facile than loss of fluoride ion. This is a result of the greater strength of the C–F bond, relative to the C–Cl and C–Br bonds.

The photo-initiated reaction of alkylmercaptide anion with aryl halides affords the corresponding alkyl aryl sulphide by direct electron transfer (rate constant, k_t); fragmentation of the intermediate anion radical (rate constant k_f) results in formation of an alkyl radical which is unable to perpetuate the chain process:[111–113]

$$Ar^{\cdot} + AlkS^{-} \longrightarrow (Ar{-}S{-}Alk)^{\cdot -} \begin{cases} \xrightarrow{k_t} ArSAlk \\ \xrightarrow{k_f} ArS^{-} + Alk^{\cdot} \end{cases}$$

The relative contributions of these two processes depends on the nature of the alkyl residue and the aryl radical (Tables 5 and 6).

Table 5. The relative amount of the products of substitution and fragmentation in the reaction

$$Ph^{\cdot} + RS^{-} \xrightarrow{h\nu} PhSR + PhS^{-},$$

depending on the nucleophile.[113]

R	Ratio of the rate constants k_t, k_f	Relative yield, %		Overall yield, %
		PhSR	PhS⁻	
Ph	$k_t \gg k_f$	100	0	94
Me, Et, *n*-Bu, Bu^t	$k_t \approx k_f$	50	50	30–70
$PhCH_2$	$k_t \ll k_f$	0	100	4

Phenyl radicals react with phenylmercaptide anion to give the substitution product only (PhSPh),[107] while the interaction with alkylmercaptide anion (R = Me, Et, n-Bu, tert-Bu) affords approximately equal amounts of substitution and fragmentation product.[111,113] The reaction with benzylmercaptide anion, however, takes place only by fragmentation.[113]

Table 6. Relative amount of the products of substitution and fragmentation

$$Ar + n\text{-}BuS^{-} \xrightarrow{h\nu} ArSBu\text{-}n + ArS^{-1},$$

depending on the nature of the substrate.[113]

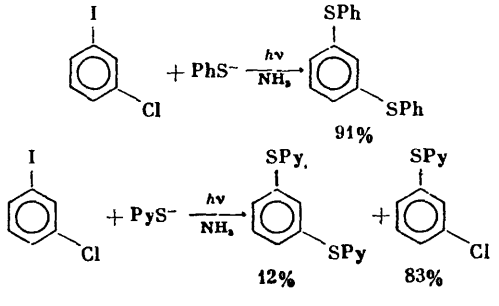
Ar	Ratio of the rate constants k_t, k_f	Relative yield, %	
		ArSBu	ArS⁻
Ph	$k_t < k_f$	50	50
1-Naphthyl	$k_t > k_f$	100	0

Since substitution proceeds as a chain reaction via electron transfer, while fragmentation is involved in the chain termination, the overall yield of substitution product will be decreased as fragmentation becomes more prominent. The relative contribution of electron transfer and fragmentation also depends on the nature of the aryl group.[112,113]

The difference between the reactivity of 1-naphthyl and phenyl radicals towards alkylmercaptide anion can be explained by the increased stability of the alkyl 1-naphthyl sulphide anion radical (relative to alkyl phenyl sulphide anion radical) and its ability to participate in the required electron transfer.

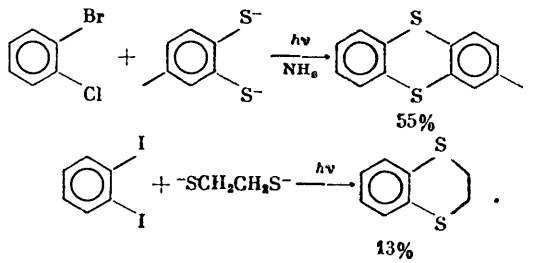
The rationale for mono- or di-substitution in the photo-initiated $S_{RN}1$ reaction of dihalogenobenzenes with RS^{-} anion has been studied.[114–117] The following factors affecting electron transfer or fragmentation have been identified:

a) the nature of the nucleophile[114,115]:



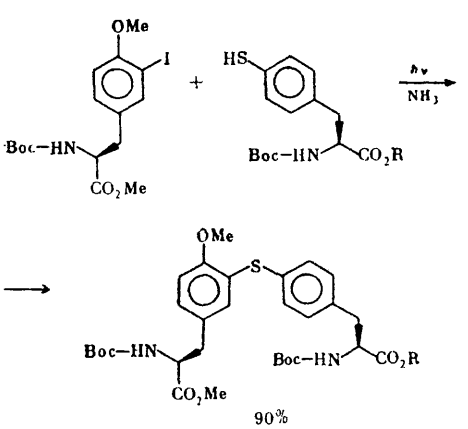
b) the structure of the substrate (in particular, the effect of electron-accepting substituents in the aromatic ring[116,117]).

Recently, heterocyclic compounds have been prepared by the $S_{RN}1$ reaction of *o*-dihalogenoarenes with dithiolate anions:[118]



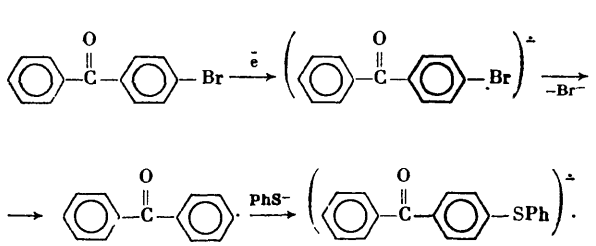
The low yield of product obtained by reaction with ethanedithiolate anion is explained by fragmentation of the intermediate anion radical.

Photo-stimulated thiylation has been applied in recent years as a mild route to complex, biologically significant, molecules. Thus, *p*-mercaptophenylalanine derivatives react effectively with iodotyrosine or iodohydroxyphenylglycine derivatives in liquid ammonia to give the corresponding diaryl sulphides by $S_{RN}1$ displacement:[119]



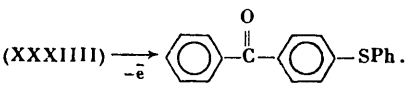
R = Me, H; Boc = ^{t}BuOCO.

It has also been shown that a number of halogenoaromatic compounds participate in electrochemically initiated $S_{RN}1$ substitution.[120–122] Thus, electrochemical reduction of 4-bromobenzophenone in DMF or acetonitrile in the presence of phenylmercaptide anion leads to 4-phenylthiobenzophenone[120] in high yield:

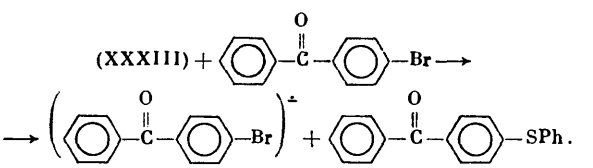


(XXXIII)

In the course of the reaction, the anion radical (XXXIII) may be oxidised at the surface of the electrode to give the desired diaryl sulphide:



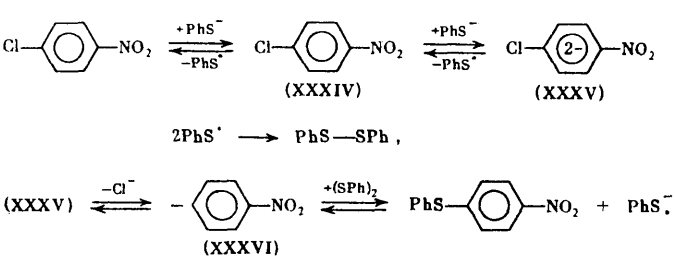
Alternatively, it may transfer its unpaired electron to another substrate molecule:



The reaction of PhS^- with 4-bromoacetophenone, *p*-bromobenzonitrile, *p*-iodobenzonitrile and 1-bromonaphthalene may, in certain instances, be complicated by competitive reduction of the aryl radical by a molecule of solvent:[122]

$$Ar^{\cdot} \xrightarrow{HA} ArH + A^{\cdot}.$$

From studies of electrochemical modelling,[123,124] it has been proposed that activated nucleophilic replacement of halogen in *p*-halogenonitrobenzenes can proceed via the intermediate formation of an anionic σ-complex. Thus, the formation of 4-nitrophenyl phenyl sulphide from *p*-chloronitrobenzene and phenylmercaptide anion is thought to involve intermediate formation of *p*-chloronitrobenzene anion radical (XXXIV) and dianion (XXXV), obtained as a result of sequential electron transfer from phenylmercaptide anion. However, the anion radicals themselves are not directly implicated in the displacement. Rather, the end product is formed by thiylation of *p*-nitrophenyl anion (XXXVI) with diphenyl disulphide, the latter anion arising by elimination of chloride ion from the dianion (XXXV);



Photochemically and electrochemically initiated thiylation of aryl halides under mild conditions is of potential interest from the synthetical and theoretical viewpoint.

* *
*

This literature survey has revealed that there is a broad spectrum of routes for the thiylation of aryl halides. Thus, the development of new methods of introducing the RS group into the aromatic ring

under mild conditions has been traced. The displacement in question is subject to a variety of activating influences, most notable from the synthesis viewpoint being transition metal catalysis, phase transfer catalysis and photochemical and electrochemical initiation. One might anticipate that further work in this area will provide more detailed information on the mechanism of these reactions as well as the nature and role of the intermediates.

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Translated from *Uspekhi Khimii* 60 2593–2618 (1991) U.D.C. 547.242

Investigations on the Arbuzov and retro-Arbuzov reactions among the organic derivatives of arsenic

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ABSTRACT. Results of attempts to effect the Arbuzov and retro-Arbuzov reactions with esters of arsinous acid and with oxides and sulphides of tertiary arsines have been correlated. The general rules and special features of these conversions are considered as well as the reactions accompanying them as a function of the environment of the arsenic atom, the nature of the electrophilic reagent and the reaction conditions. Recent and previously known results are considered from a common position.

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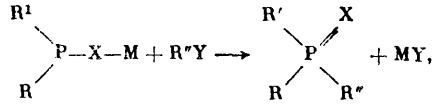
I. Introduction

The problem of nucleophilic reactivity and its link with the nature of the nucleophilic centre, with the character of its surroundings and the degree of coordination is one of the most important and pressing problems of modern chemistry. Investigation of the basic rules and, more specifically, the reactions of organoarsenic nucleophiles with electrophilic reagents is also of particular interest in connection with attempts to effect conversions analogous to the Arbuzov reaction, known in phosphorus chemistry, with the organic derivatives of arsenic. The process occurring in the reverse direction and known as the retro-Arbuzov reaction is also of interest, and has proved to be more characteristic of compounds of tetracoordinated arsenic.[1]

Numerous data have been accumulated to date by domestic investigators.[1–12] However, until now separate, sometimes contradictory, aspects of this problem have been considered which hinder an understanding of the results obtained. These problems are analysed in the present review from a common position in the light of the work of recent years.

II. Attempts to effect the Arbuzov reaction with esters of As(III) acids

After the discovery by A E Arbuzov of the reaction, which has become one of the most important synthetic methods in the chemistry of organophosphorus compounds,[13] numerous attempts were undertaken to effect a similar conversion among the organic compounds of arsenic, the closest analogue of phosphorus. On the one hand these attempts were justified by the importance acquired by the Arbuzov reaction in phosphorus chemistry. On the other hand, there is some basis to suppose that a similar reaction with the esters of trivalent arsenic is, in principle, possible. There is, in fact, the well known Michaelis–Becker reaction in the chemistry of arsenic.[14]



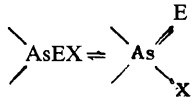
R, R′=Alk, Ar, AlkO; R″=Alk, Ac;
X=O, Y=Hal; M=metal

This reaction may correspond to one of the most important reactions in the arsenal of synthetic methods for this element, viz. the Meyer reaction and its modification proposed by Ozhe,† Scheller, Bart and others.[14]

$$Na_3AsO_3+RHal\rightarrow RAs(O)(ONa)_2+NaHal,$$
$$RAs(ONa)_2+R'Hal\rightarrow RR'As(O)ONa+NaHal,$$
$$R_2AsOAsR_2+2RI\rightarrow 2R_3AsO+2NaI,$$
$$RAs(ONa)_2+ArN_2Hal\rightarrow RArAs(O)ONa+N_2+NaHal,$$
R, R′=Alk; Hal=Cl, Br, I.

The point of this process, as for phosphorus derivatives, is an increase in the degree of coordination of the central atom, which is accompanied by the appearance of a new C–E bond and the generation of an E(O) grouping, where E = P, As. The conditions for carrying out these reactions are also closely similar.

Judging by the analogous phosphorus derivatives, the problem of tautomerism will arise in the arsenic compounds.



, where X=H, M.

However this problem has not been studied in practice. For phosphorus compounds, as is known,[15] the tautomeric equilibrium lies markedly to the right.

† This name is a transliteration and may be in error (Ed. of Translation).

Unlike phosphorus acid, arsenous acid is tribasic. Its triply substituted salts are well known. This suggests that the equilibrium of the tautomeric conversion, if it occurs among trivalent arsenic derivatives, is shifted in the direction of compounds with a lower degree of coordination of the central atom.

The need to use an alkaline medium, in spite of a whole range of side reactions, is a general feature of the conversions under examination. This is evidently linked with the high stability of tetracoordinated derivatives of arsenic in alkaline medium.

At the same time, as is well known,[16] the stability of the highest valence state of the IVth period *p* elements, as in other subgroups of the Mendeleev periodic system, is significantly less than in the IIIrd period. Consequently it might be expected that conversions accompanied by an increase in the degree of coordination must be less characteristic for arsenic derivatives than for the phosphorus analogues.

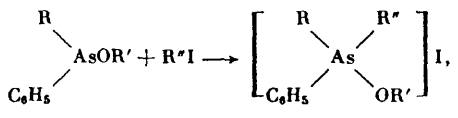
In reality, attempts to isomerise esters of As(III) acids, carried out under the conditions of the Arbuzov reaction, gave negative results. No isomerisation was observed on heating equimolar quantities of alkyl esters of phenyl- and diphenylarsinous acids with methyl and ethyl iodide for a fairly extended time (up to 18 h) at temperatures of 100–102 °C.[2]

Similar attempts were made with practically all possible classes of esters of trivalent arsenic acids, including fully esterified arsenous acid $(RO)_3As$ where R = Alk or Ar, alkyl and aryl esters of alkylarsonous acids $RAs(OR)_2$ and esters of dialkyl- and alkylphenylarsinous acids RR′AsOr″.[2]

In no case was isomerisation successfully recorded in spite of varying the reaction conditions and the reactant ratios.

Several authors have recorded cases when crystalline products were formed on reacting esters of trivalent arsenic acids with alkyl halides. Kamai and collaborators[2] first paid attention to this phenomenon but the structure of the products remained unclarified. The reaction of the triethoxypropyleneglycol ester of ethylarsinous acid with methyl iodide was also recorded and leads to the formation of a crystalline product close in composition to a trimethylethylarsonium salt.[2]

Later[17] crystalline products were isolated on reacting alkyl esters of alkylphenylarsinous acids with alkyl halides, which were assigned the structure of dialkylphenylalkoxyarsonium salts on the basis of data of arsenic and halogen analysis. The authors assumed that the reaction proceeds in a manner similar to the first stage of the Arbuzov rearrangement.



R, R′, R″=CH_3, C_2H_5, C_3H_7, C_4H_9.

Following this, communications appeared on the isolation of trialkylalkoxyaronsium salts from the reaction of esters of dialkylarsinous acids with alkyl halides.[2] The authors also used only data of elemental analysis for arsenic and halogen to infer the structure of the products formed.

Thus for esters of trivalent arsenic containing only one alkoxy group, the reaction is similar to the Arbuzov rearrangement as though stopped at the first stage.

Attention is also drawn to the fact that some properties of the products of the reaction of esters of dialkyl- and alkylphenylarsinous acids with alkyl halides do not correspond completely with the properties of alkoxy-arsonium salts. Thus dialkylphenylalkoxyarsonium iodides exchange iodide ion for nitrate ion on heating with dilute nitric acid with no change in the composition of the cation containing the alkoxy group.[2] However it is well known that an alkoxy group on an arsenic atom is fairly sensitive to hydrolysis.

The inconsistencies indicated call for a wider investigation of the products which were assigned the structure of alkoxyarsonium salts. Such investigations were subsequently undertaken.[6] The result was the unexpected conclusion that alkoxy groups were not present in the crystalline products examined. Data of IR and PMR spectra, results of conductiometry, comparison of physicochemical characteristics and data of more complete elemental analysis of the reaction products indicated that alkoxyarsonium salts were not formed by the reaction but the products were the well known quaternary arsonium salts containing no alkoxy groups.

$$RR'AsOR''+RX\rightarrow[R_3R'As]X.$$

Evidently the lack of using spectroscopic methods, the small difference in elemental composition for the compounds $[R'R_2AsOAlk]X$ and $[R'R_2AsAlk]X$, which are close in structure, and also the suggestive analogy with the first stage of the Arbuzov rearrangement biased the authors, working in this area for the first time, towards that structure for the products which seemed to be expected naturally in the reactions examined.

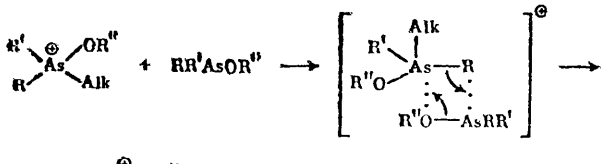
Subsequent investigations of this reaction carried out on several series of esters of dialkyl- and alkylphenylarsinous acids,[18] showed that the composition of the quaternary arsonium salts formed did not depend on the nature of the hydrocarbon residue in the ester group. This enabled exclusion of the scheme proposing exchange of hydrocarbon residues between the alkoxy group of the ester and the alkyl halide from the number of possible reaction schemes.

$$RR'AsOR''+RX\not\rightarrow RR'AsOR+R''X$$

Of the possible schemes proposed to explain the formation of quaternary arsonium salts in this reaction, two are most probable. According to one of them (Scheme 1) the increase in the coordination number of the arsenic atom occurs at the first stage.[6,9]

Scheme 1

$$RR'AsOR''+AlkHal\rightarrow[RR'AlkAsOR'']^{\oplus}Hal^{\ominus}, \quad (1)$$



$$\rightarrow R'AlkAs^{\oplus}(OR'')_2 + R_2R'As, \quad (2)$$

$$R_2R'As+AlkHal\rightarrow[R_2R'AlkAs]Hal. \quad (3)$$

The alkoxyarsonium cation formed, being unstable to nucleophilic attack, is converted into the corresponding tertiary arsine by the action of a second molecule of the initial ester [Scheme 1, stage (2)]. The appearance of a tertiary arsine in the presence of the alkyl halide leads to the formation of the quaternary arsonium salts [Scheme 1, stage (3)].

Another possible reaction route (Scheme 2) consists of a disproportionation of the initial ester, which also leads to the appearance of tertiary arsines, and as a result to the isolation of quaternary arsonium salts as final products [Scheme 1, stage (3)].[6]

Scheme 2

$$2RR'AsOR'' \rightleftharpoons R_2R'As + R'As(OR'')_2.$$

As the reaction mechanism was unexplained, an invetigation of its kinetics was later undertaken.[19] Partial reaction orders, determined by a differential method, for the case of the ethyl ester of diethylarsinous acid and ethyl iodide in acetone at 50 °C proved to be close to unity, which indicates an overall second order. The comparatively simple kinetics for a reaction which is evidently not so simple are explained by the authors by the presence of a limiting step, most probably at the beginning of the process.

It became clear later that the method of obtaining the initial ethyl ester of diethylarsinous acid has an effect on the kinetic data.

$$(C_2H_5)_2AsCl + NaOC_2H_5 \rightarrow (C_2H_5)_2AsOC_2H_5 + NaCl.$$

Haloarsine and tertiary arsine contaminants contained in the reaction product distort the kinetics of the process in the case of the simpler and therefore more frequently used method.

On making the initial ester from bis(diethylarsine)oxide the data of the kinetic investigation proved to be more stable and led to a reproducible result.[9,19]

$$[(C_2H_5)_2As]_2O + 2C_2H_5OH \xrightarrow[-H_2O]{} 2(C_2H_5)_2AsOC_2H_5.$$

It should be noted that both routes considered as most probable for forming quaternary arsonium salts propose the appearance in the reaction mixture of the same products, viz. esters of arsonous acids $R'As(OR'')_2$. These esters were successfully isolated somewhat later.[20]

$$2RR'AsOR'' + AlkX \rightarrow [R_2R'AsAlk]X + R'As(OR'')_2,$$
$$Alk=R=R'=C_2H_5,\ R''=C_6H_5,\ X=I;$$
$$Alk=R=C_2H_5,\ R'=C_6H_5,\ R''=C_4H_9,\ X=I;$$
$$R=R'=C_2H_5;\ R''=Alk=C_4H_9,\ X=Br.$$

It is interesting that the possibility of forming quaternary arsonium salts by a similar reaction was also discovered for esters of arsonous acids.[9]

$$3C_2H_5As(OC_2H_5)_2 + C_2H_5I \rightarrow [(C_2H_5)_4As]I + 2(C_2H_5O)_3As.$$

Further investigations showed that in the case of the lower esters of dialkylarsinous acids the formation of alkoxyarsonium salts may nevertheless be observed under fairly mild conditions.[21]

$$(CH_3)_2AsOCH_3 + CH_3I \rightarrow [(CH_3)_3AsOCH_3]I.$$

The structure of the product was confirmed by IR and PMR spectroscopy. However in addition to bands (655, 1013 cm^{-1}) indicating the presence of the $\rangle AsOC\langle$ grouping, signs of hydroxyl were detected which the authors link with admixture of a compound arising as a result of hydrolysis.

$$[(CH_3)_3AsOCH_3]I + H_2O \rightarrow [(CH_3)_3AsOH]I + CH_3OH.$$

The formation of hydroxyarsonium salts in the reaction of the ethyl ester of dicyclohexylarsinous acid with ethyl iodide is also linked with the increased sensitivity of alkoxyarsonium salts towards hydrolysis.[9]

Cases of the formation of difficultly separable mixtures containing, in the authors' opinion, alkoxyarsonium salts were also noted in the case of the ethyl ester of diethylarsinous acid. However, another product is proposed as contaminant here, viz. a quaternary arsonium salt containing no alkoxy group.[20]

$$(C_2H_5)_2AsOC_2H_5 + C_2H_5I \rightarrow [(C_2H_5)_3AsOC_2H_5]I + [(C_2H_5)_4As]I.$$

On the basis of this the hypothesis was made that tetraethylarsonium iodide is formed from the corresponding alkoxyarsonium salt, i.e. Scheme 1 (see above). However such an interpretation is seemingly not indisputable since the combined isolation of two products does not always indicate that one is not formed from the other. The most persuasive confirmation of the scheme in question might be to attempt to convert the alkoxyarsonium salt directly into a quaternary arsonium salt. So far this has not been successful.

Scheme 2, proposing the disproportionation of the intial ester, is less vulnerable. This property of the esters of As(III) acids was confirmed by GLC.[22] The results obtained by chromatography indicate that the disproportionation is essentially an important property of esters of arsinous acids, which it is impossible not to consider when analysing conversions involving them. The presence in the reaction mixture of haloalkanes capable of binding the generated tertiary arsine in the quaternary arsonium salt isolated in the solid may be considered as a factor assisting disproportionation.

At the same time it would be premature to make a final conclusion regarding the route of formation of the quaternary arsonium salts in the reaction.

Attempts have also been undertaken to effect conversions like the Arbuzov reaction in several thioesters of trivalent arsenic acids. However they were also unsuccessful here. The appearance of another nucleophilic centre, the sulphur atom, together with the arsenic atom evidently leads to a change in the direction of attack of the nucleophile and the reaction leads to the formation of dialkyl disulphides or sulphonium salts.[8,23]

$$R_nAs(SR')_{3-n} + (3-n)R''X \longrightarrow$$
$$\longrightarrow [R_nAs(SR')^{\oplus}_{2-n}SR'R'']X^{\ominus} \longrightarrow R_nAsX_{3-n} + (3-n)R'SR'',$$

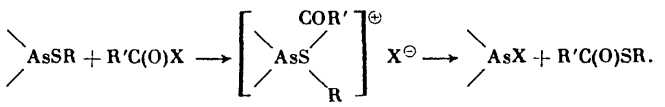
$R=C_2H_5$, C_6H_5, $NH(C_6H_4)_2$; $R'=C_2H_5$, C_4H_9,



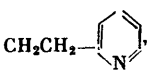
$-CH_2CH_2$, $C(O)CH_3$, CH_2CH_2OH, $C_6H_4NH_2$-*o*;

$R''=CH_3$, C_2H_5; X=Br, I; $n=0$, 1, 2.

Similarly carboxylic acid chlorides react with thioesters with fission of the As–S bond.[5] Reaction occurs at the sulphur atom as in the case of the alkyl halides.

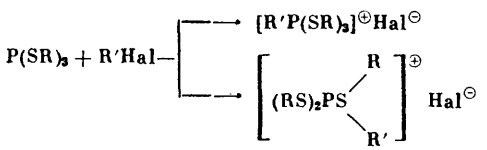


$$R=C_4H_9,\ CH_2CH_2OH,\ CH_2CH_2N(C_2H_5)_2,$$



$$R'=CH_3,\ C_6H_5;\ X=Cl,\ Br.$$

Such a reaction course is not unexpected since even thiophosphites, in which the phosphorus atom is more nucleophilic than arsenic in the thioesters of the corresponding As(III) acids, may be alkylated under analogous conditions both at phosphorus and at sulphur.[24–33]



It is interesting to compare these data with the conversions of antimonous acid under the action of halogen derivatives.[34]

$$Sb(OR)_3+nR'X\rightarrow X_nSb(OR)_{3-n}+nROR'$$

$$R=Alk,\ R'=Alk,\ Ac,\ CH_2OAlk;\ X=Cl,\ Br,\quad n=1\text{ to }3.$$

The formation of an oxonium compound was proposed at an intermediate stage and the process itself is considered as a variation of the Williamson reaction, i.e. the reaction of alkyl halides with alkoxides. In the opinion of the author, the polarity of the E–O bond changed in derivatives of the type $(RO)_3E$ (E = P, As, Sb). The phosphorus atoms acts as the nucleophilic centre in phosphites (E = P) and the oxygen atom in esters of antimonous acid (E = Sb). A similar approach was also confirmed by the results of other conversions.[34]

$$(RS)_3Sb+nR'X\rightarrow (RS)_nSbX_{3-n}+(3-n)RSR',$$
$$R=Alk;\ R'=Alk,\ Ac;\ X=Cl,\ Br,\ I,$$
$$(C_2H_5O)_3P+3HBr\rightarrow H_3PO_3+C_2H_5Br,$$
$$(C_2H_5O)_3As+3HBr\rightarrow AsBr_3+3C_2H_5OH.$$

Returning to the esters of arsinous acids it is interesting to note the attempt to alkylate their anhydrides $(RR'As)_2E$ (E = O, S),[35] which may be considered as derivatives of esters RR'AsER'' when R'' = AsRR'. It is assumed that the presence of a system of three interconnected nucleophilic centres may change the ratio of their nucleophilicities and make the first stage of the Arbuzov reaction more probable.

As it turned out, in this case also the reaction occurs in a more complex manner and led to the formation of a quaternary arsonium salt and haloarsines. When using thioanhydrides the reaction requires more forcing conditions and is accompanied by side reactions.

$$RR'AsEAsRR'+RX\rightarrow RR'AsER+RR'AsX,$$

when E = O [Ref. 35]:

$$RR'AsOR+RX\rightarrow [R_3R'As]X,$$
$$RR'AsX+RX\rightarrow R_2R'AsX_2,$$

when E = S [Ref. 36]:

$$RR'AsSR+RX\rightarrow RR'AsX+[R_3R'As]X,$$
$$R=R'=C_2H_5,\ n\text{-}C_3H_7,\ iso\text{-}C_3H_7,\ n\text{-}C_4H_9,$$
$$R=Alk,\ R'=C_6H_5;\ X=Br,\ I.$$

In similar reactions the corresponding esters and haloarsines were isolated from acid chlorides of carboxylic acids.[35]

$$(RR'As)_2E+R''X\rightarrow RR'AsER''+RR'AsX,$$
$$R=R'=Alk,\ C_6H_5;\ R''=CH_3C(O),\ C_6H_5C(O);\ X=Cl.$$

The data presented permit the conclusion that even in the most nucleophilic esters of As(III) acids and their derivatives, a reaction like the Arbuzov does not occur under similar conditions but a more complex process takes place accompanied by fission of the $\rangle As-E$ (E = O, S) bond.

The inability of esters of As(III) acids to react with halogen derivatives in a manner like their phosphorus analogues is evidently explained by the reduction of nucleophilicity on going from phosphorus to arsenic.[6] The significantly higher sensitivity of the arsenic atom to the inductive effect of substituents is an important circumstance.[37] Of the possible types of esters of As(III) acids, viz. $R_2As(OR')$, $RAs(OR')_2$ or $As(OR')_3$, only the esters of arsinous acid $R_2As(OR')$ display a clearly marked ability to react with alkyl halides. For the corresponding phosphorus derivatives with the Arbuzov reaction proceeds both with esters of phosphinic acids and with full phosphites, although at different rates. It may be proposed that with phosphorus the reduction in electron density is compensated to a greater extent than with arsenic by the attraction of the unshared electron pair of the oxygen of the alkoxy groups to the *d* orbitals of the central atom. At the same time, in spite of the abundant literature proposing conjugation with the *d* orbitals of the phosphorus atom, a fairly sound view exists on the insignificant role of similar effects in bond formation.[38] In this connection, as an alternative, it would have been useful to clarify the possibility of displaying an α-effect ("supernucleophilicity") as a feature inherent to certain phosphorus derivatives in contrast to the arsenic-containing analogues. The presence of an unshared electron pair on the atom connected directly to the nucleophilic centre is, as is known,[39,40] one of the most important factors determining the order of the nucleophilicity. However there are no literature data capable of successfully confirming a deviation from the Brønsted rule for esters of P(III) acids.

Among the other reasons explaining the difference in behaviour of esters of P(III) and As(III) acids it is impossible not to mention the unique nature of the phosphorus–oxygen bond in the phosphoryl group arising in reactions of this type. The high thermodynamic stability of this bond (estimated at 552 kJ/mol) is one of the driving forces of the Arbuzov reaction (the strength of the As–O bond is estimated at 443 kJ/mol [41]). Finally new E–C bonds arising in the course of side reactions, when E = P, prove to be more stable (for example by 40.2 kJ/mol), while the fissile E–OC bonds in esters of

As(III) acids are more labile. The latter circumstance superimposes a special imprint on the properties of these esters, imparting to them, in contrast to the phosphorus analogues, an increased hydrolytic instability, but the intermediate product containing an alkoxy group on the arsenic atom is susceptible to a different sort of side reaction, complicating significantly the course of the reaction.

Evidently these same special features may explain the more marked inclination of tetracoordinated arsenic derivatives to conversions occurring with a reduction in valency.

III. The retro-Arbuzov reaction in organic derivatives of As(V)

1. Reactions of compounds containing an arsenyl group

The first information on the possibility of conversions of esters of tetracoordinated arsenic acids occurring with a reduction of its valency were known even before the discovery by A E Arbuzov of the reaction bearing his name.

Even in 1867 Kraft[2] showed that reduction of arsenic to the trivalent state occurred on heating a mixture of arsenic acid with tetraethoxysilane to 230 °C.

However only in 1947 did Komissarov and collaborators[42] realise that the conversion of esters of alkylarsonic acids on heating to a temperature of the order of 200 °C was similar to the process occurring in the reverse direction to the Arbuzov reaction

$$CH_3As(O)(OCH_3)_2 \rightarrow (CH_3O)_3As.$$

The isomerisation was accompanied by the formation of alcohols and a fraction in which the arsenic content was higher than in the corresponding trialkyl arsenites.

These studies appear to be the starting point for the investigations of more recent times on the possibility of achieving conversions with the oxygen derivatives of tetracoordinated arsenic proceeding in a direction opposite to the Arbuzov reaction.

In reality a wider study of the behaviour of trialkylarsine oxides[4] and esters of dialkylarsinic and alkylarsonic acids[2,4] at temperatures close to 200 °C confirmed the conclusions on the thermal instability of oxygen derivatives of As(V). Certain features linked primarily with the fairly complex character of the conversions were clarified.

On pyrolysis of esters of alkylarsonic acids, in addition to the isomerisation product (I) [2,4] the yield of which proved to be generally insignificant and rarely exceeded 10%. The formation was observed of reduction products, viz. the corresponding esters of alkylarsonous acids (II).

$$RAs(O)(OR)_2 \xrightarrow{\Delta} \begin{cases} \rightarrow (RO)_2As \text{ (I), 2—11\%} \\ \rightarrow RAs(OR)_2 \text{ (II), 6—40\%} \end{cases}$$

The authors also indicated the formation in the reaction of an alcohol with the residue of the alkoxy group of the initial ester. On pyrolysis of the dibutyl ester of methylarsonic acid the presence was detected of a carbonyl compound which reacted with 2,4-dinitrophenylhydrazine.[4]

The esters of diethylarsinic acids proved to be even less stable to heat and decomposed with resinification even on attempted distillation.[2,4] It is necessary to record that the formation of isomerisation products was hardly observed by the authors in this case. In addition to the reduction products, viz. the corresponding esters of dialkylarsinous acids, alcohols containing the hydrocarbon residue of the alkoxy group and also dialkylarsinic acids were successfully identified. The dibutyl ester of ethylarsonic acid was isolated in 8% yield from the products of oxidation of the butyl ester of diethylarsinous acid as a result of thermal decomposition.

The main products of the pyrolysis of tertiary arsine oxides, as has been clarified,[4] are also reduction products, viz. the corresponding tertiary arsines and alcohols. The formation in small quantities of isomerisation products, esters of dialkylarsinous acids, was observed.

$$R_3AsO \xrightarrow{\Delta} \begin{cases} \rightarrow R_3As, ROH \\ \rightarrow R_2AsOR \end{cases}$$

The authors considered a disproportionation reaction probable, since tributylarsine was isolated from the pyrolysate of methyldibutylarsine oxide.

A more detailed investigation of the thermal conversions of derivatives containing the arsenyl group indicated the complexity of the processes taking place. The yield of isomerisation products was, as a rule, below 10%, a significant proportion of the starting material resinified.

A higher yield of isomerisation products (32—46%) was observed in the pyrolysis of the diethyl ester of ethylarsonic acid and the dibutyle ester of butylarsonic acid obtained by the method of esterification.[3,4] The authors came to the conclusion that admixture of selenium compounds, used previously to obtain the initial As(V) esters, catalyses oxidation—reduction side reactions accompanying the isomerisation. It was shown by thermography that the reaction proceeds in one stage and, depending on the character of the environment of the arsenic atom, the temperature for the initiation of conversion (TIC) varied within the limits 115—282 °C. The TIC increased with an increase in the length and branching of the hydrocarbon substituents. From the thermographic data a stability series at increased temperature was drawn up for the esters as a function of the structure of the hydrocarbon residue bound to the arsenic atoms.

$$(CH_3)_2CHCH_2 > C_4H_9 > C_2H_5 > CH_3 > C_6H_5CH_2 > CH_2{=}CHCH_2 > (CH_3)_2CH.$$

Subsequent investigations of the retro-Arbuzov reaction in esters of arsinic acids showed that on adding small quantities of electrophilic reagents (alkyl halides, salts and acids) conversion began at lower temperatures and the yield of products grew to 50—63%.[3,4] Thermographic data indicated a two-stage process and the absence of an effect on adding nucleophilic reagent (sodium ethoxide, pyridine) on the temperature for the initiation of conversion. An increase of two orders of magnitude in the specific conductivity on mixing the reactants indicated the formation of an ionic intermediate.

A study of the kinetics of the isomerisation of esters of alkylarsonic acids by alkyl halides[3] indicated the overall second order of the reaction which, together with the results of

thermographic investigations,[3,4] afforded the conclusion that the conversion occurred in the opposite direction to the Arbuzov reaction.

$$R(OR')_2AsO+R''X \rightleftharpoons [RAs(OR')_2(OR'')]^{\oplus}+X^{\ominus} \rightarrow$$

$$\rightarrow (R'O)_2AsOR''+RX.$$

Later, similar conversions were investigated for esters of dialkylarsinic acids.[1,43] Here the addition of alkyl halides also reduced the TIC significantly. The use of GLC enabled a more complete analysis of the products formed. When relatively less stable $As-C_{Alk}$ bonds were absent from the initial esters the main route of the process was an exchange of hydrocarbon residues between the alkoxy group and the alkyl halide if the reaction was carried out under conditions when the volatile products formed were continuously distilled out (yield 75–95%).

$$(C_6H_5)_2As(O)OR+R'Hal \rightarrow (C_6H_5)_2As(O)OR'+RHal,$$
$$(C_6H_5)As(O)(OR)_2+R'Hal \rightarrow (C_6H_5)As(O)(OR)(OR')+RHal,$$
$$R'=CH_2C_6H_5;\ Hal=Br;\ R=C_3H_7.$$

The following processes, which the authors regard as oxidation–reduction, occur in parallel

$$(C_6H_5)_2As(O)OR + C_6H_5CH_2Br \xrightarrow[-HBr]{} (C_6H_5)_2AsOR + C_6H_5C(O)H,$$
$$C_6H_5As(O)(OR)_2 + C_6H_3CH_2Br \xrightarrow[-HBr]{} C_6H_5As(OR)_2 + C_6H_5(O)H.$$

This reaction course predominates when R = $C_6H_5CH_2$ although it requires more forcing conditions. Triphenylarsine also appears in the reaction products, which the authors link with the disproportionation.

$$3(C_6H_5)_2AsOCH_2C_6H_5 \rightleftharpoons 2(C_6H_5)_3As+(C_6H_5CH_2O)_3As.$$

In the case of esters containing the less stable $As-C_{Alk}$ bonds the predominant reaction route is retro-Arbuzov accompanied by symmeterisation and exchange processes.

$$Alk_2As(O)OR + R'Br \xrightarrow{-RBr} Alk_2As(O)(OR') \xrightarrow[-AlkBr]{\sim 10\%} AlkAs(OR)(OR') \rightleftharpoons AlkAs(OR)_2 + AlkAs(OR')_2$$
$$\sim 65\%$$

The authors came to the conclusion that irrespective of the nature of the isolated products the first stage of the reaction is the formation of the corresponding alkoxyarsonium salt (V).

$$R_2As(O)OR' + R''CH_2Hal \rightarrow [R_2As(OCH_2R'')OR']^{\oplus}Hal^{\ominus}$$
(III) (IV) (V)

The formation of this salt is confirmed by the increase in conductivity on mixing the reactants (III) and (IV).

The further conversions of the intermediate (V) are determined by the nature of the reaction participants and conditions.

$$(V) \xrightarrow[-RHal]{a} RAs(OR')(OCH_2R'') \rightleftharpoons RAs(OR')_2 + RAs(OCH_2R'')_2$$
$$(V) \xrightarrow[-R'Hal]{b} R_2As(O)OCH_2R'' \xrightarrow{-R''CHO} R_2AsOR'$$
$$(V) \xrightarrow[-R''CHO]{c} R_2AsOR'$$

R=Alk, Ar; R′=Alk; R″=Alk, Ar.

Route *a* (retro-Arbuzov reaction) is most characteristic for esters containing an alkyl group on the arsenic atom. When alkyl groups are absent (R = Ar) route *b* predominates if conditions are created for displacing the equilibrium by removing the more volatile alkyl halide formed. In the opinion of the authors[1,43] an increase in temperature favours the oxidation–reduction reaction (route *c*). In esters having only one $As-C_{Alk}$ bond the retro-Arbuzov reaction may therefore be the main route for conversion under appropriate conditions.

A different situation is generated in attempts to effect the retro-Arbuzov reaction with tertiary arsine oxides. As was explained, on reacting triethylarsine oxide with isopropyl and isobutyl iodide a crystalline compound is formed, the analysis of which indicated a composition $C_{12}H_{31}As_2O_2I$, in place of the expected esters of arsinous acids.[44] Initially the obtained product was assigned the structure of triethyl(triethylhydroxyarsoxy)arsonium iodide.

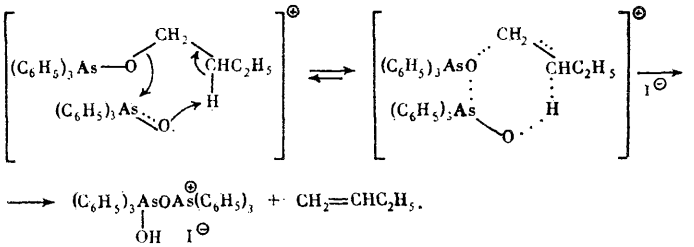
$$(C_2H_5)_3As-O-As^{\oplus}(C_2H_5)_3.\ I^{\ominus}$$
$$\quad\quad\quad

assuming the intermediate formation of an alkoxyarsonium salt capable of being later converted by an irreversible reaction (Scheme 4) to the final products.[44,45]

Scheme 3

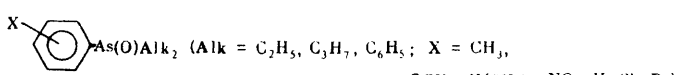
$$(C_6H_5)_3AsO + ICH_2CH_2C_2H_5 \rightleftharpoons \left[(C_6H_5)_3AsO\ldots\underset{\displaystyle CH_2C_2H_5}{\overset{\displaystyle |}{CH_2}}\ldots I\right] \rightleftharpoons$$
$$\rightleftharpoons [(C_6H_5)_3AsOCH_2CH_2C_2H_5]^{\oplus} + I^{\ominus}$$

Scheme 4



$$\longrightarrow (C_6H_5)_3AsO\overset{\oplus}{As}(C_6H_5)_3 + CH_2{=}CHC_2H_5.$$
$$\quad\ |$$
$$\quad OH\ \ I^{\ominus}$$

As was shown by further investigations,[44,46] the adducts of type $(R_2R'AsO)_2HHal$ are formed when using a fairly wide range of reactants. Alkyl halides RHal of normal and branches structure (R = CH_3, C_2H_5, n = C_3H_7, n-C_4H_9, iso-C_4H_9, $CH_2C_6H_5$; Hal = I, Br, Cl) have been used in reactions with trialkylarsine oxides Alk_3AsO (Alk = CH_3, C_2H_5, n-C_3H_7, cyclo-C_6H_{11}) and also with a series of dialkylarylarsine oxides.



The formation of hydroxyarsonium salts in place of 2 : 1 adducts occurred only in certain cases. Attempts have been made to show that hydroxyarsonium sals result from the decomposition of these adducts.[7,44]

$$(R_3AsO)_2HI \rightarrow [R_3AsOH]I + R_3AsO.$$

However the similar conversion was unsuccessful. This compelled the authors to acknowledge that it is impossible to explain the isolation of hydroxyarsonium salts in the reactions of tertiary arsine oxides with alkyl halides by more profound conversions and that the reason for the appearance of these salts remains unclear.

When analysing the first results obtained on investigating the conversions of tertiary arsine oxides by alkyl halides it is important to note that in the overwhelming majority of cases only alkyl iodides are used in these reactions[44–46] but the yield of crystalline products, as a rule, is far from quantitative. Only for trimethyl- and triethylarsine oxides reacting with methyl iodide was the yield 61.7 and 65.6% respectively while in all the remaining cases it varied between 25 and 50%.

Analysis of the gaseous reaction products indicated the formation of olefins, which is in agreement with the proposed Scheme 4. However on using methyl iodide, the presence of methane and ethane was recorded in addition to ethylene.[7] This indicates the presence of side reactions.

The problem of the composition of the liquid portion of the reaction mixture, in which the products of a retro-Arbuzov reaction would be sought, remained on one side for some time. This may be explained by the unexpected formation of crystalline products of unusual structure such as $(R_2R'AsO)_2HHal$. Only later was it discovered that on reacting diethylphenylarsine oxide with alkyl bromides were esters of ethylphenylarsinous acid isolated in up to 70% yield.[47] It was therefore shown possible to effect a conversion opposite to the Arbuzov reaction for certain tertiary arsine oxides.

$$(C_2H_5)_2(C_6H_5)AsO + AlkBr \rightarrow$$
$$\rightarrow [(C_2H_5)_2C_6H_5AsOAlk]Br \rightarrow (C_2H_5)(C_6H_5)AsOAlk + C_2H_5Br$$
$$Alk = C_2H_5,\ n\text{-}C_3H_7,\ n\text{-}C_4A_9.$$

Somewhat later an analogous route for the reaction was also reported for trialkylarsine oxides (the yield of esters was only ~10%).[48] However the closeness of the boiling points of the reaction products did not enable results to be obtained which could be acknowledged to be sufficiently clear.

Subsequent investigations were performed using diphenylalkylarsine oxides.[49] First of all evidence was obtained that this reaction may be carried out as the main process accompanied by the formation of esters of diphenylarsinous acid in 65% yield.

$$(C_6H_5)_2RAsO + AlkX \rightarrow (C_6H_5)_2AsOAlk + RX,$$

$$R = C_2H_5,\ n\text{-}C_3H_7,\ n\text{-}C_4H_9;\ Alk = CH_3,\ C_2H_5,$$

$$n\text{-}C_3H_7,\ n\text{-}C_4H_9;\ X = Br,\ I$$

The most important feature of these conversions is the formation of the corresponding haloarsines, which was noted for the first time, together with the esters of diphenylarsinous acid.[11,49]

Triphenylarsine oxide, containing no akyl groups capable of being split off by activated halogen derivatives of the type $HalCH_2Z$ (where Z = $C(O)OCH_3$, $C(O)OC_2H_5$, CN, $C(O)CH_3$; Hal = Cl, Br) forms hydroxyarsonium salts $[Ph_3AsOH]Hal$ ($Ph_3AsO.HHal$) (1 : 1) in place of adducts of composition $(Ph_3AsO)_2HHal$ (2 : 1).[50]

Similar hydroxyarsonium salts were isolated on using the usual alkyl bromides under more forcing conditions.[50] This suggested that the formation of 2 : 1 adducts such as $(Ph_3AsO)_2HHal$ or 1 : 1 adducts like $Ph_3AsO.HHal$ is determined by the nature of the halogen in the initial halogen derivative.

These facts together with the possibility mentioned above of forming haloarsines as side products enabled the following hypotheses to be put forward:

—the first stage of the process is the formation of an alkoxyarsonium salt $[R_2R'AsOAlk]Hal$ irrespective of the nature of the products isolated:

—the appearance of adducts $(R_2R'AsO)_2HHal$ is the result of the reaction of the hydroxyarsonium salt $[R_2R'AsOH]Hal$ with the initial oxide $R_2R'AsO$;

$$R_2R'AsO + [R_2R'AsOH]Hal \rightarrow (R_2R'AsO)_2HHal$$

—the hydroxyarsonium salts themselves appear as a result of the decomposition or hydrolysis of the intermediate alkoxyarsonium salts;

$$R_2R'AsO + AlkHal \rightarrow [R_2R'AsOAlk]Hal \xrightarrow{H_2O} [R_2R'AsOH]Hal + AlkOH$$
$$[R_2R'AsOAlk]Hal \xrightarrow{\Delta} [R_2R'AsOH]Hal + \text{olefin}$$

—the isolation of haloarsines together with esters of trivalent arsenic acids in those cases when a reverse Arbuzov reaction occurs is linked with the decomposition of thermally unstable hydroxyarsonium salts formed as side products:

$$[R_2R'AsOH]Hal \xrightarrow{\Delta} RR'AsHal.$$

The central point of these conversions is the formation in the first stage of an alkoxyarsonium salt $[R_2R'AsOAlk]Hal$ as an intermediate. Attempts to isolate these salts in the reactions of tertiary arsine oxides with alkyl halides were unsuccessful. The difficulty of isolating byproducts is explained by their instability linked with the increased reactivity of the alkoxyarsonium cation.[1,3,4,7]

Nevertheless the reduction of the positive charge on the arsenic atom in the cation by replacing phenyl by alkyl, the introduction of a less nucleophilic bromide anion and the use of carefully dried solvents and apparatus enabled the formation of an alkoxyarsonium salt to be recorded in one of the examples.[51]

$$(n\text{-}C_3H_7)_3AsO + C_2H_5Br \rightarrow [(n\text{-}C_3H_7)_3AsOC_2H_5]Br$$

Confirmation was also obtained for the other hypotheses in a similar manner. The synthesis and study of the thermal conversions of hydroxyarsonium salts was the subject of a special investigation.[52]

These results enabled an overall Scheme to be drawn up for the conversion of tertiary arsines by alkyl halides as a single process, the route of which is determined by the environment of the arsenic atom.[53–55]

Scheme 5

$$R_2R'AsO + R''X \rightarrow [R_2R'AsOR'']X$$
$$[R_2R'AsOR'']X \xrightarrow[-RX]{a,\ X^{\ominus}} R_2AsOR'' \rightleftharpoons R_3As + RAs(OR'')_2$$
$$[R_2R'AsOR'']X \xrightarrow[-\text{olefin}]{b,\ R_2R'AsO} [R_2R'AsOH]X \xrightarrow{R_2R'AsO} (R_2R'AsO)_2HX$$
$$[R_2R'AsOH]X \xrightarrow{-ROH} (RR'As)_2O \xrightarrow{R''X} RR'AsOR'' + RR'AsX$$

The more basic trialkylarsine oxides (R = R′ = Alk) react predominantly as bases undergoing dehydrohalogenation of the alkyl halide (Scheme 5, route *b*). If the retro-Arbuzov reaction (Scheme 5, route *a*) also takes place under these conditions then it is only a side reaction. In the case of the less basic dialkylphenyl- and alkyldiphenylarsine oxides (R = Alk, R′ = C_6H_5, R′ = Alk) the contribution of route *a*, leading to a retro-Arbuzov reaction product, is significantly increased and route *b* plays the role of a side reaction. Route *b* remains the sole possible route in the case of triphenylarsine oxide, which contains no $As-C_{Alk}$ bond capable of fission.

The Scheme represented above for the conversion of tertiary arsine oxides by halogen derivatives enables the available data to be combined, considering them as different aspects of a single fairly complex and interconnected process, certain steps of which are worthy of further study. Processes of elimination, which frequently accompany nucleophilic substitution are of particular interest in this connection. The possibility of α- and β-elimination of alkoxyarsonium salts arising in the intermediate stage was investigated in special experiments using triphenylarsine oxide.[56] The detection of tertiary arsines, olefins and aldehydes in the reaction products indicates the need to take the side reactions into account although their contribution may prove to be small (~6–10%).

2. The retro-Arbuzov reaction with tertiary arsine sulphides

Tertiary arsine sulphides are the sole representatives of the thioarsenyl compounds for which the conversions occurring with a reduction in the valency of the arsenic atom have been investigated at the present time. This may explain the unsuccessful attempts to synthesise esters of tetracoordinated arsenic containing a $\rangle As(S)$ group, although here definite progress has been planned for some time past.[57–59]

The first information on the pyrolysis of tertiary arsine sulphides was published in 1966.[60] As was explained, the pyrolysis of diethylphenylarsine sulphide in a sealed tube and in vacuum leads to the formation of an isomerisation product in 6–9% yield.

$$(C_2H_5)_2C_6H_5AsS \xrightarrow{200-240^{\circ}\,C} (C_6H_5)(C_2H_5)AsSC_2H_5.$$

The thermal decomposition of trialkylarsine sulphides proceeds in a similar manner. On heating triethyl-, tripropyl- and methyldipropylarsine sulphides in vacuum at 200 °C for 1 h the corresponding esters of dialkylthioarsinous acids were obtained in 20–26.8% yield.[60,61] The isolation of other pyrolysis products was not reported although the formation of a complex reaction mixture was obvious, as on the pyrolysis of the oxides.

An investigation of the decomposition of triethylarsine sulphide by DTA with simultaneous recording of the conductivity change showed the presence of two exo effects.[61] The position of the first of them coincided in time with an increase in conductivity. It was concluded that heterolytic fission of an As–C bond occurred with the subsequent formation of a thioether.

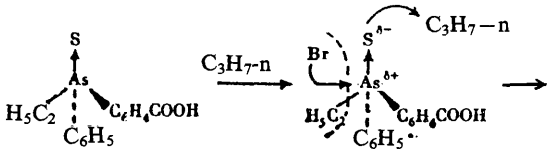
$$(C_2H_5)_3AsS \xrightarrow{\Delta} [(C_2H_5)_2As^{\ominus}S + {}^{\oplus}C_2H_5] \rightarrow (C_2H_5)_2AsSC_2H_5.$$

Similar results were obtained on investigating the thermal isomerisation of tripropyl-, and methyldipropyl- and diethylphenylarsine sulphides by DTA.[5,8,61]

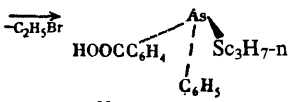
As was clarified by subsequent investigations the addition of small quantities (up to 0.1 mol) of alkyl halides and salts to tertiary arsine sulphides leads to an appreciable reduction in the temperature for the initiation of conversion.[5,8,62] The yield of product of the retro-Arbuzov reaction thereby grows significantly. The ester of

propylphenylthioarsinous acid was isolated in 60% yield by the reaction of a 1:1 ratio of ethyl bromide and dipropylphenylarsine sulphide at 100 °C for 2.5 h. Trialkylarsine sulphides are converted by alkyl halides into the corresponding thioesters in 25–67% yield.[8,62]

The retro-Arbuzov reaction was used for a series of tertiary arsine sulphides with the aim of obtaining asymmetric esters of the RR'AsSR'' type.[63] A change in the rotation of the initial (enantiomeric) sulphides to the opposite sign was recorded.



$[\alpha]_D^{20} + 19{,}12$



$[\alpha]_D^{20} - 3{,}18$

It should be noted that the esters of thioarsinous acids were not the only products isolated in the course of the retro-Arbuzov reaction with tertiary arsine sulphides. In several cases the formation was noted of the corresponding monohaloarsines as byproducts, the content of which grew with an increase in temperature, in contact time and on going from alkyl bromides to iodides.[5,8,62,64]

On reacting ethylphenyl-α-naphthylarsine sulphide with methyl iodide, diethyl-α-naphthylarsine, α-naphthyldiphenylarsine sulphide and free sulphur were isolated in addition to the corresponding ester of thioarsinous acid.[65]

The synthesis of the alkylthioarsonium salts formed as intermediates was carried out to confirm the two-stage nature of the retro-Arbuzov reaction.[66]

$$R_2R'AsS + AlkX \rightarrow [R_2R'AsSAlk]X,$$

R, R', Alk=C_2H_5, C_3H_7, C_4H_9, C_6H_5; X=Br.

The corresponding esters of thioarsinous acids were successfully obtained in up to 50% yield by the decomposition of these salts.

The retro-Arbuzov reaction was also observed for several tertiary arsine sulphides on using organic acids, their anhydrides and halogen derivatives as electrophilic reagents.[67,68]

$$Alk_2C_6H_5AsS + RC(O)X \longrightarrow [Alk_2C_6H_5AsSC(O)R]X \xrightarrow{-AlkX} \longrightarrow AlkC_6H_5AsSC(O)R,$$

Alk=C_2H_5, C_3H_7, C_4H_9; R=CH_3, C_2H_5, C_3H_7, CH_2Cl, $CHCl_2$, CCl_3; X=OH, RC(O).

When using carbon tetrachloride and alkyl chloroformates as electrophiles the authors also proceeded from an analogous reaction scheme.

$$R_2R'AsS + R''Cl \rightarrow [R_2R'AsSR'']Cl \rightarrow \rightarrow RR'AsSR'' + RCl,$$

R, R'=Alk, Ar; R''=CCl_3, $CH_2C(O)OCH_3$

A more complex character was noted for the conversions indicated requiring their further study.

The reaction of tertiary arsine sulphides with acid chlorides has been investigated in a fairly detailed manner.[69–71] On carrying out the reaction with acetyl chloride in a solvent, either the thioacetylarsine (VIII) (in benzene)[8] or the acetylthioarsonium chloride (VII) (in acetone) were formed.[8,70]

$$\underset{(VI)}{R_2R'AsS} + CH_3C(O)Cl \longrightarrow \underset{(VII)}{[R_2R'AsSC(O)CH_3]Cl} \xrightarrow{-RCl} \underset{(VIII)}{R_2R'AsSC(O)CH_3},$$

R=R'=C_2H_5, n-C_3H_7, n-C_4H_9; R'=C_6H_5, R=C_3H_7.

On carrying out the same reaction without a solvent, the corresponding chloroarsines and *S*-alkyl esters of thioacetic acid were isolated.[69]

$$\underset{(VI)}{(C_6H_5)Alk_2AsS} + CH_3C(O)Cl \rightarrow \underset{(IX)}{(C_6H_5)AsAlkCl} + \underset{(X)}{CH_3C(O)SAlk},$$

Alk=C_3H_7, C_6H_{13}.

No thioacetylarsines (VIII) were observed in the reaction products on repeatedly reproducing these experiments.[71] In this case a tertiary arsine dichloride (XI) was isolated in place of the intermediate (VII) and the corresponding chloroarsines (IX) in place of the thioacetylarsines (VIII).

$$\underset{(I)}{R_2R'AsS} + 2CH_3C(O)Cl \longrightarrow \underset{(XI)}{R_2R'AsCl_2} \xrightarrow[-RCl]{\Delta} \underset{(IX)}{RR'AsCl},$$

R=R'=C_2H_5, n-C_3H_7, iso-C_3H_7;

R=CH_3, C_2H_5, n-C_3H_7, R'=C_6H_5.

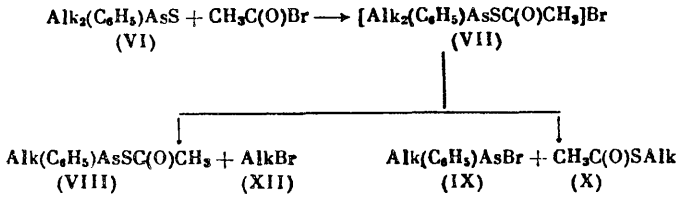
The formation of tertiary arsine dichlorides (XI) has been reported in a whole series of other cases.[72]

$$R_2R'AsS + R''Cl \rightarrow R_2R'AsCl_2,$$

R''=H, COCl, PCl_2, CH_2CN, $CH_2C(O)CH_3$, $C_6H_5C(O)$, $CH_2C(O)OCH_3$.

Considering that similar conversions are also known for teriary arsine oxides,[73] it may be proposed that here also a process alternative to the retro-Arbuzov reaction is taking place, occurring without changing the valency of the arsenic.

Reaction with acetyl bromide leads to the formation of a more complex mixture of products.[69,74]]

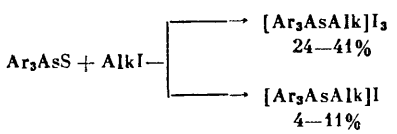


At a 1:1 ratio of starting materials the reaction occurs fairly energetically at room temperature and is completed by the formation of (VIII) and (X) contaminated with alkyl halide (XII). With a 2:1 excess of acetyl bromide and an increase in the contact time the reaction, in the authors' opinion, goes further so that it is not possible to isolate the thioacetylarsine (VIII) in the pure state or its yield is reduced. From this it was concluded that the haloarsine (IX) is formed by secondary conversions.

$$(VIII)+(XII)\rightarrow(IX)+(X)$$

In parallel to the investigations mentioned and independently of them the reaction of tertiary arsine oxides with alkyl halides has been studied by one further group of authors.[75–77]

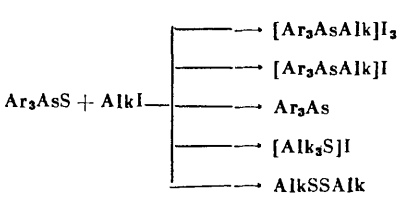
Using as starting materials triarylarsines containing the more stable As–C_{Ar} bonds these authors showed that at an excess of alkyl iodide (1:8, acetone, boiling for 15–50 h) the reaction took place without a change in arsenic valency.



Ar=C_6H_5, $CH_3C_6H_4$;

Alk=CH_3, C_2H_5, C_3H_7, $CH_2C_6H_5$, $CH_2C(O)OC_2H_5$.

One of the sulphur-containing products, trimethylsulphonium iodide, was successfully isolated in 6% yield in the case of triphenylarsine sulphide and methyl iodide. In addition it was suggested that dialkyl disulphides and tertiary arsines were present in the reaction mixture. The results of the reaction of triarylarsine sulphides with alkyl halides may be expressed by the following scheme.



It is important to note that in the experiments mentioned only the most reactive alkyl halides were used since the application of alkyl bromides led to the isolation of unreacted starting sulphide.

The trialkylarsine sulphides proved to be more reactive in alkylation reactions. Alkylthioarsonium salts are formed fairly rapidly on reaction under mild conditions.

$$Alk_3AsS+RX\rightarrow[Alk_3AsSR]X,\quad {}_{23-88\%}$$

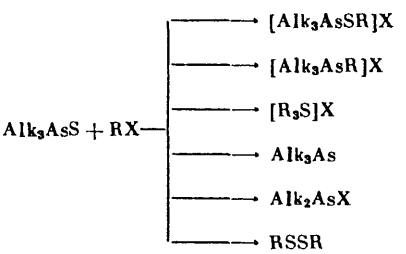
Alk=C_2H_5, n-C_3H_7 cyclo-C_6H_{11};

R=CH_3, C_2H_5, n-C_4H_9; X=Br, I

Under more forcing conditions the quaternary arsonium salt, containing no sulphur, was isolated once again.

$$(C_2H_5)_3AsS+RI\rightarrow[(C_2H_5)_3AsR]I,$$
$$R=CH_3,\ C_2H_5.$$

The impossibility of isolating the corresponding triiodides is explained by their solubility in the reaction mixture. Attempts to identify the sulphur-containing products gave no clear results. Only in the case of methyl iodide was trimethylsulphonium iodide successfully isolated from the reaction mixture. On reacting triethylarsine sulphide with n-propyl bromide a broad fraction was obtained containing, in the authors' opinion, bromodiethylarsine, triethylarsine and di-n-propyl sulphide. The data obtained indicate the formation of an even more complex mixture in the reaction of trialkylarsine sulphides with alkyl halides.



The crystalline reaction products were isolated and identified, the liquid products were not successfully separated. The formation of the latter was confirmed only indirectly. Quaternary arsonium salts may arise from trialkylarsines and sulphonium salts from dialkyl disulphides.

Comparison of the composition of the products isolated on alkylation of triaryl- and trialkylarsine sulphides indicates that these reactions have a general character. The main differences are the possibility of breaking the As–C bond in the case of trialkylarsine sulphides (haloarsine formation) and also the appearance in this case of the intermediately formed trialkyl(alkylthio)arsonium salts. Difficulties linked with the isolation of the analogous triaryl-(alkylthio)arsonium salts are explained by the authors by the stability of these salts due to the electron-accepting action of the phenyl groups and the high nucleophilicity of the anion. In fact triphenyl(ethylthio)arsonium tetrafluoroborate proved to be a completely stable compound. Addition of a carrier of more nucleophilic anions, such as sodium iodide, to a solution of this compound in acetone led to decomposition of the salt due to the reduction of its stability.

$$[(C_6H_5)_3AsSC_2H_5]BF_4+NaI\rightarrow[(C_6H_5)_3AsOH]I+$$
$$+[(C_6H_5)_3AsOH]I_3+(C_6H_5)_3As.$$

Similar observations enabled the important conclusion to be drawn that an alkylthioarsonium salt is stable if one of two factors are present. Either the anion has a low nucleophilicity or the substituents bound to the arsenic atom have a small electronegativity. This conclusion was confirmed by the synthesis of a whole series of fairly stable trialkyl- and triarylthioarsonium salts containing an anion of reduced nucleophilicity (BF_4^-, $CH_3SO_4^-$).

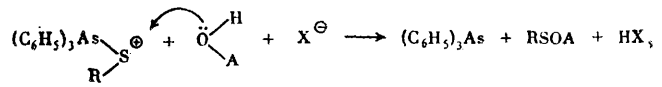
$$R_3AsS+[Alk_3O]^{\oplus}BF_4^{\ominus}\rightarrow[R_3AsSAlk]^{\oplus}BF_4^{\ominus}+Alk_2O,$$
$$R_3AsS+(CH_3)_2SO_4\rightarrow[R_3AsSCH_3]^{\oplus}CH_3SO_4^{\ominus},$$
$$R=CH_3,\ C_2H_5,\ C_3H_7,\ \text{cyclo-}C_6H_{11},\ C_6H_5;$$
$$Alk=C_2H_5,\ C_4H_9.$$

The preparation of a whole series of alkylthioarsonium halides and more stable representatives of these salts containing anions of reduced nucleophilicity was a turning point in the investigation of the features of carrying out the retro-Arbuzov reaction with tertiary arsine sulphides. The study of the structure and properties of the alkylthioarsonium salts was an important step in this investigation.[77,78] As was clarified, alkylthioarsonium salts in acetone behave as weakly associated electrolytes with fairly high specific conductivity values. This indicates their ionic structure. The action of nucleophiles depends on their nature and on the character of the environment of the arsenic atom. Thus trialkyl(alkylthio)arsonium salts are isolated unchanged after extended contact with water and alcohols at 50–60 °C. Triphenyl(alkylthio)arsonium tetrafluoroborates give triphenylarsine (70–97%) and the complexes 2 $(C_6H_5)_3AsO.HBF_4$ (40–82%) on hydrolysis and the complex $(C_6H_5)_3AsO.BF_3$ on alcoholysis.

Amines, being stronger nucleophiles, react fairly rapidly at ordinary temperatures irrespective of the environment of the arsenic atom.

$$[(C_6H_5)_3AsSC_2H_5]BF_4+(C_2H_5)_2NH\rightarrow(C_6H_5)_3As+\underset{85-89\%}{[(C_2H_5)_2NH_2]BF_4}$$
$$[(C_2H_5)_3AsSC_2H_5)Br+(C_2H_5)_3N\rightarrow\underset{90\%}{[(C_2H_5)_3NH]Br}$$

The authors considered the possibility of attack by the nucleophile at the sulphur atom

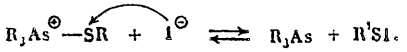


$$2RSOA\rightarrow RSSR+AOOA,$$
$$(C_6H_5)_3As+AOOA\rightarrow(C_6H_5)_3AsO+AOA,$$
if A = H, then $(C_6H_5)_3AsO+HX\rightarrow[(C_6H_5)_3AsO]_2HX.$

The notion of attack by the nucleophile at the sulphur atom is also attractive for explaining the results obtained on reacting tertiary arsine sulphides with alkyl halides.

Scheme 6

$$R_3AsS+R'I\rightarrow[R_3AsSR']^{\oplus}I^{\ominus}, \quad (1)$$



$$R'SI\rightleftharpoons[2R'S^{\cdot}+2I^{\cdot}]\rightleftharpoons R'SSR'+I_2,$$
$$R'SSR'+4RI\rightarrow2[R_3'S]^{\oplus}I^{\ominus}+I_2,$$
$$R_3As+I_2\rightarrow R_3AsI_2,$$
$$2R_3AsI_2\rightleftharpoons R_3As+[R_3AsI]^{\oplus}I_3^{\ominus},$$
$$R_3As+R'I\rightarrow[R_3R'As]^{\oplus}I^{\ominus}.$$

The proposed chain of reactions (Scheme 6) differs appreciably from the Scheme considered previously (see Section III, 2) except for stage (1) which is common..

Thus inconsistencies have been detected in relation to the interpretation of the routes of conversion of the alkylthioarsonium halides generated at the intermediate stage. In reality the results obtained indicate the conversion of the alkylthioarsonium salts to the corresponding thioesters in fairly high yield.[62–66] On the other hand the sequence of interactions proposed (Scheme 6), in which there is no place for thioesters, i.e. the route connected with the existence of the retro-Arbuzov reaction for tertiary arsine sulphides, is considered impossible.[75,76] From the point of view of one group of authors,[75,76] the main reaction products are quaternary arsonium salts $[R_3R'As]Hal$ or $[R_3R'As]Hal_3$ while the formation of such salts is not even mentioned in the communications of another group of authors.[62–66]

Nevertheless, as was clarified, the inconsistencies indicated were not differences in principle since the authors were investigating two sides of the same process. In each case attention was paid to the identification of either the liquid or the crystalline reaction proucts. In any event special investigations were necessary in order to resolve these inconsistencies.[10] It was shown by PMR spectroscopy using alkylthioarsonium tetrafluoroborates that the most probable place for nucleophilic attack in the alkylthioarsonium cation was not the sulphur atom but was the positively polarised carbon atom of the alkyl group on the arsenic.[79] In other words, the decomposition of the alkylthioarsonium salts must be effected as the second stage of the retro-Arbuzov reaction and leads to the formation of thioesters of thioarsinous acids. This posed the problem of finding a method capable of identifying the components of the complex reaction mixture containing derivatives of trivalent arsenic which are close in properties. Gas-liquid chromatography (GLC) was such a method. With the aid of GLC, the presence of esters of thioarsinous acids in the products of the reaction of tertiary arsine sulphides with alkyl halides was unequivocally confirmed and in addition one of the important properties of these esters, viz. their ability to disproportionate, was also confirmed.[80–83]

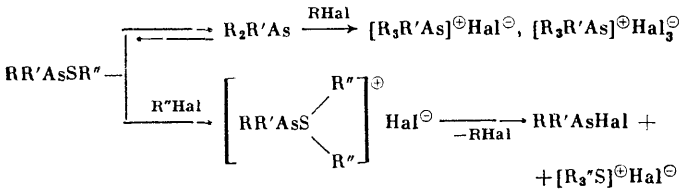
$$2RR'AsSR''\rightleftharpoons R_2R'As+R'As(SR'')_2,$$
$$3RAs(SR'')_2\rightleftharpoons R_3As+2As(SR'')_3,$$
$$R,\ R''=Alk,\ R'=C_6H_5$$

The formation of a tertiary arsine by the disproportionation of thioesters enabled the experimental data concerning the reaction of tertiary arsine sulphides with alkyl halides to be assessed in a new

way. The inconsistencies are successfully eliminated if it is assumed that the formation of the thioesters of arsinuous acids are the main course of the reaction.

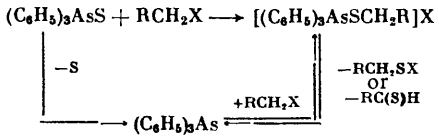
$$R_2R'AsS+R''Hal \rightarrow [R_2R'AsSR'']^{\oplus}Hal^{\ominus},$$
$$[R_2R'AsSR'']^{\oplus}Hal^{\ominus} \rightarrow RR'AsSR''+RHal.$$

Secondary processes linked with the possibility of disproportionation of the thioesters formed or with their alkylation then follow. A similar disproportionation may be the reverse process with an unfavourable position of the equilibrium. However the presence of the alkyl halide binding the tertiary arsine into an insoluble arsonium salt shifts this equilibrium to the right.



The proposed Scheme for the conversions of tertiary arsine sulphides by alkyl halides[81,82] in contrast to that put forward previously[62,76] enables a large number of features of this reaction to be understood, including the reasons for the formation of arsonium and sulphonium salts in addition to the thioesters, and also of haloarsines and tertiary arsines. At the same time this Scheme must not be considered final. In any event it is impossible to extend it to triarylarsine sulphides which do not contain a relatively readily fissile $As-C_{Alk}$ bond and consequently may not be converted into the corresponding thioesters.

It is evident that as a minimum three alternative routes of conversion must be considered in this case.



The relatively high stability of the intermediates in the retro-Arbuzov reaction involving tertiary arsine sulphides enabled a more stepwise investigation of the kinetics of this conversion.[84–86] Conductiometry was used as the method for monitoring the running concentrations of the alkylthioarsonium salts. The high sensitivity of this method enabled investigation of areas of concentration uncomplicated by the reverse reaction and by secondary conversions.

As expected the partial order of the first step proved to be close to one and its overall order close to two. A change from acetone to the more polar dimethyl sulphoxide and propan-1-ol and also replacement of ethyl bromide by the iodide leads to an increase in the reaction rate. The data obtained were interpreted from the position of an S_N2 mechanism. Comparison of these data with the results of investigations of the kinetics of the conversions of tertiary arsine oxides by alkyl halides led to the recognition of the close similarity of the nucleophilic reactivity of the oxides and sulphides.[84] This fact is particularly interesting since the basicities of these two classes of compounds differ quite appreciably.

Later an investigation was carried out of the kinetics of the second stage of the reaction using the decomposition of triethylethylthioarsonium iodide and bromide in acetone.[85,86] Processing the experimental data when calculating the overall salt concentration in the solution did not enable a conclusion to be drawn between a first or second kinetic order for the reaction. In view of the conductimetric data indicating association of the alkylthioarsonium salts in solution,[77,78] the authors proposed that not all the salt, but only the fraction present as an ion pair, is subject to decomposition under the conditions investigated. Processing the results obtained according to a kinetic equation, in which the concentration of ion pairs is expressed through the dissociation constant,[87] confirms the proposals made. It is interesting that other investigators studying the kinetics of the decomposition of alkoxyphosphonium salts are also inclined to the conclusion of the possibility of association through hydrogen bond formation.[88]

IV. Conclusion

In conclusion it may be recorded that the numerous attempts to bring about the Arbuzov reaction in esters of trivalent arsenic acids proved to be unsuccessful. Ideas on the possibility of a simple and unequivocal carrying out of the first stage of this reaction with esters of dialkyl- and alkylphenylarinous acids have not been confirmed. In spite of the difference in interpretation of the routes of forming quaternary arsonium salts as one of the products of the conversions being considered, the conclusion on the appreciable reduction of the nucleophilic reactivity of the esters of trivalent arsenic acids in comparison with their phosphorus-containing analogues undoubtedly seems more important. The reason for this lies in the characteristics of the reaction centres and the differences in character of the effect of substituents in the derivatives of phosphorus and arsenic. This, together with the reduction in strength of the E(O) and E–C (E = P, As) bonds on going from phosphorus to arsenic and the enhanced lability of the As–OR bond, strictly limits the possibility of using the Arbuzov reaction in the chemistry of organoarsenic compounds. The unusually high nucleophilic reactivity of esters of trivalent phosphorus acids singles them out among similar derivatives along the period and group and also determines the amazingly unique nature of the Arbuzov reaction.

Conversions accompanied by a reduction in the degree of coordination of the central atom proved to be more characteristic of the organic derivatives of arsenic. The possibility of effecting a retro-Arbuzov reaction among the oxides and sulphides of tertiary arsines is determined by the special features of the arsenic–heteroatom bond, by its strength, by the basicity of the initial nucleophile and by the presence in them of an $As-C_{Alk}$ bond capable of fission. The investigation of the general rules and distinctive features of these conversions and the reactions accompanying them as a function of the environment of the arsenic atom, of the nature of the electrophilic reagent and the reaction conditions, indicates the complexity of the processes taking place and the need for their further study. Inconsistencies emerging in the first stages of the investigations in this field may be connected with the fact that in a large number of studies either the liquid or the crystalline products of the reaction were examined preferentially, which could not possibly give a complete picture. Investigations in recent years have shown the possiblity of effecting a retro-Arbuzov reaction among tertiary arsine oxides containing just one alkyl group

in the environment of the arsenic atom. The isolation of byproducts from this reaction, such as haloarsines and hydroxyarsonium salts, enabled the character of the processes occurring to be linked with the environment of the arsenic atom. The more basic trialkylarsine oxides react predominantly in the direction of dehydrohalogenation of the electrophilic reactant. The retro-Arbuzov reaction occurs as a competing reaction on going to the less basic oxides of dialkylphenyl- and alkyldiphenylarsines. Due to the absence of alkyl groups capable of fission triphenylarsine oxide reacts as a base under these conditions.

The retro-Arbuzov reaction may be considered as the main process for tertiary arsine sulphides, complicated by secondary conversions of the thioesters formed. The necessary conditions for the retro-Arbuzov reaction are here the participation of a soft electrophile, alkyl halide, and the presence in the initial sulphide of at least one $As-C_{Alk}$ bond. In the case of harder chlorine-containing electophiles (hydrogen chloride, acetyl and benzoyl chlorides), chloroacetonitrile, chloromethyl methyl ether, etc.) the reaction may proceed without a change in the degree of coordination of the arsenic atom and is completed by the formation of tertiary arsine dichlorides or the products of their thermal decomposition, viz. the corresponding chloroarsines.

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Translated from *Uspekhi Khimii* **60** 2619–2632 (1991) U.D.C. 541.124:542.91:546.18:547.34

Elemental phosphorus-strong base as a system for the synthesis of organophosphorus compounds

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ABSTRACT. A systematic review is presented on the reactions of elemental phosphorus with organic compounds in the presence of base, proceeding via polyphosphide and polyphosphinite anions. Particular attention has been paid to new effective methods of activating red phosphorus by superbase complexes, formed from alkali metal hydroxides and polar, non-hydroxylic solvents (HMPA, DMSO, DMF, triethylphosphine oxide), by the sodium/liquid ammonia system, or under phase transfer catalysis. The direct phosphorylation of organic halides, activated alkenes, acetylenes and oxiranes is also discussed.

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I. Introduction

Organophosphorus compounds occupy an important place in the chemistry of elementoorganic compounds. Their influence on living organisms is well known,[1] and a wide spectrum of organophosphorus compounds has been prepared for use as extractants,[2,3] antipyretics[4,5] and emulsifiers,[6,7] as fuel additives and in lubricating materials,[8,9] as plasticizers,[10,11] and as biologically active agents for medicinal and agricultural application.[12,13] Triorganophosphines and -phosphine oxides have also been used, and are currently being developed, as effective ligands for complex metal catalysts.[10,14–16]

Organophosphorus compounds with a P–C bond are usually prepared from phosphorus halides or phosphines, which are toxic and ecologically unsuitable for industrial-scale syntheses. Furthermore, it is reported that many important organophosphorus compounds prepared from phosphorus chlorides have been threatened with liquidation because "hydrogen chloride, a by-product, corrodes steel apparatus and leads to the formation of a number of poisonous compounds in the aqueous effluent. For each ton of useful product, around six tons of effluent are produced, the refinement of which is sometimes more costly than that of the product itself".[17]

In view of this, the synthesis of organophosphorus compounds from elemental phosphorus (primarily from non-toxic and non-flammable red phosphorus) has attracted far more interest both from the point of view of the simplicity of the procedures and the fact that organophosphorus compounds can be prepared by this means in one step. The ecological advantages of this methodology also enhances the marketability of organophosphorus compounds in the difficult times which the economy faces.[17]

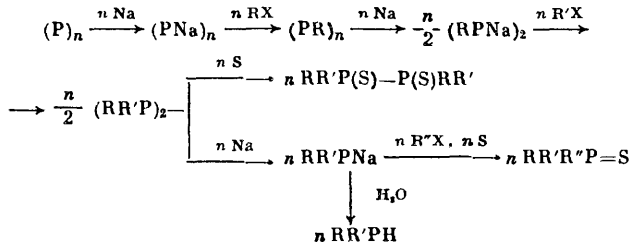
Information published prior to 1979 on the reactions of elemental phosphorus with organic compounds has been covered systematically in five short reviews.[18–22] It is pointed out in these that classical phosphorylation is normally carried out with white phosphorus at high temperatures (200–400 °C), i.e. under conditions for radical initiation.

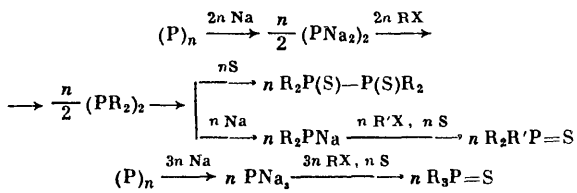
In the present review we have surveyed data on the reactions of elemental phosphorus with electrophilic agents in the presence of strong base. This relates to information published in the last 10–15 years, during which time a number of novel and effective routes to organophosphorus compounds (notably organic phosphines and phosphine oxides) have been developed. Among these new procedures for phosphorylation, much attention has been paid to syntheses with red phosphorus, which may be activated by superbases, such as Na/liquid ammonia,[23–25] alkali metal hydroxide in polar, non-hydroxylic solvent (e.g. HMPA, DMSO),[26–28] or under phase transfer catalysis.[28–30] It should be emphasised that the superbase system, KOH–DMSO (or KOH–HMPA), has already been successfully utilised for direct chalcogenation with elemental sulphur and metallic selenium or tellurium. Here, the superbasic hydroxide ion reacts with the chalcogen to generate the milder, more nucleophilic chalcogen anions, which react subsequently with suitable electrophiles (notably acetylenes).[31–33]

II. Reactions of elemental phosphorus with organic halides in superbasic systems

In 1966, Bogolyubov and Petrov published for the first time a general procedure for carrying out reactions of red phosphorus with organic halides in the presence of the classical superbasic system, Na/liquid ammonia.[23,24] This resulted in the development of new routes to organic phosphines and their derivatives. Depending on the proportion of the reactants, the process takes place with the

participation of polyphosphide anions, according to the following generalised scheme:[23]

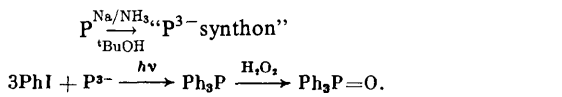




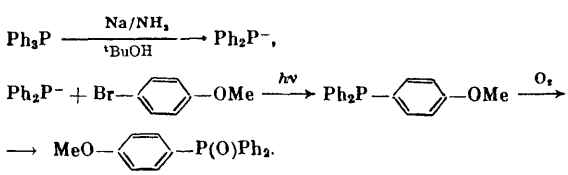
R=Me, Et, $PhCH_2$; X=Cl, Br, I.

The products are obtained in 17–34% yield.

Continuing this theme, the direct phosphorylation of aryl halides with red phosphorus was subsequently carried out with the system, Na/liquid ammonia, under UV-activation.[25] As a result, an effective route to symmetrical and unsymmetrical triarylphosphine oxides has been developed. Thus, triphenylphosphine oxide was obtained in 75% yield from iodobenzene and red phosphorus, followed by oxidation of the intermediate triphenylphosphine with hydrogen peroxide.[25]



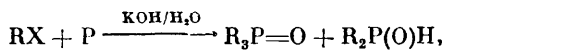
p-Anisyldiphenylphosphine oxide was prepared in 55% yield by treatment of triphenylphosphine with *p*-bromoanisole in the system, Na/liquid ammonia, under irradiation on exposure to air.[25]



The authors of this research[25] did not provide additional supporting evidence in favour of the ion-radical mechanism which they proposed. There was no reference to an earlier finding that there is a noticeable increase in the rate of the reaction of diphenylphosphide[34] and diphenylphosphinite ion[35] with aryl halides on UV-irradiation in the systems, potassium *tert*-butoxide/liquid ammonia and potassium *tert*-butoxide/DMSO.

The same authors[25] also consider that an ion-radical mechanism prevails for the reaction of aryl halides with elemental arsenic and antimony on UV-irradiation in the system, Na/liquid ammonia. The yield of triphenylarsine and triphenylstibine by this procedure was 75% and 40%, respectively. No indication was given by the authors[23–25] of the manner in which they calculated the product yield.

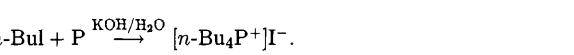
Superbases generated under phase transfer catalysis (50–60% aqueous solution with an organic solvent in the presence of a phase transfer catalyst)[36,37] have been used for the synthesis of trialkylphosphine oxides from alkyl halides and red phosphorus.[28,29,38,39] The reaction also produces a small amount of the corresponding dialkylphosphinous acid.[29]



R = Et, *n*-Pr, *n*-Bu, *n*-Am, n-C_8H_{17}; X = Cl, Br, I. (1)

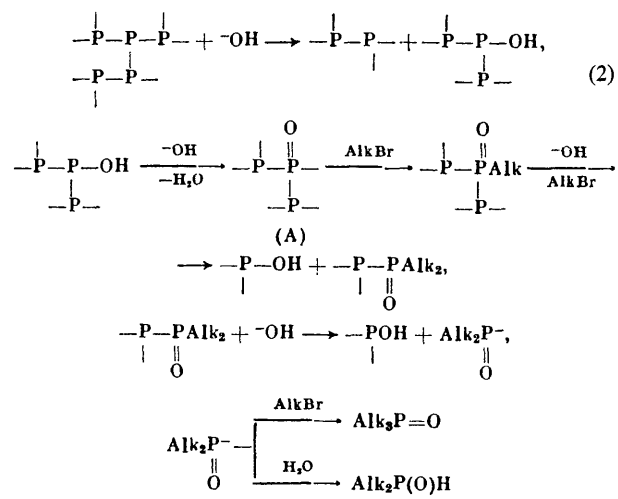
Under optimum conditions (on heating at 93–95 °C for 6–7 h with dioxane as the organic solvent), the yield of trialkylphosphine oxides was 60–65% (based on the alkyl halide).[28]

In studying the above reaction with butyl halides, it was found that butyl bromide was the most suitable substrate. The yield of tributylphosphine oxide was noticeably less with butyl chloride under the same conditions, while butyl iodide reacted with red phosphorus to give a low yield of tetrabutylphosphonium iodide.[29]



It should be stressed that tiralkylphosphines were not detected among the products of reaction (1), even on carrying out the conversion under argon.

Evidently, the interaction of alkyl bromides with the system, P–KOH–H_2O, proceeds with the participation of the polyphosphinite anion (A), formed by cleavage, with hydroxide ion, of a P–P bond of the irregular trimeric phosphorus clusters which unite the red phosphorus macromolecule.[40]



On heating benzyl chloride with red phosphorus in the system, KOH–DMSO (or KOH–HMPA), at 70–80 °C, tribenzylphosphine oxide (I) was isolated as the main product in 30% yield

(based on benzyl chloride), together with small amounts of tribenzylphosphine (II) and tetrabenzylphosphonium chloride (III).[41]

$$PhCH_2Cl + P \xrightarrow{KOH/DMSO} \underset{(I)}{(PhCH_2)_3P{=}O} + \underset{(II)}{(PhCH_2)_3P} + \underset{(III)}{[(PhCH_2)_4P^+]Cl^-}. \quad (3)$$

The process is thought to involve generation of polyphosphide ions by action of the superbase on red phosphorus, followed by reaction with benzyl chloride. This leads to tribenzylphosphine (II), which is then quaternized with a further molecule of benzyl chloride to give the phosphonium chloride (III) prior to its reaction with base to give the phosphine oxide (I). Toluene, eliminated in the final step of the reaction was identified by g.l.c.[29]

$$P_n + {}^-OH \rightarrow P_m^- + P_k{-}OH,$$

$$P_m^- + 3PhCH_2Cl \longrightarrow (PhCH_2)_3P_m \xrightarrow[-P_{m-1}]{} \underset{(II)}{(PhCH_2)_3P} \xrightarrow{PhCH_2Cl} \underset{(III)}{[(PhCH_2)_4P^+]Cl^-} \xrightarrow{KOH} [(PhCH_2)_4P^+]OH^- \xrightarrow[-PhMe]{} \underset{(I)}{(PhCH_2)_3P{=}O}.$$

Since only traces of dimethyl sulphide were detected during the course of the reaction, it can be assumed that the phosphine oxide (I) is not formed from the corresponding phosphine (II) by oxidation with DMSO.[29]

The selectivity and efficiency of conversion (3) can be increased by carrying out the reaction in the 3-phase system comprising red phosphorus, aqueous KOH, dioxane, and benzyltriethylammonium chloride at 94–96 °C. The yield of the phosphine oxide (I) under these conditions increases to 50% on complete conversion of phosphorus.[28,42]

Heating allyl halides with red phosphorus at 60–65 °C in the system, KOH–H_2O–THF containing benzyltriethylammonium chloride, affords *tris*-(*E*-propen-1-yl)phosphine oxide as well as the expected *tris*(propen-2-yl)phosphine oxide.[28,29,43,44]

$$CH_2{=}CHCH_2X + P \xrightarrow{KOH/H_2O} \underset{35\%}{(E\text{-}MeCH{=}CH)_3P{=}O} + \underset{30\%}{(CH_2{=}CHCH_2)_3P{=}O}$$

X=Cl, Br.

1,1-Dialkoxy-2-bromoethanes also serve as electrophile. Thus, heating these compounds in the system, P–KOH–DMSO, at 70–100 °C in the presence of a small amount of water provides the corresponding *tris*(2,2-dialkoxyethyl)phosphine oxide in up to 15% yield. The products are potentially useful synthons, having three protected aldehyde functions.[45]

$$(RO)_2CHCH_2Br + P \xrightarrow{KOH/H_2O} [(RO)_2CHCH_2]_3P{=}O$$

R = Et, *n*-Bu

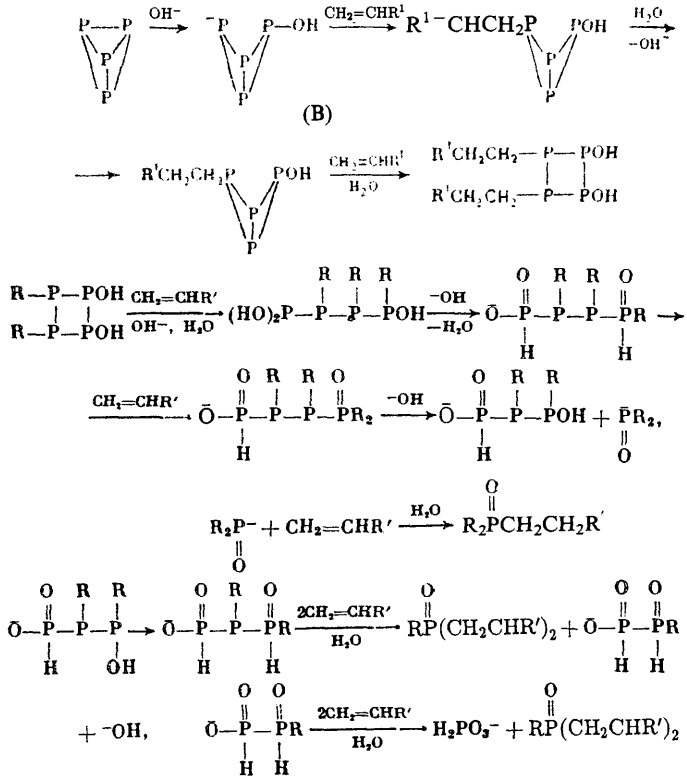
A brief reference has been made to the alkylation of red phosphorus with butyl bromine in the superbasic system, KOH–hydrazine hydrate.[46] When the molar proportion of P : KOH : BuBr is 1 : 12 : 3, reaction proceeds on heating at 80–85 °C, and is reported to lead, not only to tributylphosphine oxide, but also to a small proportion of tributylphosphine. The latter evidently forms by reduction of the phosphine oxide with hydrazine hydrate. Further products were also isolated in 8 and 1.4% yield (based on butyl bromide), but, unfortunately, these were unidentified.

III. Phosphorylation of alkenes with elemental phosphorus in the presence of base

Some interesting results have been obtained by studying the reaction of white phosphorus with acrylonitrile and acrylamide in the presence of KOH.[47] The reaction was conducted at –5 to 35 °C in a system containing an organic solvent (acetonitrile) and 10 N aqueous KOH under an inert atmosphere. The principal products of the reaction were *tris*(2-cyanoethyl)phosphine oxide and *tris*(2-carbamoylethyl)phosphine oxide, the optimum yields of which were 53 and 74%, respectively (based on phosphorus).

$$P_4 + 2KOH + 4H_2O + 9CH_2{=}CHR \rightarrow 3(RCH_2CH_2)_3P{=}O + K_2HPO_3,$$
R=CN, $CONH_2$.

In the opinion of the authors,[47] reaction is initiated by attack of hydroxide ion on the tetrahedral white phosphorus clusters to give the phosphide anion (B), which then undergoes Michael addition to the activated double bond of the starting alkene:



R=CH_2CH_2R', R'=CN or $CONH_2$.

Subsequently, the same reaction was performed with *N*-alkyl- and *N,N*-dialkyl-acrylamides to give the corresponding *N*-substituted *tris*(2-carbamoylethyl)phosphine oxides in 45–87% yield (based on phosphorus).[48]

$$P_4+2KOH+4H_2O+9CH_2=CHCONR^1R^2\rightarrow$$
$$\rightarrow 3(R^1R^2NCOCH_2CH_2)_3P=O+K_2HPO_3,$$
$$R^1=Me,\ R^2=H\ (45\%);\ R^1=R^2=Et\ (87\%);$$
$$R^1=R^2=CH_2CH=CH_2\ (72\%);\ R^1-R^2=(CH_2)_4\ (75\%);$$
$$R^1-R^2=(CH_2)_5\ (84\%).$$

Vinyldiorganophosphine oxides and sulphides,[48] and dialkyl vinylphosphonates,[49] also undergo Michael addition with phosphide ions (generated from yellow phosphorus and KOH) under mild conditions (25–30 °C) to give the corresponding functionalised phosphine oxide (in 50–100% yield).

$$P_4+KOH+H_2O\xrightarrow{R_2P(X)CH=CH_2}[R_2P(X)CH_2CH_2]_3P=O$$
$$\xrightarrow{(AlkO)_2P(O)CH=CH_2}[(AlkO)_2P(O)CH_2CH_2]_3P=O$$
$$R=Alk,\ Ar;\ X=O,\ S.$$

Recently, it was found that styrene and 4-vinylpyridine may also be phosphorylated with red phosphorus in the system, KOH–DMSO or KOH–HMPA.[50,51] Thus, the phosphorylation of styrene at 75–125 °C affords *tris*(2-phenylethyl)phosphine oxide (IV) in 65% yield (based on styrene) together with a small amount of *bis*(2-phenylethyl)phosohinous acid (V).[28,50]

$$P+PhCH=CH_2\xrightarrow[KOH/DMSO/H_2O]{KOH/HMPA/H_2O}\underset{(IV)}{(PhCH_2CH_2)_3P=O}+$$
$$+\ \underset{(V)}{(PhCH_2CH_2)_2P(O)H}. \qquad (4)$$

For the above reaction, the system, KOH–HMPA–H_2O, is somewhat more effective than the system, KOH–DMSO–H_2O. However, the base generated in the system, 70% aqueous KOH–dioxane– benzyltriethylammonium chloride, is not strong enough to activate the process, only traces of (IV) being detected. Neither the standard radical initiator, azodiisobutyronitrile, nor the radical quencher, hydroquinone, have any effect on the reaction. Evidently, a polyphosphinite anion is involved in the formation of (IV) and (V), i.e. the reaction takes place in the same manner as the previously described phosphorylation of alkyl halides, as outlined in scheme (2).[29]

4-Vinylpyridine reactions in the same way with red (or white) phosphorus in the system, KOH–DMSO–H_2O, leading to *tris*-[2-(4-pyridyl)ethyl]phopshine oxide in 20% yield.[51]



In spite of the lowish yields, the method described above is of preparative value since, at present, there are no other available routes to functionalised phosphine oxides, which are key synthetic intermediates and synthons.

IV. The interaction of elemental phosphorus with alkynes in the presence of superbase

By studying the reactions of phenylacetylene, it was shown for the first time that red phosphorus interacts with acetylenes on heating (at 60–90 °C) in the system, alkali metal hydroxide-polar (non-hydroxylic) solvent (HMPA, DMSO, DMF, Et_3PO), as well as under phase transfer catalysis (aqueous alkali metal hydroxide-organic solvent-phase transfer catalyst). Thus, phenylacetylene affords *tris*(*Z*-styryl)phosphine (VI) in up to 44% yield (based on the alkyne) together with a small amount of *tris*(*Z*-styryl)phosphine oxide (VIII).[26–28,39,44,52–58]

$$PhC\equiv CH+P\xrightarrow{KOH/H_2O}\underset{(VI)}{(Z\text{-}PhCH=CH)_3P}+$$
$$+\ \underset{(VII)}{(Z\text{-}PhCH=CH)_3P=O}.$$

Evidently, reaction involves attack of the triple bond by polyphosphide anion, P_m^- generated from red phosphorus and the superbase.[28]

$$P_n+{}^-OH\rightarrow P_nOH+P_m^-,$$
$$P_m^-+HC\equiv CPh\longrightarrow P_mCH=\bar{C}Ph\xrightarrow[-OH^-]{H_2O}P_mCH=CHPh\xrightarrow[-P_kOH]{-OH}$$
$$\longrightarrow PhCH=CHP_g^-\xrightarrow[H_2O]{PhC\equiv CH}(PhCH=CH)_2P_g\xrightarrow[-P_hOH]{OH^-}$$
$$\longrightarrow (PhCH=CH)_2P_e^-\ \text{etc.}$$

According to ^1H and ^{31}P NMR spectroscopic data, all the styryl groups in (VI) and (VII) are in the *Z*-configuration, i.e. of the four possible stereoisomers, only the *Z,Z,Z*-isomer is formed. This would be anticipated as *trans*-nucleophilic addition to triple bonds in the norm.[28]

For the phosphorylation of phenylacetylene, the 2-phase systems, KOH–DMSO, KOH–Et_3PO and KOH–DMF, and the 3-phase system comprising red phosphorus, 50–70% aqueous KOH and an organic solvent (THF, toluene, dioxane), with or without benzyltriethylammonium chloride,[28] are less effective than the system, KOH–HMPA. Replacement of KOH by NaOH under the same conditions leads to a clear (3-fold) decrease in the yield of (VI).

At the same time, the activity of red phosphorus towards phenylacetylene is enhanced on ultrasonic irradiation in the presence of a strong base. Under these conditions, reaction takes place without external heating, and the yield of (VI) is increased by 50% while the reaction time is reduced to 1 h.[52]

The reaction of phenylacetylene with red phosphorus proceeds equally well under inert atmosphere and on exposure to air. The yield of the phosphine oxide (VII) is always around 2–4%.[28]

Naturally, the question arises: why is it that phenylacetylene affords the corresponding phosphine (VI) almost exclusively, while, under the same conditions, styrene and 4-vinylpyridine afford predominantly the corresponding phosphine oxide? In the original publications,[26,28,50,51] there was no comment on this anomaly. One possible explanation is the competing behaviour of the two different types of P-nucleophile (i.e. the polyphosphide and polyphosphinite anions). With alkynes, the polyphosphide anion is more complementary (according to the principle of hard and soft acid and

base), while the polyphosphinite anion (A) is more complementary with alkenes.

More recently, phosphorylation of acetylene with red phosphorus was carried out under pressure at 105–115 °C in the system, KOH–hydrazine hydrate–aqueous HMPA.[46] Trivinylphosphine was identified in the reaction product by chromato-mass spectrometry. A 10% yield was quoted, but the method by which the yield was calculated was not given. It was not possible to isolate the product nor characterise it further.[46]

V. Reactions of elemental phosphorus with oxygen- and sulphur-containing compounds in the presence of base

By studying the reactions of α-aminoalcohols, Maier was first to demonstrate that white phosphorus reacts with such compounds by an ionic mechanism via intermediate formation of polyphosphide and polyphosphinite ions.[59,60] Almost equal amounts of the corresponding *tris*(dialkylaminomethyl)phosphine oxide (VIII), *bis*(dialkylaminomethyl)phosphinic acid (IX), and dialkylaminomethylphosphonic acid (X) were obtained in a total yield of 90% (based on phosphorus).

$$2P_4+20R_2NCH_2OH \rightarrow 5(R_2NCH_2)_3P{=}O+$$
(VIII)
$$+2(R_2NCH_2)_2P(O)OH+R_2NCH_2P(O)(OH)_2+8H_2O.$$
(IX) (X)

$R_2N = Me_2N$, Et_2N, C_4H_8N, $C_5H_{10}N$, $CH_2CH_2OCH_2CH_2N$, $(n\text{-Bu})_2N$, $(cyclo\text{-}C_5H_{11})_2N$.

It was not possible to carry out this reaction with red phosphorus.[60]

Later, a series of publications appeared on the interaction of white phosphorus with alcohols and alkali metal alkoxides in carbon tetrachloride at 50–60 °C under N_2, leading to the formation of trialkyl phosphites as the main product (in 70–80% yield), together with small amounts of trialkyl phosphates and dialkyl alkanephosphonates (in up to 10% yield).[61–66]

$$P_4+ROH+ROM+CCl_4 \rightarrow (RO)_3P+(RO)_3P{=}O+(RO)_2P(O)R,$$
M – alkali metal, R = Alk.

This reaction involves initial nucleophilic attack of the P–P bond of the phosphorus cluster with alkoxide, as proposed by Brown, et al.[66]

$$P_4+6RO^-+6ROH+6CCl_4 \rightarrow 4(RO)_3P+6CHCl_3+6Cl^-.$$

The reaction of white phosphorus with sodium alkylmercaptides in the presence of the corresponding mercaptan and an excess of CCl_4 proceeds in a similar way at room temperature. Trialkyl trithiophosphites were thus obtained in high yield.[67,68]

$$P_4+6RSH+6RSNa+6CCl_4 \rightarrow 4(RS)_3P+6CHCl_3+6NaCl,$$
R = Et, *n*-Bu.

The corresponding dialkyl disulphides and *tris*(alkylthio)methanes were formed as by-products.

The reaction of white phosphorus with alkali metal phenoxide and CCl_4 in an aprotic dipolar solvent (DMF at 0–100 °C under a dry, inert atmosphere) leads to a mixture of organophosphorus compounds, of which the main component is triphenyl phosphite (70% yield).[69]

$$P_4+PhOM+PhOH+CCl_4 \rightarrow (PhO)_3P+ClCH_2P(OPh)_2+$$
$$+Cl_2CHP(OPh)_2+[(PhO)_2P]_2CH_2,$$
M – alkali metal.

Recently, Ivanov, et al. extended this reaction to other phenols (in the presence of the corresponding phenoxide), and found that the composition and yield of product depends on the acidity of the phenol and the nature of the ring substituent.[70] Phenols with a pK_a in the range 9–11 participate in this reaction.

A number of patents has appeared on the reaction of phosphorus (white or yellow) with alcohols and epoxy compounds in the presence of a catalyst (alkali or alkaline earth hydroxide or alkoxide) at 25–200 °C.[71–76] The products of the reaction have P–H, P–C and P–O linkages in varying proportion, the molecular formula approximating to $(RO)_{3-n}PR'_n$ (where R is an alkyl radical from the alcohol, and R′ = H or a ZOH residue, where Z represents an alkylidene (–C–C–) residue formed by cleavage of the epoxide). These products are potentially useful for the preparation of surface-active compounds and as epoxy resin hardeners.

White phosphorus reacts with alkene oxides in the presence of compounds with an acidic hydrogen and metal alkoxides (or amides) to give phosphorus-containing polyols.[77–79] This reaction was studied in more detail by Ivanov, et al.,[80] who found that a mixture of P_4, propylene oxide, Me_3N and HX (HX = $MeCO_2H$, PhOH, MeC_6H_4OH, H_2O, ^{t}BuOH) in 1 : 5 : 0.8 : 1 proportion leads to the formation of oligomers containing the fragment C–C–P(O)–O as repeating unit.

By studying the reactions of propylene oxide and [2-(vinyloxy)-ethoxy]methyloxirane, it was shown for the first time that epoxides may react with the less toxic, and more convenient, red phosphorus. Phosphorylation proceeds effectively in the 3-phase system comprising red phosphorus, 50% aqueous KOH and an organic solvent (dioxane, toluene or THF) in the presence of benzyltriethylammonium chloride at 60–93 °C. The resulting phosphorus-containing polyols were shown to have structures (XI–XIV) from ^{31}P NMR and IR spectroscopic data, and by elemental analysis.[81,82]

$$P + R^1\text{–}\underset{O}{\text{CH}}\text{–}\text{CH}_2 \rightarrow R^2_{3-n}P(O)[(CH_2CHO)_mH]_n \quad (5)$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad R^1$$
(XI)–(XIV)

(XI): R^1 = Me, R^2 = H, n = 2, m = 3;

(XII): R^1 = Me, R^2 = OK, n = 2, m = 4;

(XIII): $R^1 = CH_2{=}CHO(CH_2)_2OCH_2$, R^2 = OK, n = 2, m = 1;

(XIV): $R^1 = CH_2{=}CHO(CH_2)_2OCH_2$, R^2 = OK, n = 1, m = 4.

As seen with the formation of (XIII) and (XIV), the vinyloxy group remains intact, which further supports the anionic (nucleophilic) character of the reaction.[81] Our finding that butyl vinyl ether remains inert to the above phosphorylation is consistent with this view.

VI. Reactions of elemental phosphorus with organometallic compounds

Carbanions of certain organometallic compounds may also be used to generate polyphosphide anions from elemental phosphorus.[83–91] This was first demonstrated by Rauhut, et al., who studied the interaction of white phosphorus with phenylmagnesium bromide or phenyllithium at 25–40 °C in diethyl ether or THF, followed by treatment with water.[83] Among the products of the reaction, the following were identified: phenylphosphine (in 40% yield based on the conversion of phosphorus); small amounts of diphenyl- and triphenyl-phosphine; and organopolyphosphines, being insoluble, amorphous compounds with a yellow colouration.[83]

$$P_4 \xrightarrow{\text{PhMgBr, PhLi}} \xrightarrow{H_2O} PhPH_2 + Ph_2PH + Ph_3P + Ph_mH_{3-m}P_n,$$

$m=1-3$.

Later, Kaabak, et al. discovered suitable conditions (240–250 °C) for increasing the selectivity and efficiency of this reaction.[84] Thus, triarylphosphines were obtained in 70–83% yield (based on phosphorus) from white phosphorus and arylmagnesium iodides.[84]

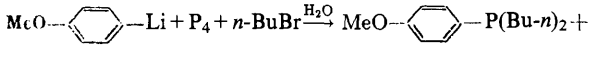
$$P_4 + RMgI \xrightarrow{H_2O} R_3P,$$
$$R=Ph,\ 4\text{-}MeC_6H_4.$$

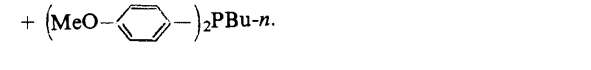
The same authors developed a method of preparing *tris*(*sec*-alkyl)phosphine oxides (in 57–82% yield) by heating white phosphorus with *sec*-alkyl halides and Mg (or Zn) at 120–210 °C, followed by treatment of the mixture with base at 270 °C.[85]

Unsymmetrical tertiary phosphines may be obtained under mild conditions (20–50 °C in an inert organic solvent) by the simultaneous treatment of white phosphorus with an organometallic compound and an alkyl halides.[86,87] The main products from the reaction of white phosphorus with butyl halide and phenyl-lithium or -sodium are dibutylphenyl- and butyldiphenyl-phosphine, obtained in 20–44% yield (based on phosphorus).[86] In certain instances, small amounts (8–11%) of butyldiphenylphosphine oxide were also detected.[86]

$$PhM + P4 + n\text{-}BuHal \xrightarrow{H_2O} PhP(Bu\text{-}n)_2 + Ph_2PBu\text{-}n +$$
$$+\ Ph_2P(O)Bu\text{-}n,$$
$$M=Li, Na;\quad Hal=Cl, Br.$$

The reaction of white phosphorus with 4-methoxyphenyllithium and butyl bromide proceeds in a similar way, though less efficiently, to give dibutyl(4-methoxyphenyl)phosphine and butyl-*bis*(4-methoxyphenyl)phosphine (in 15 and 20% yield, respectively).[87]

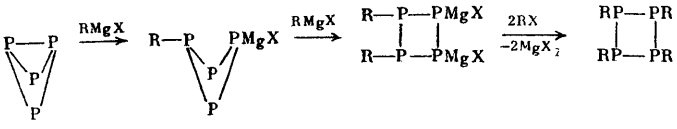




At the same time, it was found that only trace amounts of the expected di- and tri-butylphosphine were formed by using butylmagnesium bromide as the organometallic compound. The main product of this reaction was tetrabutylcyclotetraphosphine (42% yield).[86]

$$P_4 + 2n\text{-}BuMgBr + 2n\text{-}BuBr \rightarrow \begin{matrix} n\text{-}BuP-PBu\text{-}n \\ | \quad | \\ n\text{-}BuP-PBu\text{-}n \end{matrix}$$

The authors consider that the reaction proceeds as follows:[86]



R = Alk.

Later, it was shown that other tetraalkylcyclotetraphosphines, e.g. $(EtP)_4$ and $(n\text{-}PrP)_4$, were obtainable by this route.[87]

However, the reaction of white phosphorus with isopropylmagnesium bromide or cyclohexylmagnesium bromide and the corresponding alkyl bromide proceeds by a quite different pathway, leading to products of composition R_2P_8 (R = isopropyl, cyclohexyl).[88]

Comparatively recently, unambiguous evidence was provided for the formation of polyphosphide ions from white phosphorus and methyllithium. Thus, organopolyphosphines (XV–XVII) were obtained by quenching intermediate polyphosphide ions with trimethylsilyl chloride or methyl bromide.[89]

$$P_4 + LiMe \rightarrow Li_3P_7 + Li_2P_7Me + LiP_7Me_2 \rightarrow$$

$$\xrightarrow{Me_3SiCl} P_7(SiMe_3)_3 + P_7(SiMe_3)_2Me$$
(XV) (XVI)

$$\xrightarrow{MeBr} P_7Me_3$$
(XVII)

Alkali metal pentaphosphides were also obtained by interaction of white phosphorus with Na (or Li) in diglyme or THF in the presence of a phase transfer catalyst (18-crown-6).[90]

References have been given in the patent literature to the formation of lithium aminophosphides, (XVIII) and (XIX), by heating white phosphorus with butyllithium and dialkylamines in benzene.[91,92] The two products were

$$P_4 + n\text{-}BuLi + R_2NH \rightarrow R_2NPLi_2 + (R_2N)_2PLi,$$
(XVIII) (XIX)
$$R=Me,\ Et.$$

obtained in quantitative yield.

Attempts to carry out the reaction of organometallic compounds (methylmagnesium iodide and diethylzinc) with red phosphorus met with failure.[40]

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Simple, convenient, and efficient routes to triorganophosphines and -phosphine oxides (including unsaturated derivatives) have been developed, based on the novel activation of red phosphorus by multi-phase superbasic systems (e.g. KOH–HMPA, KOH–DMSO, 50–70% aqueous KOH–organic solvent–phase transfer catalyst).[9,26–30,41–45,50–58,81] This method is currently being developed broadly. In particular, technological aspects of these processes are being improved, and the search continues for suitable electrophiles for redox phosphorylation with red phosphorus.

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Translated from *Uspekhi Khimii* **60** 2633–2662 (1991) U.D.C. 547.822.3:547.514:547.78:547.811:547.818

Synthesis of spiro[piperidine-4,C'_n-hetero(carbo)cycles]

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ABSTRACT. **A systemic survey is presented on methods of preparing *N*-containing spiroheterocycles in which a piperidine ring is spiro-condensed at the four position with various carbocycles and heterocycles. The biological properties of these compounds is also discussed.**

The bibliography contains 250 references.

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I. Introduction

In recent years much attention has been focussed on methods of preparing spiroheterocycles, in particular spiro-N-heterocycles, and studying their biological activity. This was intensified after the isolation of the biogenic amine, histrionicotoxin, from the skin of the tree frog, *Dendrobates histrionicus*.[1] This amine is a derivative of 1-azaspiro[5.5]undecan-8-ol, having highly unsaturated groups at the 2- and 7-positions, the structure and absolute configuration of which has been established by X-ray analysis. Subsequently, more than ten other 1-azaspiro[5.5]undecanes having a variety of unsaturated functions at the same ring positions were isolated from the genus *Dendrobates*.[2–5] In view of the biological significance of histrionicotoxin (which blocks the transmission of nervous impulses following activation by acetylcholine[1,6,7]), and because it is difficult to isolate in large amounts from the tree frog, much research has been devoted to the chemical synthesis of histrionicotoxin and variously hydrogenated derivatives.

Racemic octahydrohistrionicotoxin has been prepared by several routes, but, at the present time, no total synthesis of histrionicotoxin itself has been reported, primarily because of the lability of the unsaturated residues. A review published in 1982[8] covers this aspect, but since this time new data has been published, largely in connection with stereoselective and non-stereoselective routes to variously hydrogenated histrionicotoxin derivatives.[9,10] A further impetus to research in this field came with the discovery that the biological activity of histrionicotoxin is not entirely associated with the unsaturated functions in the side chain. For example, perhydrohistrionicotoxin—2-amyl-7-butyl-1-azaspiro[5.5]undecan-8-ol—has a biological activity very similar to that of histrionicotoxin. The development of non-stereoselective and stereoselective routes to 1-azaspiro[5.5]undecanes has already born fruit.[11–25]

At the beginning of the 1980's, Yunusov, et al. isolated the alkaloids, nitramine, isonitramine and sibirine, from *Nitraria schoberi, Nitraria sibirica* and *Nitraria sibirica Pall*, respectively.[26,27] These compounds were shown to have the 2-azaspiro[5.5]undecane skeleton, the first two having an asymmetric centre at C_7. Although the biological properties of these alkaloids are unknown, much work has been published on their non-stereoselective and stereoselective synthesis.[28–34]

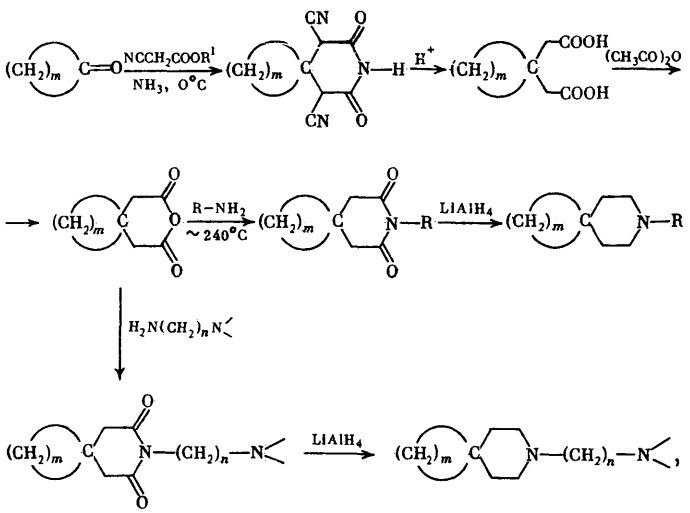
Spirocycles without a nitrogen atom have also been isolated from plants and living organisms. Thus, the components of the pheromone complex from the olive fly, *Dacus olfae*, have the 1,7-dioxaspiro[5.5]undecane skeleton.[35] Although few spiro compounds have been isolated from nature, there is sufficient evidence that spiroheterocycles perform key biological functions. It is for this reason that much research has been devoted both to the synthesis of analogues of spiro-fused alkaloids and biogenic amines, and to methods of preparing new spiroheterocyclic bases. Such compounds possess a wide spectrum of biological activity, and certain derivatives have been used medicinally, notably as pyschotropic drugs.[36–38]

The volume of literature on the synthesis of spiroheterocycles and the study of their chemistry and biological activity is so large that it would be impossible to digest in one review. The present review covers the methods of preparing, and the biological activity, of nitrogen-containing spiroheterocycles in which a piperidine ring is spiro-fused at the 4-position with a variety of carbo- and heterocycles. However, there has been no attempt to present an all-embracing review of the literature. Rather, the objective has been to highlight the problems which chemists have experienced in the synthesis of such compounds as potential drugs.

II. Spiro-*N*-heterocycles in which a piperidine ring is spiro-condensed at the four position with carbo- and heterocycles

It was in the 1960's that research into the synthesis and biological activity of spirocycles, such as azaspiranes, commenced. 1,1-Bis-(carboxymethyl)-carbocycles and -heterocycles were the key intermediates used for the preparation of azaspiranes in which a piperidine ring is spiro-fused at the 4-position by various carbo- and heterocycles. The well-established route to such intermediates involves interaction of a ketone with ethyl cyanoacetate under mild conditions in ammonia-saturated ethanol to give the corresponding Guareschi's imide, subsequent hydrolysis of which affords the desired *gem*-disubstituted diacetic acid.[39] The latter are then

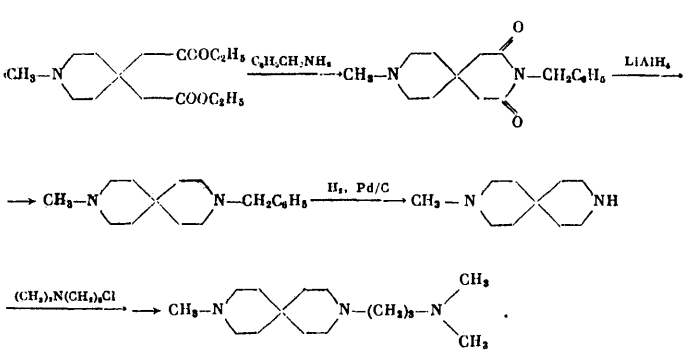
converted to the corresponding cyclic anhydride spiro-fused with a variety of carbo- and heterocycles, and subsequent treatment with a whole range of amines or diamines yields the corresponding imide in reasonably high yield. These undergo hydride reduction, as shown below.[40–57]



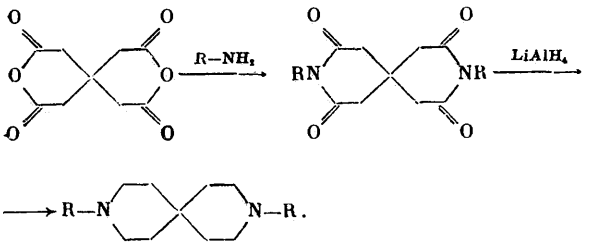
R = H, alky, isoalkyl, aryl; n = 2, 3; m = 2–7.

Depending on the nature of the substituent on the piperidine nitrogen and the nature of the ring fused at C_4, the resulting 3-azaspiranes and their salts display a variety of biological activities. The compounds act on the central nervous system,[40–43,46–49,55,57] possess analgesic,[41] antihypertensive,[41–43,45–47] antihistamine,[48] antimicrobial and antibacterial activity,[40,41] and suppress the growth of tumour cells.[52–54] In certain instances, the intermediate 3-azaspirane-2,4-diones were submitted to biological tests and shown to have both antimicrobial[58,59] and, notably, psychotropic activity.[60–63]

The above-described 3-azaspirane synthesis is also applicable to 1-methyl-4-piperidone as the cyclic ketone, so that it is possible to prepare diazaspiranes having two piperidine rings spiro-fused at the 4-position. The intermediate 1-methylpiperidine-4,4-diacetic acid was converted to the diethyl ester (rather than the cyclic anhydride), which reacted with benzylamine to give the corresponding imine; hydride reduction of the latter then gave the desired 3-benzyl-9-methyl-3,9-diazaspiro[5.5]undecane, as shown below. Cleavage of the *N*-benzyl group was effected by hydrogenation over palladium-on-carbon, and the resulting secondary amino function was further alkylated to give, for example, the γ-(dimethylamine)propyl derivative as a useful intermediate for the preparation of pharmacologically active agents.[64,65]

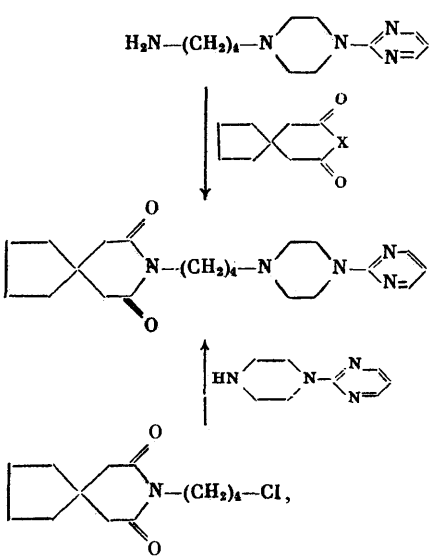


In an alternative synthesis of 3,9-diazaspiranes, methanetetraacetic acid was converted to its spirocyclic bisanhydride, which afforded the desired product on treatment with primary amine followed by hydride reduction.[64]



The main advantage of the previous route over this alternative procedure is that the resulting diazaspiranes may have different substituents on the two nitrogen atoms.

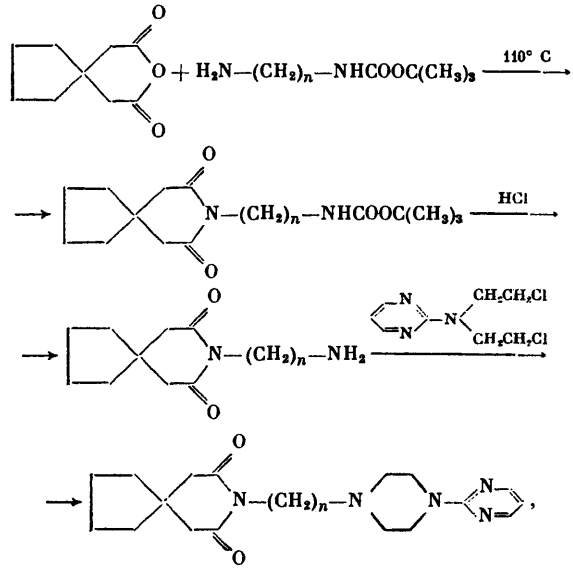
One of the 3-azaspiranes obtained by the first method is 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione, which displays neuroleptic properties and is used medicinally under the name buspirone.[66] In one synthesis of this drug, 3,3-tetramethyleneglutaric anhydride is converted to the corresponding imide with 1-(4-aminobutyl)-4-(2-pyrimidinyl)piperazine in pyridine; alternatively, it can be prepared by interaction of *N*-(4-chlorobutyl)-3,3-tetramethyleneglutarimide with *N*-(2-pyrimidinyl)piperazine in butanol.[67,68]



X=O, NH.

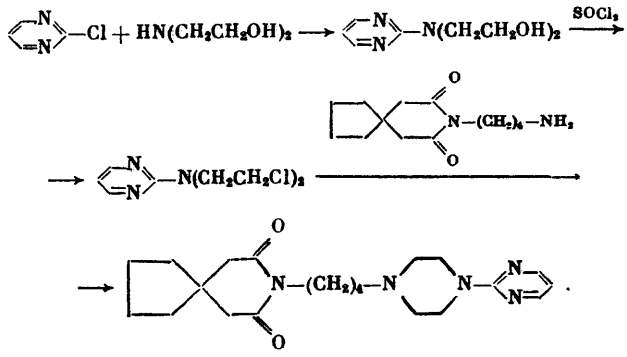
In recent years, a variety of methods has been used for the synthesis of buspirone and its analogues. Thus, treatment of 3,3-tetramethyleneglutaric anhydride with *tert*-butyl *N*-(ω-aminoalkyl)carbamates affords the corresponding imides, which undergo

selective hydrolysis to the corresponding *N*-ω(aminoalkyl)-3,3-tetramethyleneglutarimides. Interaction of the latter with 2-[*bis*(2-chloroethyl)amino]pyrimidine gives buspirone and its analogues in high yield, according to the following scheme.[69]



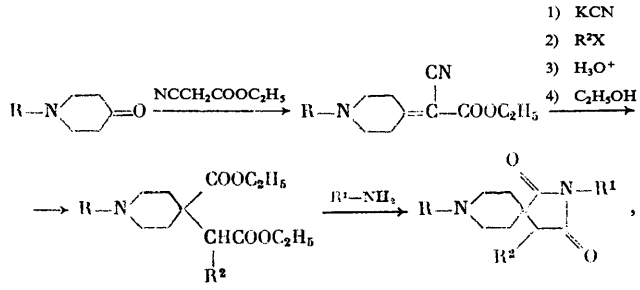
$n = 2-5$.

Buspirone was also obtained by the route shown below. Thus, 2-chloropyrimidine interacts with diethanolamine to give *N*-(2-pyrimidinyl)diethanolamine, which is converted to the corresponding bis(2-chloroethyl)amine with thionyl chloride. Subsequent condensation with *N*-(ω-aminobutyl)-3,3-tetramethyleneglutarimide affords the desired compound in high yield.[70]



Other routes to buspirone,[71–73] its precursors,[74] and novel analogues[75–78] have been reported. For diagnostic purposes, a buspirone derivative having a dideuteriated piperazine ring has also been prepared.[79]

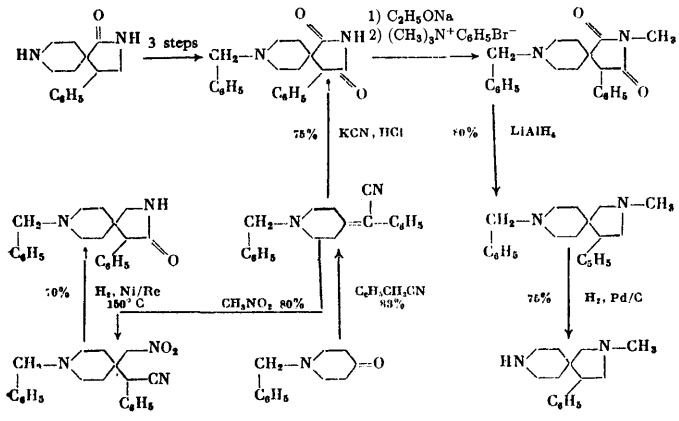
The Knoevenagel reaction has been applied in a useful synthesis of azaspiranes in which a piperidine ring is spiro-fused at the 4-position with a succinimide ring. The latter may have a variety of substituents in the 2- and 4-positions. Thus, 4-piperidones condense with ethyl cyanoacetate to give the Knoevenagel product, which undergoes Michael addition with HCN to give the corresponding dicyanoester; hydrolysis of the latter, followed by decarboxylation and esterification affords the corresponding *gem*-disubstituted diethyl succinate, which reacts with primary amines to give the desired 2-substituted 2,8-diazaspiro[4.5]decanes.[80–87] The same authors have also prepared spirosuccinimides with substituents in both the 2- and 4-position. This was achieved by hydrolysing the dicyanoesters, and then α-alkylating (or α-arylating) with various alkyl (or aryl) halides prior to succinimide ring closure.[81]



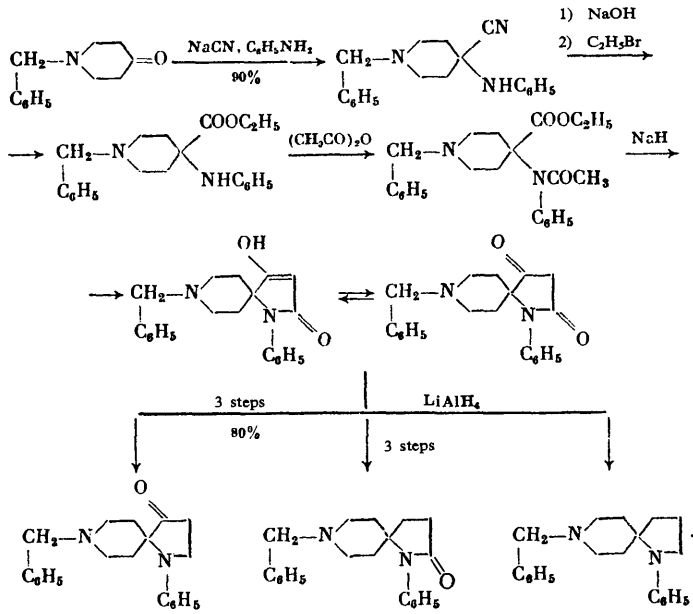
R = H, alkyl, isoalkyl, phenyl, benzyl, phenylethyl, allyl, benzoylethyl; R^1 = H, alkyl, isoalkyl, allyl, phenyl, benzyl, phenylethyl; R^2 = H, alkyl, isoalkyl, aryl, allyl.

Having prepared *N*-benzylpiperidine derivatives by this route, the benzyl group may then be readily cleaved by standard methods to give the corresponding *N*-unsubstituted derivatives; the latter may then be *N*-alkylated to give compounds with potential pharmacological activity. Thus, alkylation with 3-chloropropyl *p*-fluorobenzoate affords an azaspirosuccinimide with neuroleptic activity.[82,83]

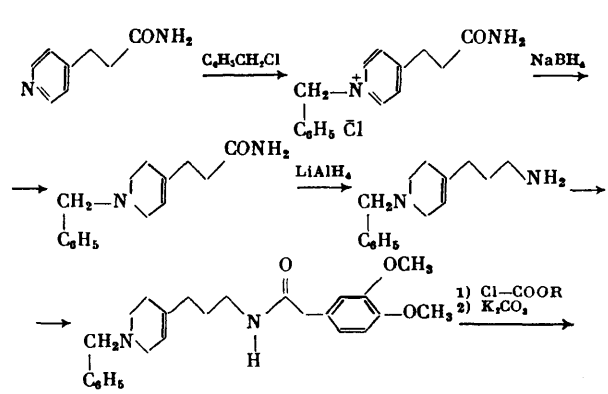
In a modification of the above 2,8-diazaspiro[4.5]decane synthesis, it is also possible to prepare azaspiranes with a phenyl group. Thus, Knoevenagel condensation of *N*-benzyl-4-piperidone with phenylacetonitrile, followed by addition of HCN leads to the corresponding dinitrile by Michael addition; without isolation, this is cylised with HCl to give 4-phenyl-8-benzyl-2,8-diazaspiro[4.5]decane-2,4-dione, which is partially or completely reduced to give 4-phenyl-8-benzyl-2,8-diazaspiro[4.5]decane or the corresponding 1-oxo- and 3-oxo-derivatives.[88] The latter may also be prepared by addition of nitromethane to α-[*N*-benzylpiperidin-4-ylidene]benzyl cyanide, followed by hydrogenation over Raney nickel under pressure.[88] These conversions are shown below.

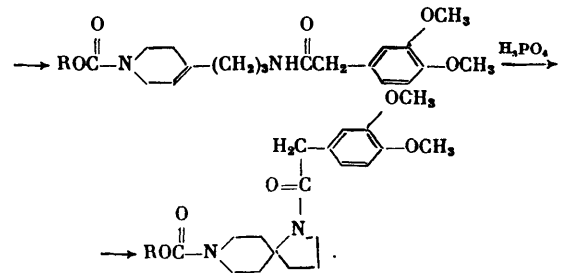


1,8-Diazaspiro[4.5]decanes have also been synthesised from *N*-benzyl-4-piperidone. Thus, treatment of the latter under Strecker conditions affords 1-benzyl-4-cyano-4-anilinopiperidine, from which the corresponding α-anilinocarboxylic acid ethyl ester is obtained and then *N*-acetylated with acetic anhydride. Subsequent intramolecular Dieckmann cyclisation provides *N*-benzyl-1-phenyl-1,8-diazaspiro[4.5]decane-2,4-dione (in 45% yield), which is completely or partially reduced to 8-benzyl-1-phenyl-1,8-diazaspiro-[4.5]decane or the 2-oxo- and 4-oxo-derivatives, as shown below.[89]

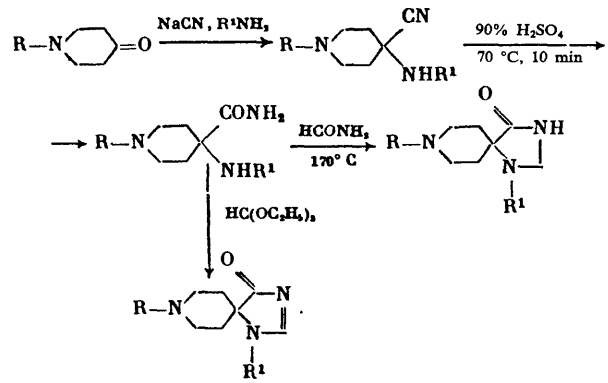


Alternatively, the 1,8-diazaspiro[4.5]decane ring can be prepared from 4-(2-carbamylethyl)pyridine. Thus, treatment of the latter with benzyl chloride affords the corresponding *N*-benzylpyridinium salt, which undergoes sequential reduction, first with $NaBH_4$ to give 1-benzyl-1,2,3,6-tetrahydro-β-(4-pyridyl)propionamide, reduction of which with $LiAlH_4$ affords the corresponding 3-substituted propylamine. Condensation of the latter with 3,4-dimethoxyphenylacetic acid gives the corresponding amide (in 70% yield), which, in the key step, is converted to the *N*-carbalkoxy derivative by treatment with chloroformic acid ester. Cyclisation with 80% phosphoric acid then provides the desired 1,8-diazaspiro-[4.5]decane.[90]



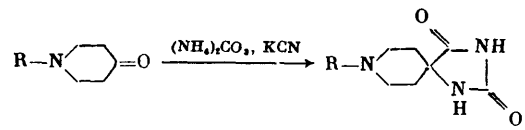


In an extension of these routes, biologically active 1,3,8-triazaspiro[4.5]decanes have also been prepared from 4-piperidones. The synthesis involves Strecker conversion to the corresponding α-aminonitriles, followed by hydrolysis to the corresponding amides and cyclisation of the latter with formamide or ethyl orthoformate.[91,92]

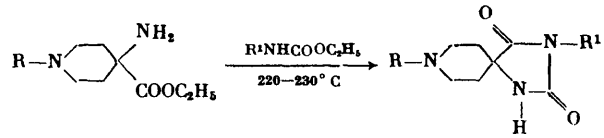


A large number of 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-ones have been prepared by this route by varying the substituent on the piperidine nitrogen atom. These have been shown to possess neuroleptic,[93–95] tranquilizing,[96–98] analgesic,[97–101] sedative,[100,105] hypotensive, and antiinflammatory[97] activities, and, furthermore, are apomorphine antagonists and CNS depressants.[102–104] One of these compounds—8-[3-(4-fluorobenzoyl)propyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one—is a neuroleptic drug used medicinally under the name 'spiperone'.[106] Labelled spiperone derivatives having an isotopic carbon, fluorine, iodine or bromine atom have also been prepared for diagnostic purposes.[107–114]

The 1,3,8-triazaspirane skeleton also incorporates spiro[piperidine-4,5′-hydantoins], obtained in high yield by interaction of 4-piperidones with a mixture of KCN and ammonium carbonate.[115–120]



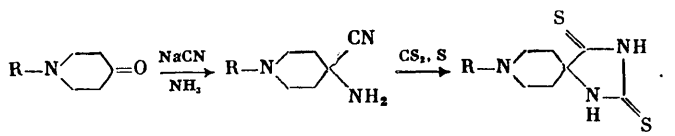
Such spirohydantoins are also obtainable by condensing 4-amino-4-ethoxycarbonylpiperidines with *N*-substituted carbamates.[121,122]



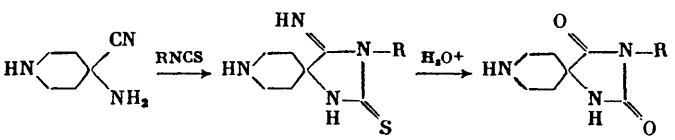
R = phenyl, benzyl; R^1 = alkyl, cyclohexyl, phenyl.

Spirohydantoins possess analgesic, antispasmolytic and antiinflammatory activities.

Antiinflammatory 1,3,8-triazaspiro[4.5]decane-2,4-dithiones are obtained from 4-piperidones via Strecker synthesis, followed by treatment of the resulting α-aminonitriles with carbon disulphide.[123]

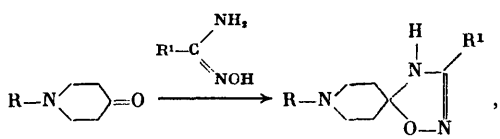


These same α-aminonitriles interact with isothiocyanates to provide a new route to 4-imino-1,3,8-triazaspiro[4.5]decane-2-thiones,[124] hydrolysis of which leads to the corresponding hydantoins.[125]



R = alkyl, cyclohexyl, phenyl, α-naphthyl.

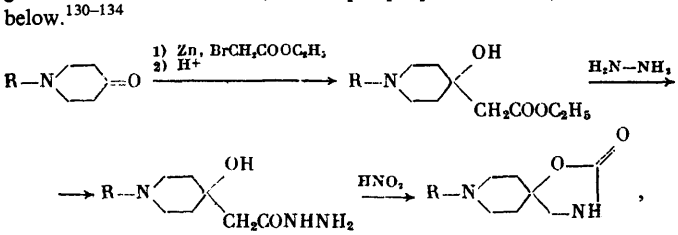
Piperidines spiro-fused with the 1,2,4-oxadiazoline ring have been prepared by interaction of 4-piperidones with amidoximes in the presence of various acids.[126–129]



R = H, alkyl, acyl, aryl; R^1 = alkyl, phenyl, benzyl, *p*-tolyl.

Such 1-oxa-2,4,8-triazaspiro[4.5]dec-2-enes possess sedative, analgesic, and antiinflammatory activity, and reduce blood levels of sugar and cholesterol.

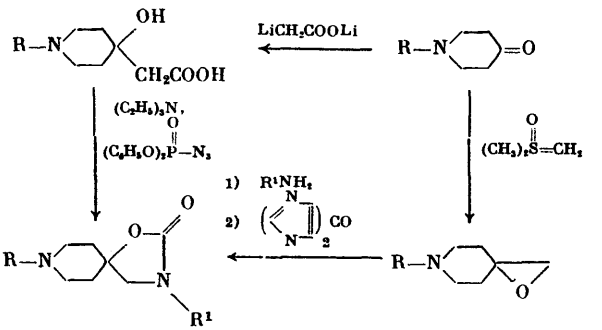
Piperidines spiro-fused at the 4-position with the 2-oxazolidone ring have been obtained via Reformatskii reaction with 4-piperidones. The resulting β-hydroxycarboxylic acid esters are converted to the corresponding hydrazides which undergo Curtius rearrangement to give the desired 1-oxa-3,8-diazaspiro[4.5]decan-2-ones, as shown below.[130–134]



R = alkyl, aryl.

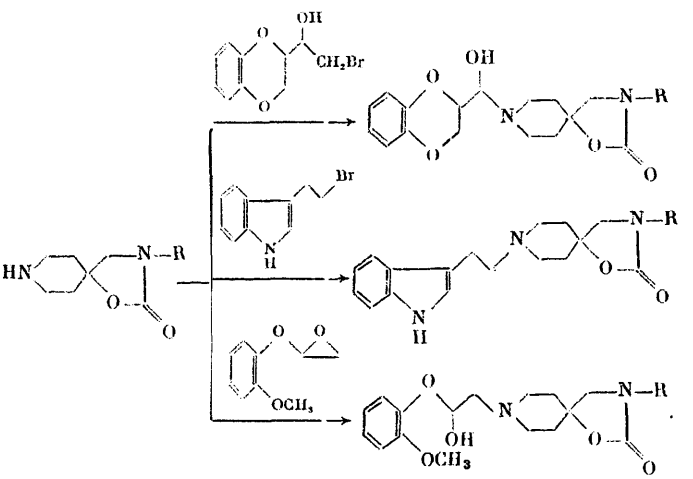
These compounds possess antiinflammatory, antiasthmatic, analgesic, and tranquillizing activity.

A wide range of 1-oxa-3,8-diazaspiro[4.5]decan-2-ones has been prepared by other researchers, both by the route shown above and by two other methods.[135] One of these is based on the conversion of 4-piperidones to the corresponding spirooxirane which is cylised to the desired 1-oxa-3,8-diazaspiro[4.5]decan-2-ones in two steps. Alternatively, in a one-step route, the same products are obtained by interaction of 4-carboxymethyl-4-hydroxypiperidines with diphenyl phosphorazidate.[135]

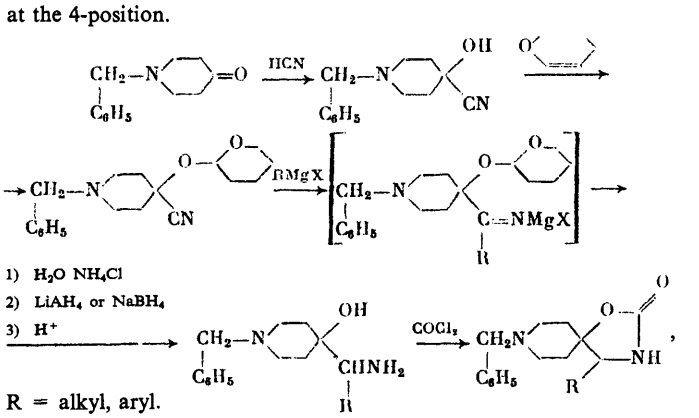


R^1 = H, alkyl.

Treatment of 1-oxa-3,8-diazaspiro[4.5]decan-2-ones with a variety of halides or epoxides affords *N*-substituted derivatives with antihypertensive properties.[135]



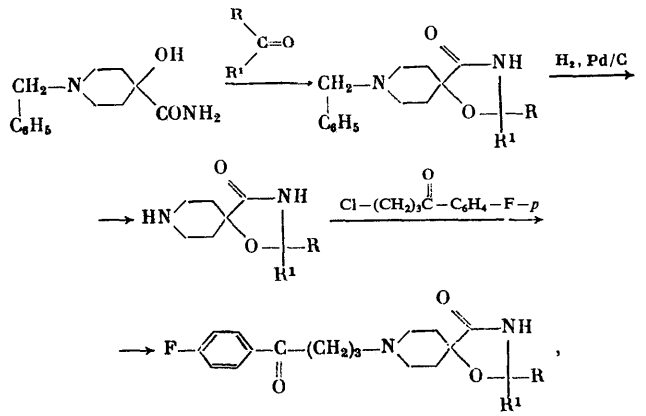
In an alternative 1-oxa-3,8-diazaspiro[4.5]decan-2-one synthesis, 4-piperidone cyanohydrins are protected as their tetrahydropyran-2-yl ethers, which afford the corresponding 2-aminoalcohol derivatives by reaction with Grignard reagents followed by reduction and deprotection. Cyclisation with phosgene then secures the desired spirocyclics.[136] This method has been applied to the preparation of 1-oxa-3,8-diazaspiro[4.5]decan-2-ones with a variety of substituents at the 4-position.



R = alkyl, aryl.

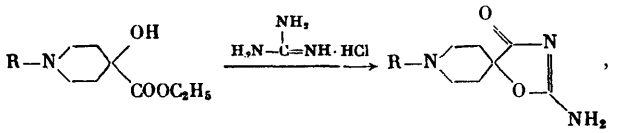
Debenzylation of these compounds, followed by *N*-alkylation (notably with 2-chloromethyl-1,4-benzodioxane) leads to *N*-substituted derivatives which possess pharmacological activity and are suitable for the treatment of diseases of the cardiovascular system.[137]

1-Oxa-3,8-diazaspiro[4.5]decan-4-ones have been prepared by interaction of 1-benzyl-4-hydroxypiperidine-4-carboxamide with carbonyl compounds in acidic media. Subsequent debenzylation and *N*-alkylation with 3-(4-fluorobenzoyl)propyl chloride affords the desired spirocyclics which possess neuroleptic, cataleptic, adrenolytic, and sedative properties.[138]



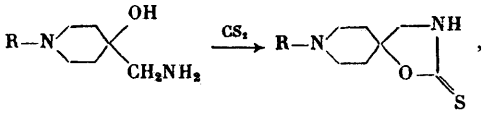
R = H, methyl; R^1 = methyl, phenyl, benzyl.

Condensation of 4-carbethoxy-4-hydroxypiperidines with guanidine hydrochloride affords 2-amino-1-oxa-3,8-diazaspiro-[4.5]dec-2-en-4-ones which display CNS depressant activity.[139]



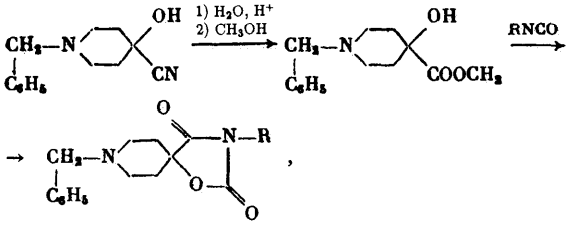
R = H, alkyl, aralkyl.

1-Oxa-3,8-diazaspiro[4.5]decane-2-thiones have been prepared by interaction of 4-aminomethyl-4-hydroxypiperidines with carbon disulphide.[140,141] Compounds of this type possess neuroleptic, broncodilator, analgesic, antibacterial, and hypotensive properties.



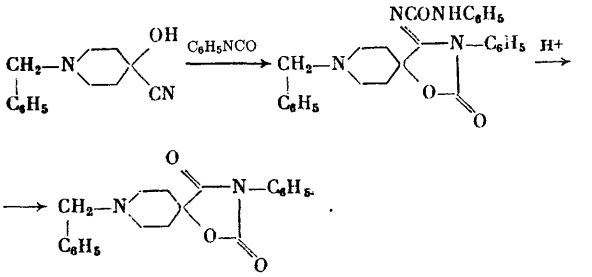
R = benzyl, 4-fluorobenzoylpropyl.

1-Oxa-3,8-diazaspiro[4.5]decane-2,4-diones have been synthesised from *N*-benzyl-4-piperidone cyanohydrin by hydrolysis, esterification, and subsequent interaction with isocyanates.[142–144]



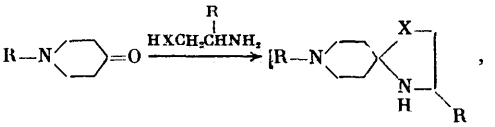
R = alkyl, benzyl, aryl.

The same authors have prepared 8-benzyl-3-phenyl-4-phenylcarbamylimino-1-oxa-3,8-diazaspiro[4.5]decan-2-one from the same cyanohydrin and phenyl isocyanate; hydrolysis of the product in acidic media leads to 8-benzyl-3-phenyl-1-oxa-3,8-diazaspiro-[4.5]decane-2,4-dione.[145]



Derivatives of this ring system possess CNS depressant activity.

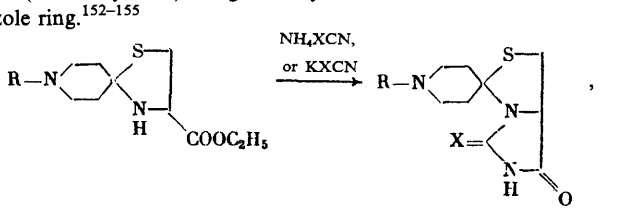
A general method of preparing 1-oxa-4,8-diazaspiro[4.5]decanes and 1-thia-4,8-diazaspiro[4.5]decanes has also been devised. This is based on the interaction of 4-piperidones with 2-aminoalcohols and 2-aminomercaptans, respectively, under acidic catalysis.[146–149]



X = O, S; R = H, alkyl, phenyl, acetyl, ethoxycarbonyl; R^1 = H, carboxyl, ethoxycarbonyl.

For the preparation of 1-thia-analogues, a mixture of the corresponding aziridine and hydrogen sulphide may be used in place of 2-aminomercaptans.[149]

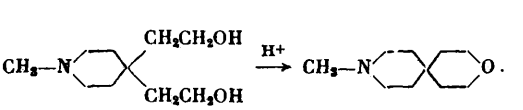
Similar results have been obtained by using *N*-substituted 2-aminoalcohols.[150,151] Compounds in this class possess analgesic,[146,147] psychotropic, CNS stimulatory,[146–148] and antibacterial activity.[149] 1-Thia-4,8-diazaspiro[4.5]decanes with an ethoxycarbonyl group at the 3-position react further with potassium or ammonium cyanate (or thiocyanate) to give tricyclic derivatives with a fused imidazole ring.[152–155]



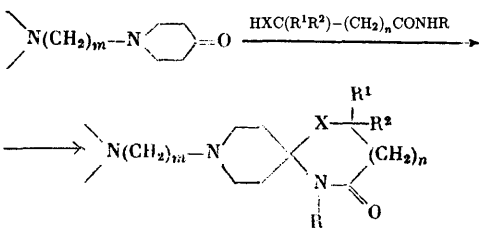
X = O, S; R = H, alkyl, acyl, aryl, ethoxycarbonyl.

Of the numerous derivatives with this ring system, some have shown neuroleptic properties,[155] while others display anti-hallucinogenic, sedative,[152] psychotropic,[153] and antithromotoxic properties.[154]

9-Methyl-3-oxa-9-azaspiro[5.5]undecane has been prepared from 1-methyl-4,4-*bis*(2-hydroxyethyl)piperidine by heating in an acidic medium.[156] The substrate is obtainable by reduction of the 4,4-*bis*-(carboxymethyl) derivative with $LiAlH_4$.



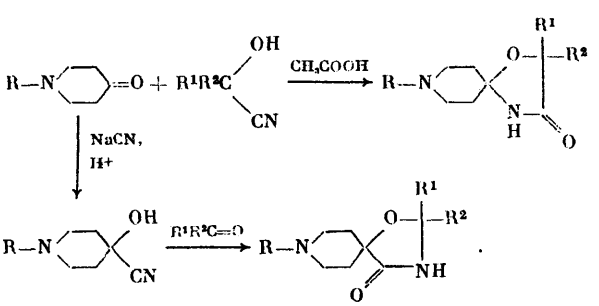
Much research has been devoted to the synthesis of derivatives of 1-oxa- or 1-thia-4,8-diazaspiro[4.5]decan-3-one and 1-oxa- or 1-thia-5,9-diazaspiro[5.5]undecan-4-one.[157–187] All routes to these compounds are based on *N*-substituted 4-piperidones, which cyclise to the desired spirocyclics on reaction with various hydroxy- or mercapto-carboxylic acids under acidic catalysis.



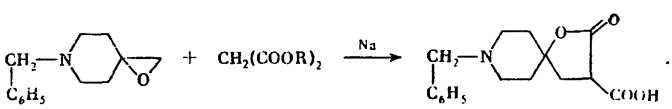
R = H, alkyl, aryl, benzyl, 2-furfuryl, 2-pyridyl; R^1 and R^2 = H, alkyl, phenyl; n = 0, 1; m = 2, 3; X = O, S, SO, SO_2.

Similar results are obtained if the hydroxy- or mercapto-carboxamides are replaced by a mixture of the corresponding hydroxy- or mercapto-carboxylic acid and a primary amine or ammonium carbonate.[188–193] Interest in these spiroheterocyclic systems has increased since certain of the compounds possess CNS stimulating activity,[161] reserpine antagonist,[158,163] tranquillizing,[167,173] analgesic,[167,179] psychotropic,[168,169,180,192] depressant,[191] neuroleptic,[174] and antiinflammatory[160,172,184] activities; certain compounds also reduce cholesterol levels,[159,184] the toxicity of carbon tetrachloride in the liver,[157,166] and sugar levels in the blood;[158] certain also suppress the activity of acetylcholine, and are used in the treatment of intestinal spasms and ulcers;[186] sedative and anticonvulsant activities have also been reported.[187] It should be noted that a number of these compounds are used medicinally as drugs.

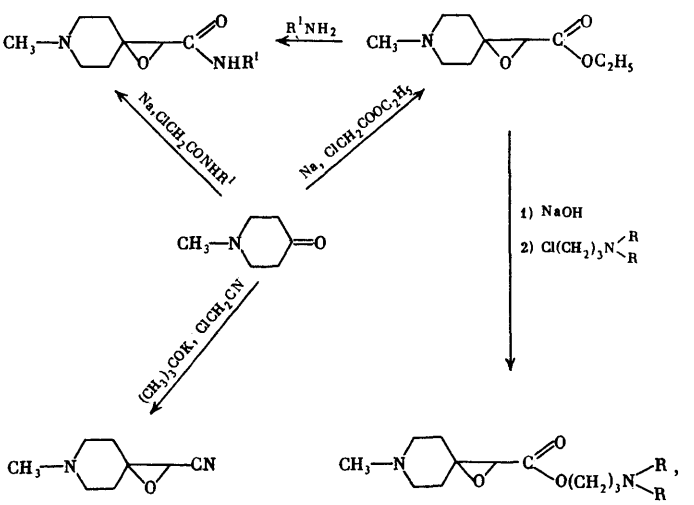
1-Oxa-4,8-diazaspiro[4.5]decan-3-ones have also been obtained by condensation of 4-piperidones with cyanohydrins.[194] Treatment of 4-cyano-4-hydroxypiperidines with ketones, however, leads to 1-oxa-3,8-diazaspiro[4.5]decan-4-ones.[194]



1-Oxa-6-azaspiro[2.5]octanes interact with malonic acid esters to give 3-carboxyazaspirocyclic lactones.[195]



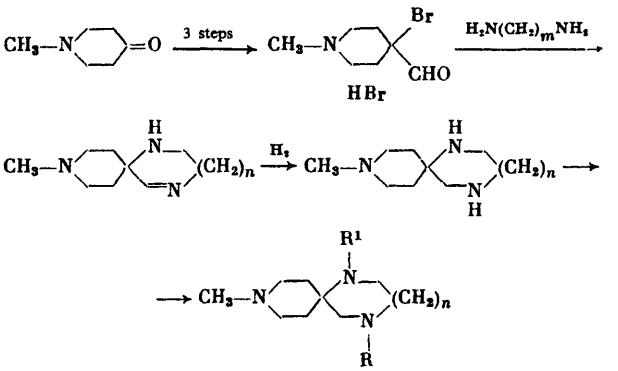
Derivatives of 1-oxa-6-azaspiro[2.5]octane having a carbalkoxy, amino-substituted carbalkoxy, carbamyl, or cyano groups at the 2-position have been prepared from 4-piperidones by the Darzens condensation.[196–199] For the cyano derivatives, potassium *tert*-butoxide was used as base, while metallic sodium was preferred for the preparation of the other derivatives.



R = methyl, ethyl, piperidyl, morphoyl; R^1 = H, methyl, ethyl, phenyl.

The mass spectrometric fragmentation of aminoalkyl 1-oxa-6-azaspiro[2.5]octane-2-carboxylates has been studied.[200]

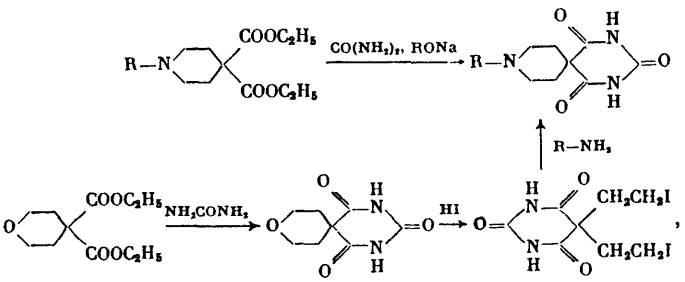
Spirocyclics with a piperidine ring spiro-fused at the 4-position with the piperazine or perhydrodiazepine ring (or partially dehydrogenated derivatives) have also been prepared.[201,202] It has been shown that the nitrogen atom situated alpha to the spirocarbon atom in both 9-methyl-1,4,9-triazaspiro[5.5]undecane and 3-methyl-3,7,11-triazaspiro[5.6]dodecane is relatively unreactive, so that it is possible to prepare both mono- and di-*N*-substituted derivatives.



R=CH_2CH_2CN, CH_2CN, CH_2CONH_2, $CH_2CH_2CONH_2$, $CH_2COOC_2H_5$, $CH_2CH_2COOC_2H_5$, $CH_2CH_2NH_2$, $(CH_2)_3-NH_2$, $CH_2CONHNH_2$; R'=H, $CH_2COOC_2H_5$, $CH_2CONHNH_2$; m=2, 3; n=1, 2.

2,4,9-Triazaspiro[5.5]undecane-1,3,5-triones have been prepared by two different routes. One is based on the cyclocondensation of 4,4-bis(carbethoxy)piperidines with urea in the presence of sodium

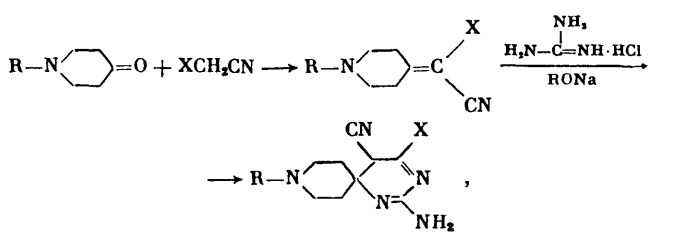
ethoxide, while the other involves cyclisation of 5,5-bis-(2-iodoethyl)barbituric acids with primary amines.[203] These barbituric acids are obtainable from 9-oxa-2,4-diazaspiro[5.5]-undecane-1,3,5-trione, as shown below.[204]



R = alkyl, allyl, aryl, benzyl, cyclohexyl.

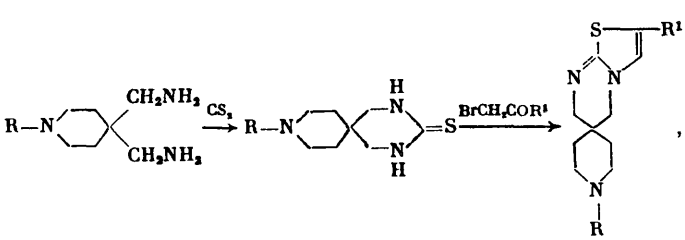
Recently it was shown that 2,4,9-triazaspiro[5.5]undecane-1,3,5-trione derivatives with various substituents on the piperidine nitrogen possess neuroleptic properties.[205,206]

1,3,9-Triazaspiro[5.5]undecane-1,3-dienes have been prepared by interaction of unsaturated nitriles with guanidine.[207] These products are effective for the treatment of Parkinson's disease.



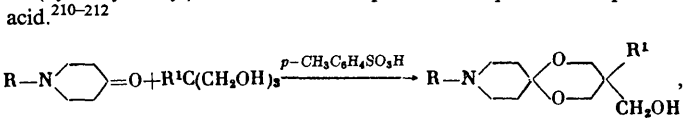
R = methyl, phenylethyl, dimethylaminoethyl; X = OH, NH_2.

The interaction of 1-substituted 4,4-bis(aminomethyl)piperidines with carbon disulphide leads to 9-substituted 2,4,9-triazaspiro-[5.5]undecane-4-thiones, which condense with α-halogenoketones to give spiro[piperidine-4,6-thiazolo[3,2-a]pyrimidines. The latter display antidepressant and thymoanaleptic properties.[208,209]



R = alkyl, aryl, benzyl, furyl, thienyl.

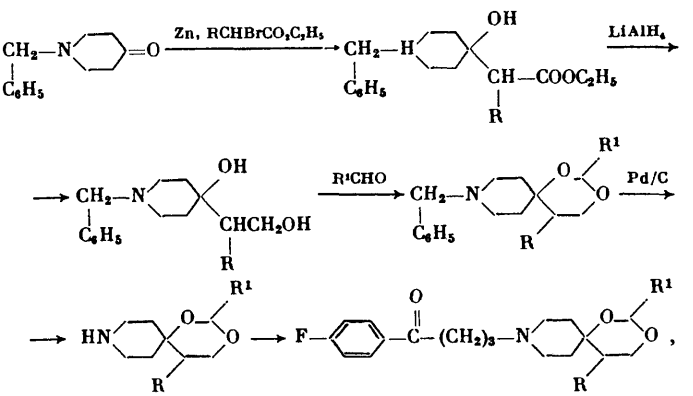
Substituted 1,5-dioxa-9-azaspiro[5.5]undecanes have been synthesised by condensation of 4-piperidones with alkyl-substituted tris(hydroxymethyl)methanes in the presence of *p*-toluenesulphonic acid.[210–212]



R = H, alkyl, aryl, aralkyl, acyl, ethoxycarbonyl, thienylalkyl; R^1 = alkyl.

In the above scheme, 4-piperidone ketals have been used in place of 4-piperidones,[213] and substituted 1,3-dioxanes in place of the triols.[214] Certain of the resulting azaspirodioxanes have been shown to possess tranquillizing activity.[215]

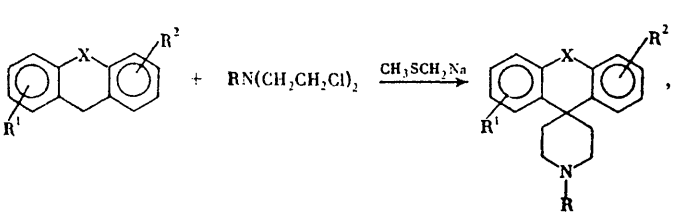
1,3-Dioxa-9-azaspiro[5.5]undecanes have been prepared from 1-benzyl-4-piperidone.[215] Thus, Reformatskii reaction with the latter, followed by reduction of the resulting β-hydroxyesters with $LiAlH_4$, yields the corresponding 1,3-diols, which are cyclised to the desired spiro[piperidine-1,3-dioxanes] with aldehydes:



R = H, alkyl; R^1 = H, alkyl, aryl.

III. Spiro-*N*-heterocycles in which the piperidine ring is spiro-condensed at the four position with condensed heterocycles

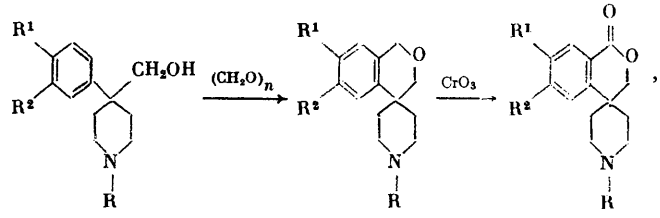
Xanthenes, thioxanthenes and dihydroanthracenes with various substituents in the benzene ring undergo cycloalkylation with bis(2-chloroethyl)amines to give the corresponding 4-spiropiperidines. Certain of these compounds have been used medicinally as analgesics.[216–218]



R = alkyl, aryl, benzyl, alkenyl; R^1 = R^2 = H, OMe, Cl, OH, etc.

References have also been made to the preparation of spiro-[isochroman-4,4'-piperidines] and spiro[isochroman-3,4'-piperidines]. One route to the former involves hydroxymethylation, followed by ring closure of the resulting 4-aryl-4-hydroxymethylpiperidines.[219–223] The starting 4-hydroxymethylpiperidines were obtained by reduction

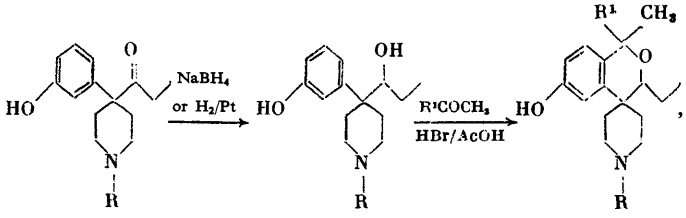
of the corresponding 4-carbalkoxy-derivatives. The spiroisochromans prepared by this method were oxidised to the corresponding spiroisocoumarins with CrO_3.[219,222]



R = alkyl, aryl, benzyl, aralkyl; $R^1 = R^2 = H$, MeO, etc.

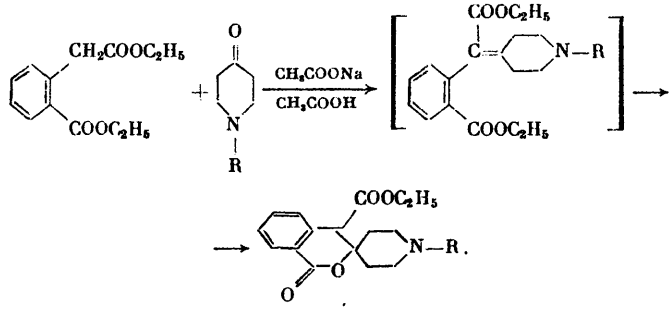
N-Substituted spiro[isochroman-4,4′-piperidines] may also be prepared by reductive *N*-debenzylation, followed by *N*-alkylation.[219]

In an alternative route to these spirocycles, 4-aryl-4-acylpiperidines may be reduced to the corresponding alcohol, and subsequently condensed with alkyl methyl ketones. In this way, derivatives with substituents at the 1 and 4 positions may be prepared.[224]

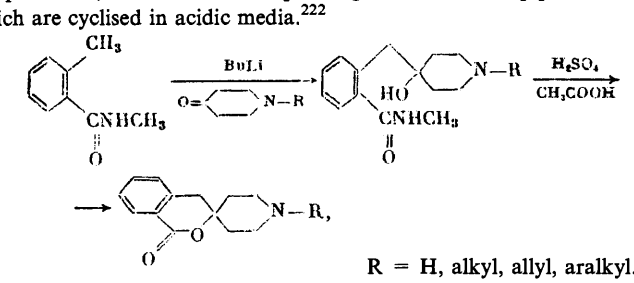


R = alkyl, allyl; R^1 = methyl, ethyl.

Spiro[isochroman-3,4′-piperidines] have been prepared by interaction of diethyl homophthalate with 4-piperidones, followed by cyclisation of the resulting 4-piperidinylidene-derivatives in acidic media.[219]



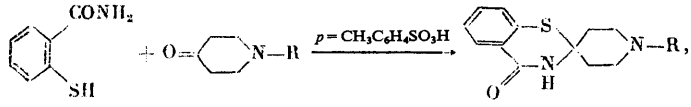
Alternatively, benzylic metallation of *o*-(*N*-methylcarbamyl)-toluene with *n*-butyllithium, followed by treatment with 4-piperidones, affords the corresponding 4-substituted 4-piperidinols, which are cyclised in acidic media.[222]



R = H, alkyl, allyl, aralkyl.

Such spiroisochromans possess analgesic activity.

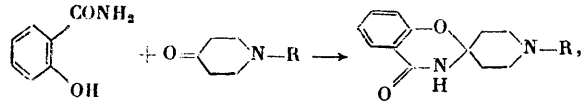
4-Oxospiro[1,3-benzothiazine-2,4′-piperidines] may be obtained by condensation of thiosalicylamide with 4-piperidones.[225]



R = H, butyl, acetyl, benzyl, benzoyl.

These compounds possess sedative, analgesic and hypoglycaemic properties.

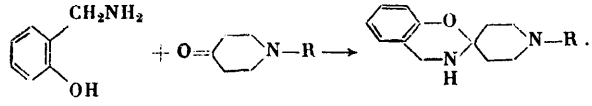
In a similar way, 4-oxospiro[1,3-benzoxazine-2,4′-piperidines] may be prepared by condensation of 4-piperidones with salicylamide.[226]



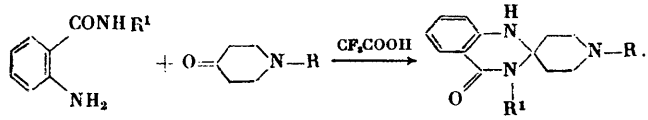
R = H, acetyl, benzyl, ethoxycarbonyl.

It is interesting that these compounds also possess sedative, analgesic, and hypoglycaemic properties.

Spiro[1,3-benzoxazine-2,4′-piperidines] are obtained if *o*-aminomethylphenols are used in place of salicylamides.[227]

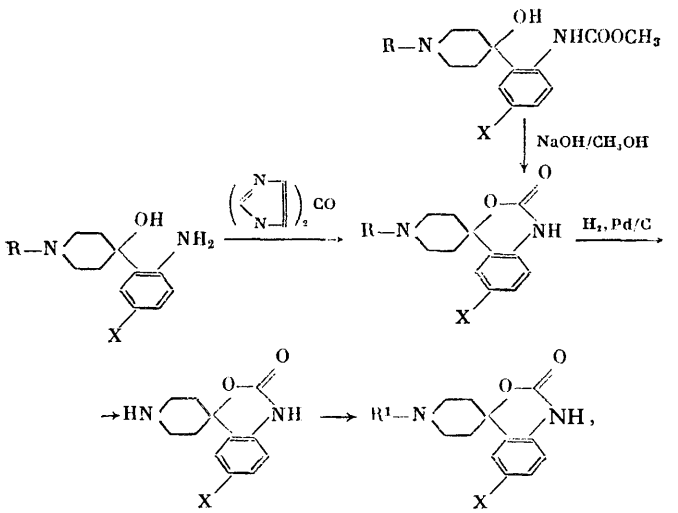


The condensation of anthranilamides with 4-piperidones in the presence of trifluoroacetic acid affords 4-oxospiro[tetrahydroquinazoline-2,4′-piperidines], which display bronchodilator and CNS depressant activity.[228]



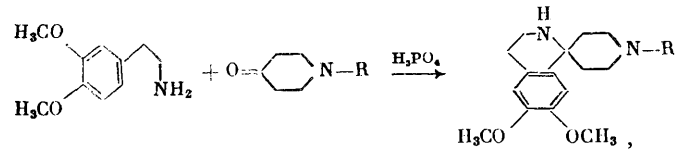
There are two routes to 2-oxospiro[4*H*-3,1-benzoxazine-4,4′-piperidines] based on *N*-substituted 4-hydroxy-4-(2-aminophenyl)piperidines.[229,230] In one of these methods, the latter compounds are converted to *N*-carbomethoxy derivatives with methyl chloroformate, and then cyclised in aqueous ethanolic NaOH. In the other method, the starting 4-piperidinols are cyclised directly with *N*,*N*′-carbonyldiimidazole. A variety of *N*-substituted derivatives may be obtained by reductive cleavage of *N*′-benzyl-2-oxospiro[4*H*-3,1-benzoxazine-4,4′-piperidines], followed by appropriate *N*-alkylation of the *N*-unsubstituted derivatives. These

products possess hypotensive properties and are used medicinally in combination with other drugs.



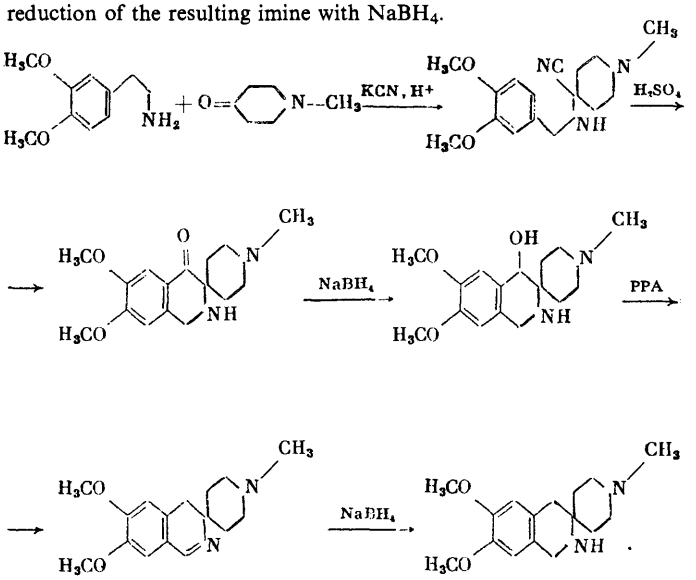
R = H, alkyl, benzyl; R^1 = benzoylbutyl; X = H, Cl.

There are convenient one-step routes to spiro[tetrahydroisoquinoline-1,4′-piperidines] by Pictet-Spengler ring closure of 3,4-dimethoxyphenylethylamine with 4-piperidones in polyphosphoric acid.[231]

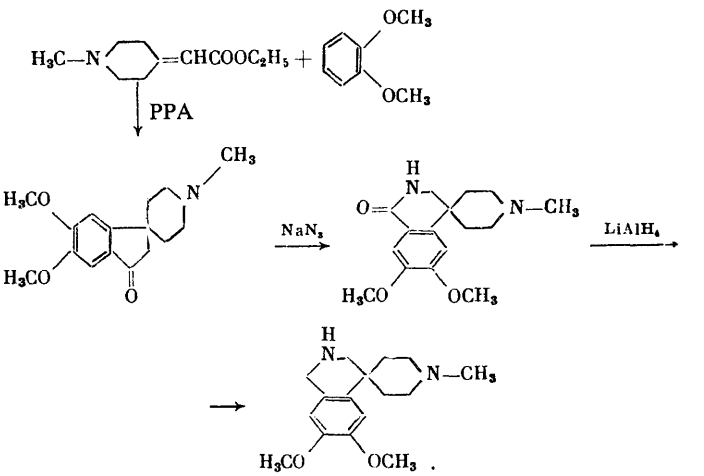


R = methyl, benzyl.

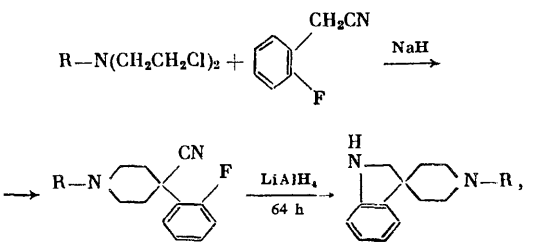
The synthesis of spiro[tetrahydroisoquinoline-3,4′-piperidines] has also been reported.[231] Thus, 3,4-dimethoxyphenylethylamine condenses with 1-methyl-4-piperidone in the presence of KCN to give the corresponding 4-amino-4-cyanopiperidine, which cyclises to 4′-methyl-4-oxo-6,7-dimethoxyspiro[1,2,3,4-tetraisoquinoline-3,4′-piperidine]. The 4-deoxy derivative is obtained by reduction to the corresponding alcohols, followed by dehydration and a second reduction of the resulting imine with $NaBH_4$.



Spiro[isoquinoline-4,4′-piperidines] have been prepared by Schmidt rearrangement of the corresponding spiroindanones, followed by hydride reduction of the resulting lactams.[231] The starting spiroindanones are obtained under Friedel-Crafts conditions by interaction of the corresponding phenolethers with the appropriate 4-carboxymethylenepiperidines or their esters.[232]



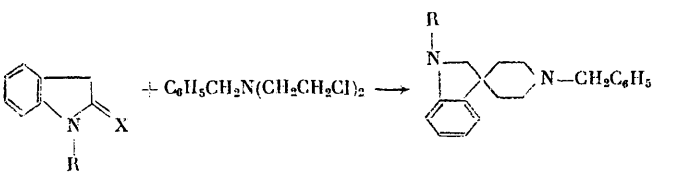
Methods of preparing spiro[indoline-3,4′-piperidines] have been reported in the patent literature.[233,234] These involve condensation of bis(2-chloroethyl)amines with *o*-fluorobenzyl cyanide in the presence of NaH. The resulting 4-cyano-4-(*o*-fluorophenyl)-piperidines are reduced with $LiAlH_4$ over > 60 h, during which time indoline ring closure takes place with liberation of fluoride ion.



R = H, alkyl, CN, acyl, phenyl.

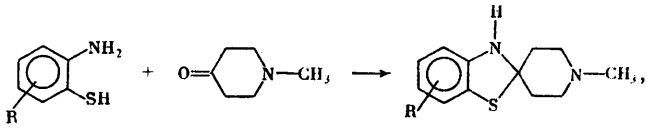
The obtained *N*-substituted indolines are used medicinally as anticonvulsant, antidepressant, and transquillizing drugs.

The preparation of spiro[indoline-3,4′-piperidines] and their 2-oxo-derivatives has been achieved by cycloalkylation of the corresponding indolines with *N*-benzylbis(2-chloroethyl)amine, followed by debenzylation and subsequent *N*-alkylation with various alkyl halides.[235,236] According to the authors, these compounds possess antiarrhythmic, analgesic and antihypertensive activity.



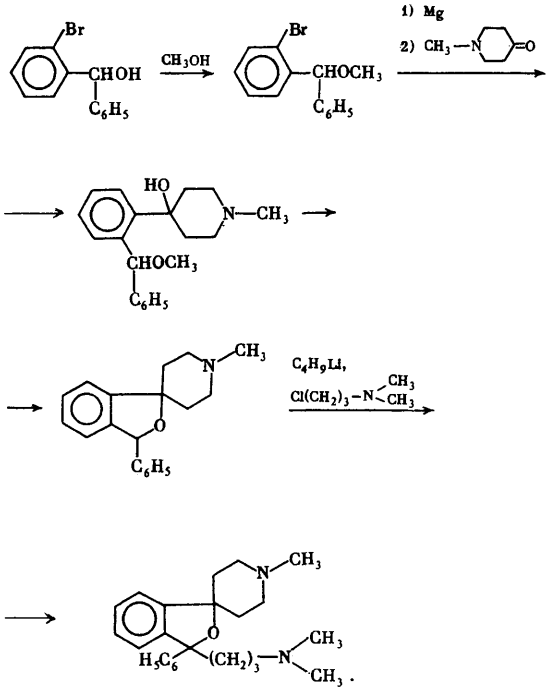
R = H, alkyl, phenyl; X = H_2, O.

o-Aminothiophenols condense with 1-methyl-4-piperidones to give spiro[benzthiazoline-2,4′-piperidines] which possess antiasthmatic properties.[237]

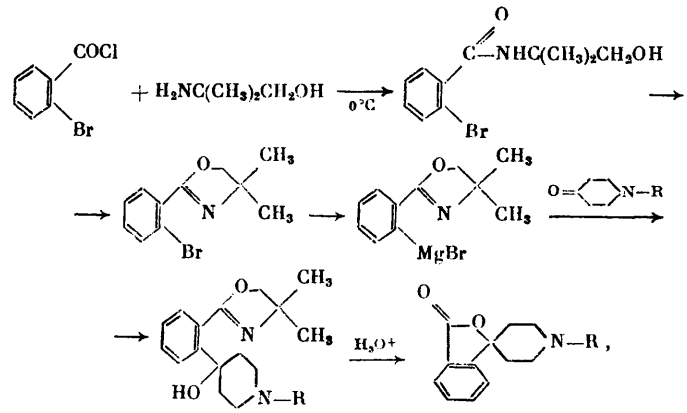


R = H, Cl, Me, MeO.

Spiro[isobenzofuran-1,4-piperidines] are obtained by conversion of *o*-bromobenzhydryl alcohol to the corresponding methyl ether, which, following conversion to the corresponding Grignard reagent, adds to 4-piperidones to give the corresponding 4-aryl-4-piperidinols; the latter are then cyclised to the desired spirocycles, as exemplified below. The resulting 3-phenyl-1,3-dihydrospiro[isobenzofuran-1,4′-piperidine] is converted to the 3-(3-dimethylaminopropyl) derivative by metallation with butyllithium followed by alkylation with 3-dimethylaminopropyl chloride.[238] A number of such spiroisobenzofurans have been discussed in the patent literature.[239]

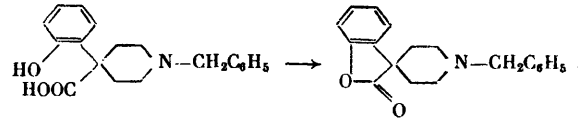


3-Thienyl-1-spiroisobenzofuran analogues have been prepared by the same method and shown to possess tranquillizing and antidepressant activity.[240] The following route is available for preparing 3-oxospiro[isobenzofuran-1,4′-piperidines]. Thus, *o*-bromobenzoyl chloride condenses with 2-amino-2-methylpropanol to give the corresponding benzamide, which undergoes cyclodehydration with $SOCl_2$ to give 2-(2-bromophenyl)-4,4-dimethyl-2-oxazoline. The corresponding Grignard reagent reacts with 4-piperidones to give the corresponding 4-aryl-4-piperidinols which cyclise to the desired spirocycles in acidic media. A number of these compounds possess analgesic, tranquillizing, antidepressant and anticonvulsant activities.[241,242]



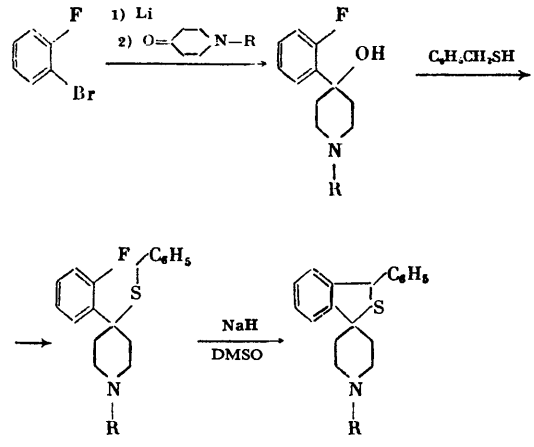
R = methyl, benzyl.

2-Oxospiro[benzofuran-3,4′-piperidines] are formed by cyclisation of *N*-benzyl-4-carboxy-4-(*o*-hydrophenyl)piperidines.[243]



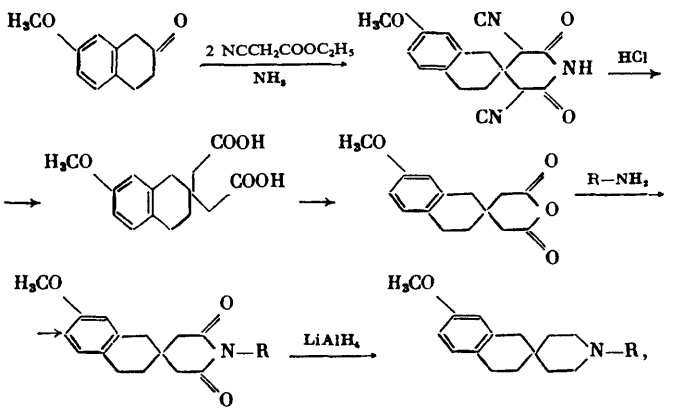
A 3-methylenespiro[benzofuran-2,4′-piperidine] has also been prepared and shown to possess hypotensive properties.[244]

Spiro[benzo[c]thiophene-1,4′-piperidines] have been synthesised as follows. *o*-Fluorophenyllithium, obtained from *o*-fluorobromobenzene by bromine-lithium exchange, condenses with 4-piperidones to give the corresponding 4-aryl-4-piperidinols, which are converted to the desired spirocycles by condensation with benzyl mercaptan followed by ring closure.[245,246]



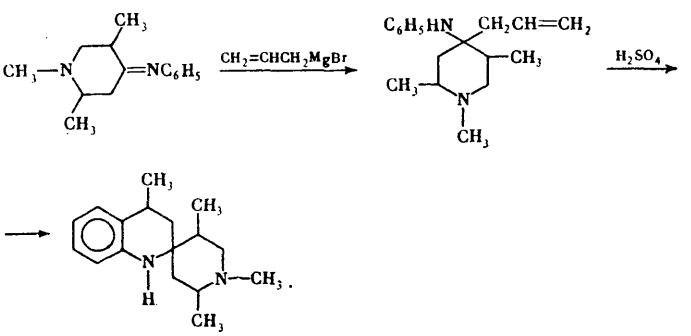
Such spirobenzothiophenes possess anticholinergic properties and are effective antidepressants and sedatives.

Spiro[tetrahydronaphthalene-2,4'-piperidines] have been obtained by conversion of 7-methoxy-2-tetralone to the corresponding Guaveschi's imide, followed by the sequence of steps shown below.[247]

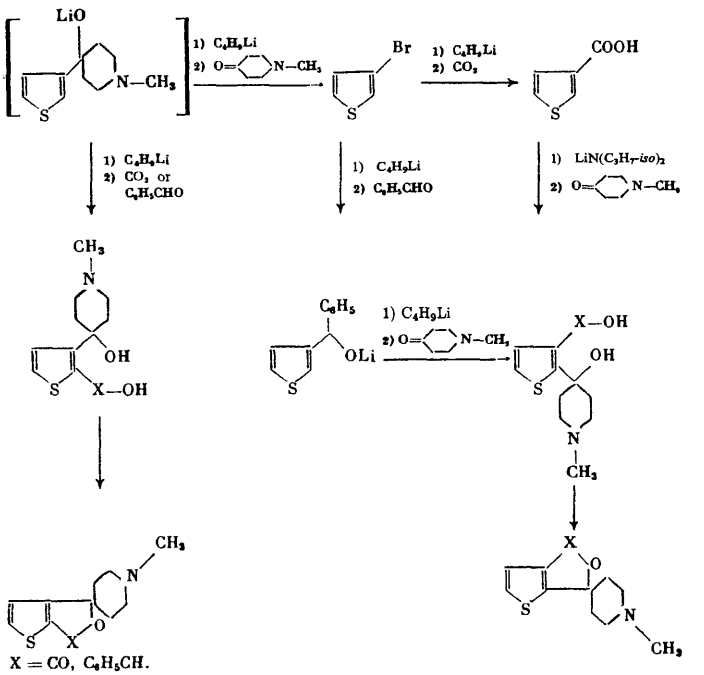


R = dimethylaminopropyl.

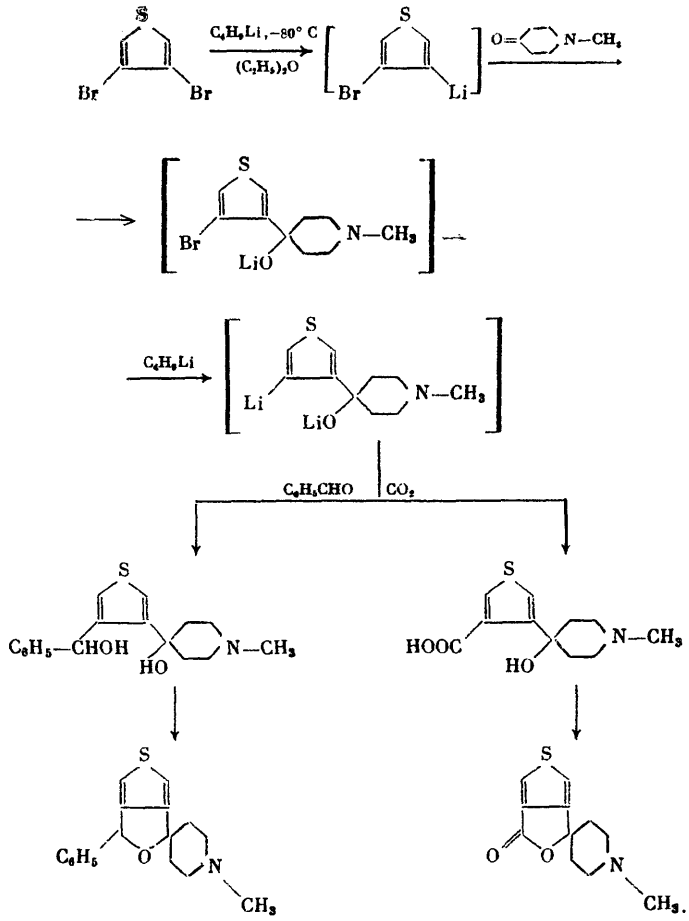
Tetrahydro-1,3,5,7-tetramethylspiro[quinoline-2,4'-piperidine] has been prepared by the high-yielding reaction of 1,2,5-trimethyl-4-phenyliminopiperidine with allylmagnesium bromide, followed by heating the resulting 4-allyl-4-anilinopiperidine in acidic media.[248]



Spiropiperidines having a spiro-condensed thieno[2,3-c]furan ring at the 4-position have been prepared from 3-bromothiophene, which offers scope for incorporating further substituents in the thiophene ring via metallation.[249] Thus, sequential treatment of 3-bromothiophene with butyllithium and 1-methyl-4-piperidone affords the corresponding 4-(3-thienyl)-4-piperidolate, which reacts, sequentially, with a second equivalent of butyllithium and carbon dioxide or benzaldehyde to give the corresponding 2-carboxy- or 2-hydroxyalkylthiophenes. The latter then undergo cyclodehydration as shown below. Alternatively, 3-lithiothiophene reacts with carbon dioxide or benzaldehyde to give the corresponding 3-substituted thiophenes which undergo lithiation at the 2-position. These derivatives then condense with 1-methyl-4-piperidone to give the desired spirocycles.



Piperidines having a spiro-fused thieno[3,4-c]furan ring at the 4-position have been prepared by the above method from 3,4-dibromothiophene. Thus, treatment of the latter with butyllithium at low temperature affords 3-bromo-4-lithiothiophene, which, without isolation, adds to 1-methyl-4-piperidone; the intermediate 4-piperidolate (again without isolation) is further lithiated and the resulting *O,C*-dianion is converted to the desired spirocycle by quenching with benzaldehyde or carbon dioxide, followed by cyclodehydration of the intermediate diol or hydroxyacid in acidic media, as shown below:[250]



- - - o0o - - -

The discovery of spiropiperidine-type biogenic amines and alkaloids has stimulated intense research, notably in the chemistry of azaspiranes having a piperidine ring spiro-fused at the 4-position with various heterocycles containing both nitrogen and other heteroatoms.

Studies of the biological properties of these compounds have shown that they possess a broad spectrum of activity, certain of which have been utilised medicinally. From this survey, one might predict that in the near future these azaspiranes will be used as effective drugs for treating irregularities of the central nervous system.

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Translated from *Uspekhi Khimii* 60 2663–2684 (1991) U.D.C. 541.128

Pyrolysis of methane in the temperature range 100–1700 K

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ABSTRACT. The results of studies on the pyrolysis of methane in the temperature range 1000–1700 K, which is of greatest practical importance, are surveyed. The influence of heterogeneous factors, pressure, temperature, and the products formed on the process is examined. The composition of the products is analysed and the mechanism of the process is discussed.

The bibliography includes 61 references.

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I. Introduction

The enhancement of the role of natural gas in the fuel–energy system as well as in many technological processes has aroused a new wave of interest in fundamental problems of the processing of the simplest hydrocarbons, including the main primary processes involved in the conversion of methane—its oxidation and pyrolysis. The complexity of the problem and the enormously wide variety of the real conditions encountered in technological processes have precluded to date a unique theoretical description of these processes. Depending on the specific purpose of the process, the pyrolysis of methane can be carried out over a wide temperature range. This range can be divided arbitrarily into three regions: low temperatures (up to 1000 K), moderate temperatures (1000–1800 K), and high temperatures (above 1800 K). Fairly reliable kinetic data have been obtained for the low temperature range and have already been surveyed.[1,2] Studies in the high-temperature range have developed by virtue of the wide scale adoption of the experimental shock wave method.[3,4] However, the specific features of the method resulted in mainly the initial stages of the pyrolysis being investigated.

The range of moderate temperatures, in which most of the technological processes are carried out, for example, the reduction of sulphur dioxide by methane at 1200–1500 K in the waste gases from non-ferrous metallurgy,[5] has in fact been least investigated at the present time. The pyrolysis of methane in this temperature range is the initial and rate-limiting stage of the entire SO_2 process.[6] During the last six years, many studies have been published on the pyrolysis of methane in the range of moderate temperatures, but these were mainly studies with a technological bias. Their fragmentary nature and association with specific conditions precluded a reliable answer to three principal questions: concerning the rate of pyrolysis in this temperature range and its dependence on external parameters, the concentration of the main gaseous pyrolysis products and the kinetic mechanism of the pyrolysis under these conditions. The aim of the present review is to survey the available data on these problems.

The study of the pyrolysis of methane was initiated in 1809 by Dalton, who demonstrated the possibility of decomposing methane into its elements by an electric discharge. On the other hand, the thermal decomposition of methane was first achieved by Davy with the aid of an electrically heated platinum wire. The first study devoted to the thermal decomposition of methane was carried out by Berthelot[7,8] in 1862. He passed methane through a heated porcelain tube and observed the formation, together with carbon, of a mixture of different hydrocarbons, primarily acetylene and olefins, as well as traces as more complex hydrocarbons—benzene and naphthalene. He assumed that the primary stage of the process is the bimolecular reaction

$$2CH_4 \rightarrow C_2H_2 + 3H_2. \quad (1)$$

In 1908 Bone and Coward,[9] who investigated the kinetics of the decomposition of CH_4 at temperatures in the range 773–1473 K, put forward the hypothesis of the intermediate formation of the fragment species CH_3, CH_2, and CH. The experimental demonstration of the formation of hydrocarbon radicals (methylene and methyl) in the pyrolysis of methane was first obtained by Belchetz[10] and Rice and Dooley[11] using Paneth's method (the metallic mirror method). Mayer and Altmayer,[12,13] who investigated the equilibrium

$$CH_3 \rightleftharpoons C + 2H_2, \quad (2)$$

at atmospheric pressure and different temperatures, demonstrated the reversibility of the decomposition of methane into the elements.

The most fundamental study of the kinetics of the pyrolysis of methane up to the 1950s remains that of Kassel,[14] who carried out the pyrolysis under static conditions in a quartz reactor in the temperature range 973–1123 K. He concluded that the reaction is homogeneous and of first order although under certain conditions an induction period of unknown nature is observed. The expression which he obtained for the methane pyrolysis rate constant $k = 7.3 \times 10^{11} \exp(-79\,385/RT)\ s^{-1}$ describes the process satisfactorily up to temperatures in the region of 1500 K. Having

surveyed the results of earlier studies[15,16] concerning the influence of hydrogen on the pyrolysis of methane, Kassel established that the rate of pyrolysis decreases markedly in the presence of hydrogen and he derived the empirical relation $W \propto [CH_4]^2/[H_2]^3$. The experiments carried out by Storch,[17] who carried out the pyrolysis of methane on an incandescent carbon filament in a flask whose surface was cooled to a definite low temperature which made it possible to stabilise and isolate the primary reaction product, were very important for the understanding of the mechanism of the decomposition of methane. On cooling with liquid nitrogen (77 K), 95% conversion of methane into ethane was observed, on cooling with liquid oxygen (91 K) cracking resulted in the formation of ethane, ethylene, and acetylene, while on cooling the surface of the flask to 203 and 273 K the cracking products were carbon and hydrogen. On the basis of these data, the following scheme for the consecutive dehydrogenation of methane was put forward:[14]

$$CH_4 \rightarrow CH_2 + H_2, \quad (3)$$

$$CH_4 + CH_2 \rightarrow C_2H_6, \quad (4)$$

$$C_2H_6 \rightarrow C_2H_4 \rightarrow C_2H_2 \rightarrow C + H_2. \quad (5)$$

Subsequently Storch[18] interpreted data for the rate of the thermal decomposition of methane obtained in earlier investigations,[16,19–21] etc. His conclusions will be partly considered below.

Two important factors in the study of the pyrolysis of ethane were established by Kobozev and co-workers.[22–24] Firstly, a change in the nature of the surface does not affect the rate of decomposition of methane itself but can influence greatly the rate of formation of solid carbon products[22,23] and, secondly, the pyrolysis is accelerated by the addition of ethane.[24] Subsequently the accelerating effect of all C_2 hydrocarbons (ethane, ethylene, acetylene) was demonstrated in many investigations. In a series of studies by Germain and Vaniscotte,[25–27] etc. at temperatures near 1273 K and atmospheric pressure, the induction periods in the pyrolysis process were thoroughly investigated and their dependence on the process conditions was established.

Since the end of the 1950s, the shock wave method came to be used widely for the study of the early stages of the pyrolysis of methane,[28,29] but most of the results obtained by this method refer to the high-temperature range. The studies of this period have been briefly surveyed by Khan and Crynes.[1] At the same time, a series of studies devoted to practical problems of the preparation of acetylene by the pyrolysis of methane have been carried out.[30–33]

II. Heterogeneous factors in the pyrolysis of methane

The results of early studies of the influence of heterogeneous factors on the pyrolysis of methane are fairly contradictory. Whereas Kassel[14] and Holliday and Exell[15] did not detect the influence of a change in the ratio S/V on the pyrolysis of methane in the range of moderate temperatures in quartz reactors and reactors coated with a layer of carbon formed on pyrolysis even when this parameter was varied widely (by a factor of 20 in Kassel's study[14]), Wheeler and Wood[20] claimed that the pyrolysis of methane in a quartz reactor is mainly a surface process (an appreciable catalytic effect in the presence of iron was also noted). The study of Kobozev et al.[22] was devoted to the influence of the nature of the surface (quartz or porcelain) and also of the known catalytic poisons on the pyrolysis of methane at 1433 K. It was established that the rate of formation of products such as ethylene and acetylene is independent of changes in the material of the surface or the presence of catalytic poisons, but these factors do affect greatly the rate of formation of soot on the surface of the reactor. The conclusion that the reaction is homogeneous was confirmed[24] by the identical yields of ethylene and acetylene in carbon and porcelain tubes at 1883 K.

It has been shown[25,34] that at temperatures of about 1273 K an increase in the ratio S/V diminishes the induction period and increases somewhat the maximum rate of reaction. The influence of the state of the surface on the process during the induction period was also noted. However, at higher temperatures (1373 and 1423 K) a change in S/V ceases to influence even the initial stage of the pyrolysis.[35] The claim that the pyrolysis of methane is heterogeneous, made in the study of Shantorovich and Pavlov[36] on the basis of experiments under flow conditions at low pressures, also refers to the initial stage involving the self-acceleration of the reaction. An increase in the rate of reaction as carbon was deposited on the surface of the porcelain reactor was also noted in the above investigation, the activation energy for the pyrolysis on the carbon-coated surface amounting to only 60 kcal mol^{-1} compared with 90 kcal mol^{-1} on the procelain surface.

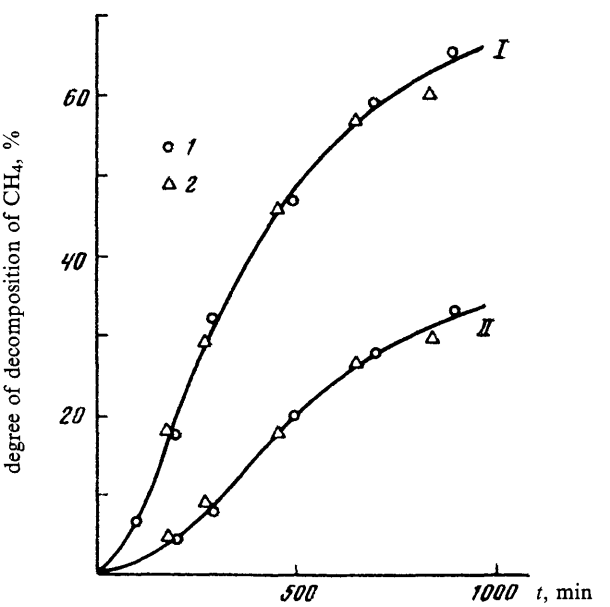


Figure 1. Kinetics of the decomposition of methane for S/V = 2 cm^{-1} (*1*) and 4 cm^{-1} (*2*): *I*, initial CH_4 concentration C_0 = 10% at T = 1423 K; *II*, C_0 = 16% at T = 1373 K. P = 740 torr.[35]

A dependence of the pyrolysis of methane on heterogeneous factors was not observed in many studies.[35,37–40] The independence of the degree of conversion of methane and of the quasi-stationary rate of pyrolysis of the surface area of the reactor for times exceeding the induction period has been demonstrated[35,37] for mixtures of methane (10–16%) with nitrogen and helium at temperatures of about 1400 K (Fig. 1). Chen et al.[38] demonstrated

this for lower temperatures (995–1103 K). Arutyunov et al.[39] observed in a static reactor a satisfactory agreement between the kinetics of the decomposition of methane at 1200 K and the kinetics of the production of hydrogen when S/V was altered by a factor of approximately 2.2. They noted that it is virtually impossible to observe differences in the process kinetics and in the composition of the products when the pyrolysis is carried out in a clean quartz reactor, in a reactor where a large number of experiments have already been carried out, or in a reactor flushed repeatedly with oxygen at 1200–1300 K after pyrolysis. The independence of the final composition of the pyrolysis products of the diameter of an alumina flow reactor has been demonstrated.[40]

The formation of soot in the volume of the reactor apparently influences greatly the pyrolysis of methane. Thus it has been shown[35] that the introduction of 1% of naphthalene vapour into the reactor leads to a thirtyfold increase in the rate of decomposition of methane. On the basis of these experiments, the authors concluded that the initial autoacceleration of the pyrolysis on the soot nuclei, formed in the volume of the reactor and on the surface, is heterogeneous.

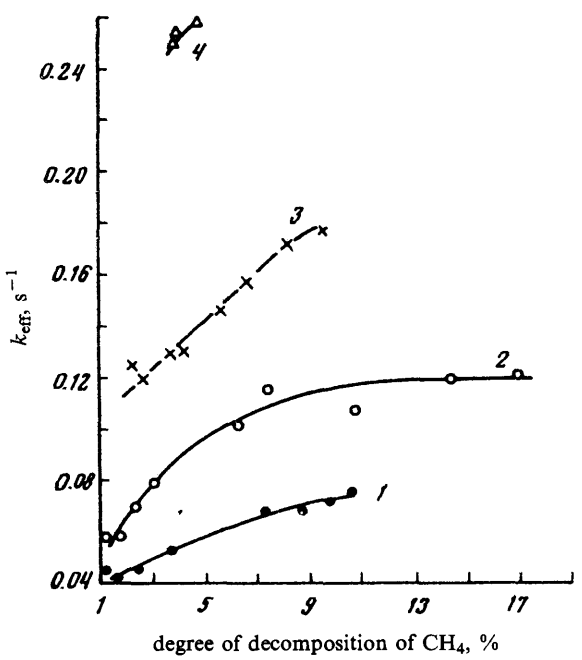


Figure 2. Dependence of the effective unimolecular rate constant for the decomposition of methane (k_{eff}) on the degree of conversion of the latter at different temperatures (K) (pressure 1 atm): *1*, 1280; *2*, 1306; *3*, 1326; *4*, 1346.

Many workers suggest the existence of a pathway leading to the direct decomposition of methane into carbon and hydrogen, bypassing the formation of intermediate C_2 hydrocarbons,[33,41,42] on the surface of the reactor,[42] which might explain the low activation energies for the carbon deposition process on the surfaces of graphite (36.0 kcal mol^{-1} [41]) and alumina (16.2 kcal mol^{-1} [33]) reactors. Similar activation energies (~25 kcal mol^{-1}) have been obtained for the methane decomposition and carbon deposit formation reactions in a tubular graphite reactor with a high ratio S/V = 10 cm^{-1} in the temperature range 1573–2473 K, while the temperature dependence of the yield and of the rate constants for the formation of ethylene and acetylene was more marked.[42] This led the authors[42] to the conclusion that a single dehydrogenation mechanism [reaction (5)] is insufficient for the description of the pyrolysis of methane under these conditions.

Only for the very high ratios $S/V > 10^4$ cm^{-1}, obtained[43] by introducing finely disperse materials (gas carbon black, Al_2O_3 powder) into the reaction zone in quartz and copper flow reactors, does the reaction become fully heterogeneous. According to the authors,[43] this is associated with the fact that the rate of formation of active centres per unit volume is greater by a factor of 10^4 than per unit surface. Therefore, even for $S/V < 20$ cm^{-1}, the induction period reappears.

On the whole, despite the existence of fairly notable contradictions between the results of individual studies, one may conclude that in the range of moderate temperatures and for the usual S/V ratios and reactor materials, heterogeneous factors have an appreciable influence on the pyrolysis of methane only in the initial period of the autoacceleration of the reaction and that with increase in temperture this influence gradually weakens and at $T > 1400$ K is virtually inappreciable. Heterogeneous factors affect much more strongly the deposition of solid carbon on the surface, but examination of these processes is outside the scope of the present review.[44]

III. Autocatalysis of the initial stage of the pyrolysis of methane

In the vast majority of cases, the pyrolysis of methane is regarded as a first-order reaction and is described by the corresponding kinetic equation. However, the presence of an induction period in this reaction was already established in the early studies. Kassel[14] noted that the presence of the induction period is most striking at low pressures and in reactors which have not yet been coated by a layer of carbon; in the case of large S/V ratios, there are no induction periods. An increase in the rate of pyrolysis of methane with increase in the degree of pyrolysis, i.e. the occurrence of autocatalysis, has been demonstrated[34] for low degrees of conversion (Fig. 2). The phenomenon of autocatalysis and its dependence on the process parameters have been investigated by Germain and Vaniscotte[25–27] at temperatures near 1273 K. According to their results, changes in the S/V ratio for the reactor have a fairly appreciable albeit not very strong influence on the induction period and the rate of reaction in the initial period (Figs. 3 an 4). Evidently an increase in S/V approximatley by a factor of 10 leads to only a twofold decrease in the induction period and increase in the maximum rate of reaction. Small amounts of added ethane (0.5–3%) have approximately the same effect.[27] The influence of added ethane on the initial period of the pyrolysis has been investigated[45] over a wider temperature range: from 1323 to 1823 K. At 1323 K, the presence of even 0.21% of ethane alters qualitatively the nature of the methane decomposition curve, leading to the disappearance of the reaction autoacceleration section (Fig. 5). Similar changes have been obtained also for the kinetics of the evolution of hydrogen in this process. With increase in temperature,

the autoacceleration becomes less marked and at $T > 1500$ K neither autoacceleration (Fig. 6) nor the influence of added ethane (0.69%) on the kinetics of the pyrolysis are observed.[45] Apart from an increase in temperature, an appreciable increase in the S/V ratio (S/V > 20 cm^{-1}) leads to the disappearance of the autoacceleration period.[43]

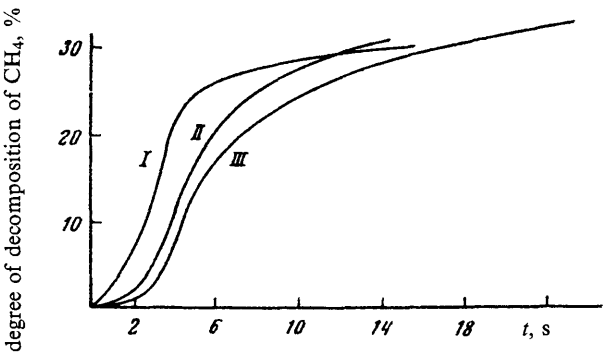


Figure 3. Kinetics of the decomposition of methane for different S/V ratios (cm^{-1}): *I*, 25.3; *II*, 5.0; *III*, 2.8. Temperature 1273 K; pressure 1 atm; methane concentration 95%.[25]

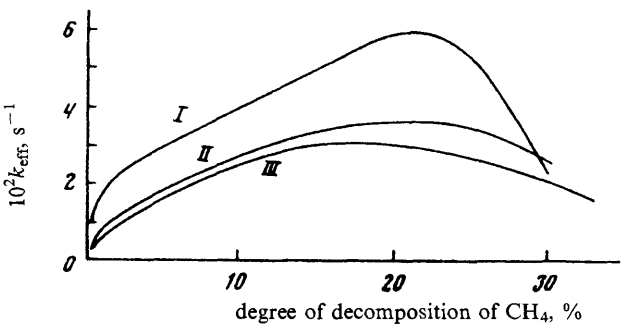


Figure 4. Dependence of the effective unimolecular rate constant k_{eff} for the decomposition of methane on the degree of conversion of the latter for different S/V ratios (cm^{-1}): *I*, 25.3; *II*, 5.0; *III*, 2.8.[25]

In a review[2] devoted to the pyrolysis of methane at temperatures of about 1000 K, it was shown on the basis of a series of experimental studies that the autocatalysis in this reaction cannot be accounted for by the formation of a layer of carbon on the surface of the reactor. Thus the formation of carbon on the surface of the reactor was followed from the absorption of light in a static system at about 1000 K.[46] The sensitivity of the method made it possible to detect less than a monolayer of the carbon formed. It was noted that carbon begins to be formed appreciably after the start of the autoacceleration of the reaction (Fig. 7). Furthermore, the use of a reactor in which the initial stage of the pyrolysis had already been carried out up to the onset of autocatalysis and then all the volatile products were removed did not affect appreciably the formation of products, i.e. the autoacceleration effect cannot be attributed to the presence of small amounts of undetected carbon on the surface. Probing of the volume of the reactor with the beam from a helium–neon laser also demonstrated the absence in this stage of even small carbon particles in the reactor volume which could be responsible for the autocatalysis, since their presence should have given rise to the corresponding scattering of the laser beam.[2] Thus it was necessary to seek an explanation of the phenomenon of autocatalysis in the gas-phase processes, which was in fact done for the above conditions (T = 1038 K, P = 433 torr) by Roscoe and Thompson[47] and Dean.[48] Mathematical modelling of the process showed[47] that the main causes of the autoacceleration are the secondary initiation of the pyrolysis by hydrocarbon products more complex than ethane and the subsequent chain processes involving methyl radicals. With increase in temperature, the role of higher hydrocarbons in the pyrolysis of methane diminishes, which reduces the autocatalytic effect up to its complete disappearance at $T > 1500$ K.

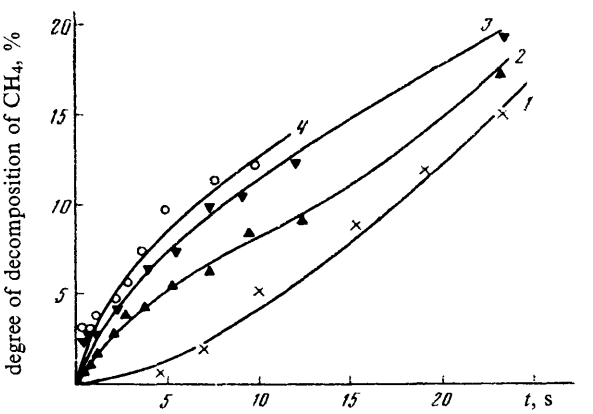


Figure 5. Dependence of the kinetics of the decomposition of methane on the initial C_2H_6 concentration C_0 (T = 1323 K, P = 760 torr); C_0 (%): *1*, 0; *2*, 0.21; *3*, 1.02; *4*, 1.45.[45]

IV. The influence of hydrocarbons on the pyrolysis of methane

The acceleration of the pyrolysis of methane in the presence of added ethane was already observed by Kobozev and Shneerson.[24] Gordon[34] showed for pyrolysis under flow conditions at temperatures near 1273 K that the addition of 0.72% of acetylene increases the rate of pyrolysis by a factor of 2–2.5 and that acetylene itself is initially vigorously consumed in the reaction. At the addition of 1% of ethylene to methane being pyrolysed has a similar effect but in this case the concentration of ethylene itself does not fall below 0.85% and the catalytic effect was attributed solely to the acetylene formed in the reaction and detected in the products in approximately the same amount as for the addition of acetylene itself.

A detailed study of the influence of small amounts of added ethane on the initial stage of the pyrolysis of methane was carried out by Germain and Vaniscotte[27] under flow conditions at T = 1273 to

1373 K. A decrease in the induction period and an increase in the maximum rate of pyrolysis after the addition of 0.5–3% of ethane were demonstrated, but with increase in the ethane concentration the relative efficiency of the additive fell. With increase in temperature in the above range, the influence of ethane also diminishes. The accelerating effect of ethane on the pyrolysis of methane under flow conditions was also observed in the temperature range T = 1100–1200 K.[37] The influence of ethane on the initial period of the process, manifested by the disappearance of the induction period and of the reaction acceleration region,[45] was examined in a previous section. It is of interest that, regardless of the initial concentration of the added ethane, a concentration characteristic of the pyrolysis of pure methane is established after a certain time (Fig. 8), i.e. the accelerating effect of hydrocarbon additives is manifested in the initial period of the reaction.

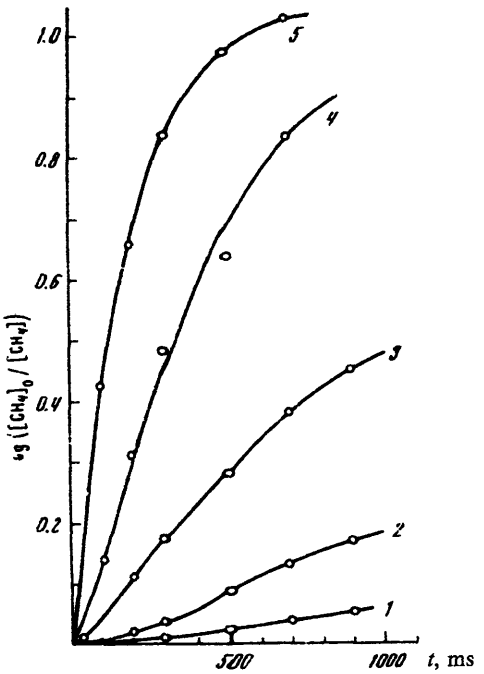


Figure 6. The influence of temperature on the kinetics of the decomposition of methane in the initial period; pressure 740 torr; methane concentration 10%;[35] T (K): *1*, 1323; *2*, 1373; *3*, 1423; *4*, 1473; *5*, 1523.

Using a radiochemical method,[49–51] the influence of the addition of 0.5–3% of acetylene, ethylene, and ethane on the pyrolysis of methane at T = 1293 and 1343 K was studied systematically. A clear accelerating effect of the C_2 hydrocarbons was observed in all cases, but, as in the study of Germain and Vaniscotte,[27] the effectiveness of the additives fell appreciably as their concentration approached 3%. Apparently further increase in the concentration of the additive has only a weak effect on the pyrolysis.

Added hydrocarbons exert the greatest influence on the yield of hydrogen for short reaction times. For example, in the pyrolysis of methane at 1293 K for 1.96 s, the presence of 1.5% of ethane increases the yield of hydrogen by a factor of approximately 10.[51] The yield of C_2 hydrocarbons can also increase severalfold under these conditions. With increase in the reaction time (8–8.5 s) and especially at a higher temperature (1343 K), the addition of hydrocarbons has almost no effect on the yield of hydrogen and C_2 hydrocarbons. In all three cases, the use of initiating additives with the ^{14}C radioactive isotope results in almost the entire radioactivity being concentrated in methane even after the shortest period of observation. This agrees well with the concept of the leading role of the CH_3 radicals in the pyrolysis, whose ready formation on decomposition of C_2 hydrocarbons is apparently responsible for the initiating effect in the initial period of the pyrolysis of methane.

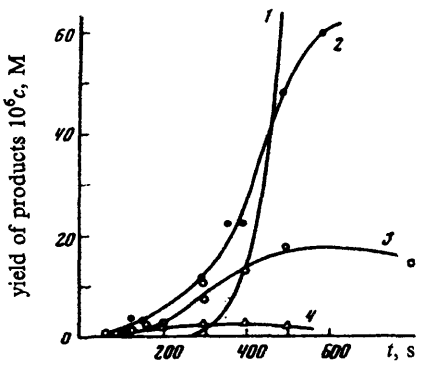


Figure 7. The yield of certain methane pyrolysis products at T = 1118 K and P = 307 torr;[2] products: *1*, carbon; *2*, C_2H_6; *3*, C_2H_4; *4*, C_4H_6.

V. The influence of hydrogen on the pyrolysis of methane

The inhibiting effect of hydrogen on the pyrolysis of methane was already established by Holliday and Exell[15] and Wheeler and Wood,[20] who explained it by the formation of a layer of adsorbed hydrogen on the reactor surface. According to the authors, this layer does not allow the heterogeneous pyrolysis of methane to go to completion, which results in the establishment of a false equilibrium in the system which is far from thermodynamic equilibrium.[20] On the basis of the scheme involving the consecutive dehydrogenation of methane [Eqns. (3)–(5)], Kassell explained the inhibiting effect of hydrogen by the occurrence of the corresponding reverse hydrogenation reaction, which enabled him to obtain, in terms of the approximation of quasi-stationary concentrations, a relation for the rate of pyrolysis, namely $W \propto [CH_4]^2/[H_2]^3$, describing satisfactorily the experimental results which he obtained in a static reactor at T = 1033 K. The only study where the accelerating effect of hydrogen was reported was that of Gordon,[34] who described the pyrolysis of methane at T = 1280 K and P = 1 atm in a porcelain

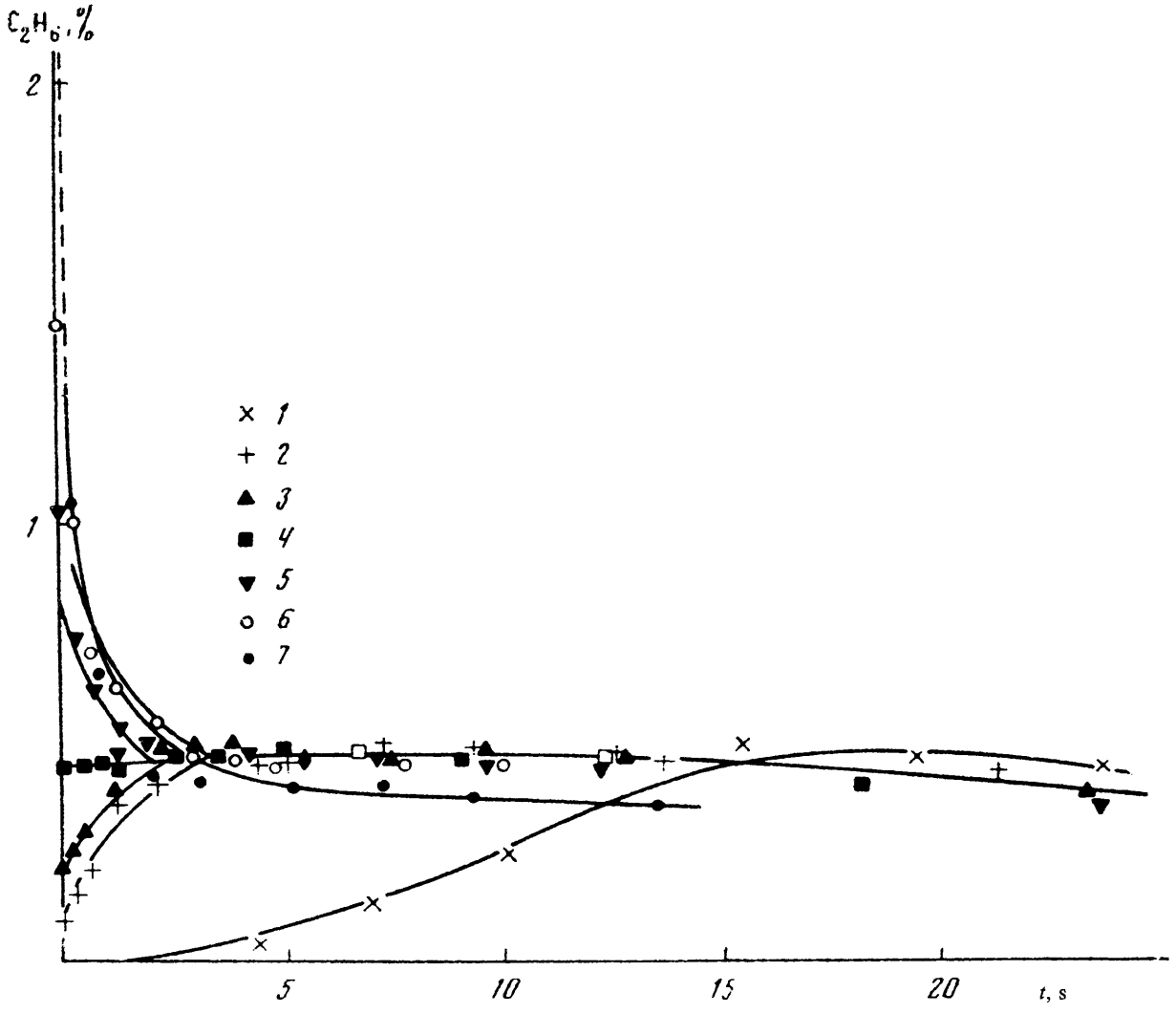


Figure 8. Kinetics of the formation and decomposition of C_2H_6 in the pyrolysis of methane at different initial C_2H_6 concentrations (T = 1323 K, P = 760 torr);[45] C_2H_6 concentration (%): *1*, 0; *2*, 0.09; *3*, 0.21; *4*, 0.45; *5*, 1.02; *6*, 1.45; *7*, 4.56.

flow reactor. It was noted that the addition of 2% of H_2 accelerates the rate of the initial stage of the decomposition of methane by 20–30% (degree of decomposition of methane 1.64–3.09%). There has been yet another study[52] in which an inhibiting effect of hydrogen was not observed when the decomposition of methane was investigated by the shock wave method in the higher temperature range 1656–1695 K. This may be explained by the fact that the effect of hydrogen is associated with later stages of the reaction, which do not manage to be manifested for the short times characteristic of the processes in shock waves.

The identity of the inhibiting effects of the hydrogen formed during the reaction and specially added to the initial mixture has been demonstrated[53] at T = 1123 K, P = 150 torr, and for degrees of decomposition of methane not exceeding 1% (Fig. 9).

The influence of the addition of 50% of hydrogen on the pyrolysis of methane at 1273–1373 K has been investigated.[26] In contrast to nitrogen, the addition of which has only a slight effect on the pyrolysis, dilution of the mixture with hydrogen in proportions of 1 : 1 led to an appreciable increase in the induction period and to an approximately fivefold decrease in the maximum rate of the process (Fig. 10). However, such appreciable dilution with hydrogen and nitrogen had no effect on the process activation energy (87 kcal mol^{-1}).[26] These results have been confirmed[37] in a flow reactor at 1458 K for mixtures containing 15% of CH_4 in nitrogen and H_2/CH_4 ratios ranging from 0.1 to 2. It has been shown[39] in a static reactor at 1200 K and a pressure of 400–450 torr that dilution of methane with hydrogen in proportions of 1 : 3 diminishes the maximum concentration of ethylene in the course of the reaction by a factor of 10–15 and entails a decrease in the overall rate of pyrolysis by a factor of 2–3. The formation of ethane and acetylene under these conditions could not be detected at all (volume concentration < 0.01%).

In a number of studies devoted to practical aspects of the pyrolysis of methane, the influence of dilution of the reaction

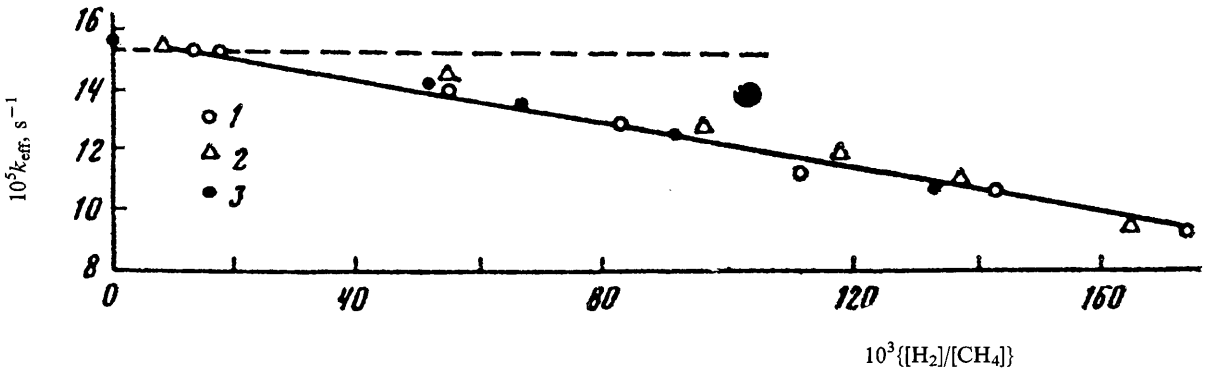


Figure 9. Dependence of the effective unimolecular rate constant k_{eff} for the decomposition of methane at 1123 K on the degree of accumulation of H_2 in the reacting gas:[53] *1*, P = 150–162 torr, H_2 added to the initial mixture; *2*, P = 101.0 torr; *3*, P = 158.3 torr, H_2 accumulating in the reacting gas.

mixture with hydrogen on the yield of acetylene in this reaction was investigated. Kunugi et al.[30] carried out the process in a quartz flow reactor, filled with lumps of quartz, in the temperature range 1373–1673 K. The dependence of the yield of acetylene on the dilution of methane with hydrogen is illustrated in Fig. 11. Evidently, the yield of acetylene increases with increase in the hydrogen/methane ratio and reaches a maximum when the ratio is approximately 2.5 at 1473 K and approximately 3.5 at 1573 and 1673 K. With increase in the hydrogen/methane ratio, the time required for the attainment of the maximum yield of acetylene also rises. The increase in the yield of acetylene on dilution with hydrogen, which clearly diminishes the rate of pyrolysis, is associated with the fact that it suppresses to an even greater extent the rate of formation of hydrocarbon products from acetylene. It may be that the latter process is heterogeneous and takes place when hydrogen interacts with the soot deposits in the system.[33]

Yampol'skii et al.,[42] who investigated the pyrolysis of methane in a graphite flow reactor for high dilutions with hydrogen (H_2/CH_4 up to 21) and at high temperatures (2003–2173 K) also concluded that hydrogen inhibits certain heterogeneous processes associated with the pyrolysis of methane. Under these conditions, dilution with hydrogen reduced the formation of carbon deposits in the reactor and diminished the concentration of unsaturated C_3–C_4 hydrocarbons in the reaction products, increasing simultaneously the yield of acetylene. However, the decrease in the yield of carbon deposits on dilution of methane with hydrogen was attributed[42] primarily to the selective inhibition of the direct heterogeneous decomposition of methane into carbon and hydrogen.

A marked influence of hydrogen on the heterogeneous decomposition of methane at 1088–1373 K has been observed[43] in a reactor with a high S/V ratio (up to 10^5 cm^{-1}). However, the effect diminishes with increase in temperature. Thus at 1073 K the addition of 10% H_2 reduces the rate of formation of pyrocarbon by a factor of 140, while at 1573 K the decrease is only by a factor of 5. According to the hypothesis put forward by Makarov and Pechik,[43] the much stronger inhibiting effect of hydrogen under the conditions of pure heterogeneous pyrolysis is associated with the fact that under these conditions the inhibition is by atomic hydrogen, while in homogeneous pyrolysis the inhibitor is molecular hydrogen.

VI. Dependence of the process on the concentration of methane and on pressure

Data concerning the influence of the concentration of methane on its pyrolysis have been obtained in a number of studies. An appreciable influence of 50% dilution of methane by nitrogen or water vapour on the rate of pyrolysis was not observed in a study[34] at P = 1 atm and 1280 K. A similar dilution of methane with nitrogen in proportions of 1:1 and 1:2 at 1273–1373 K led to a slight increase in the degree of decomposition of methane (Fig. 10).[26] The reverse effect was observed in a study[27] where an increase in the methane concentration in nitrogen in a flow reactor from 15 to 25% (T = 1373 K, P = 1 atm) resulted in a slight (~10%) increase in the degree of its decomposition for a fixed observation time. On the other hand, in another study,[35] when the concentration of methane in helium was increased from 1 to 10%, the degree of its decomposition in a porcelain flow reactor at T = 1473 K and P = 740 torr remained virtually constant. Only for short reaction times was an increase in the degree of decomposition with increase in the methane concentration observed, but it was so slight that the authors themselves expressed doubts about the reliability of the effect. The contradictory nature of the data presented above combined with the smallness of the effect in those cases where it was observed apparently mean the dilution with inert gases in the above temperature range at atmospheric pressure hardly affects the pyrolysis of methane.

The dependence of the rate of pyrolysis of methane on pressure is related primarily to the pressure dependence of the reaction rate constant:[38,54]

$$CH_4 \rightarrow CH_3 + H. \qquad (6)$$

It has been established[55] that this transitional range of pressures in the above temperature range extends almost up to 500 atm. Fig. 12 illustrates the increase in the unimolecular rate constant for the pyrolysis of methane with pressure, observed[39] in the range 115 to 700 torr at T = 1100 and 1200 K. Although in certain early studies, for example, those of Kassel[14] (pressure range 13.0–296.4 torr, temperature 1008 K) and Shantorovich and Pavlov[53] (low degrees of conversion not exceeding 2–2.5%, methane pressure range 28.7 to

232.0 torr, temperature 1123 K), no pressure dependence of the rate of pyrolysis of methane was observed, nevertheless, such a dependence undoubtedly exists.

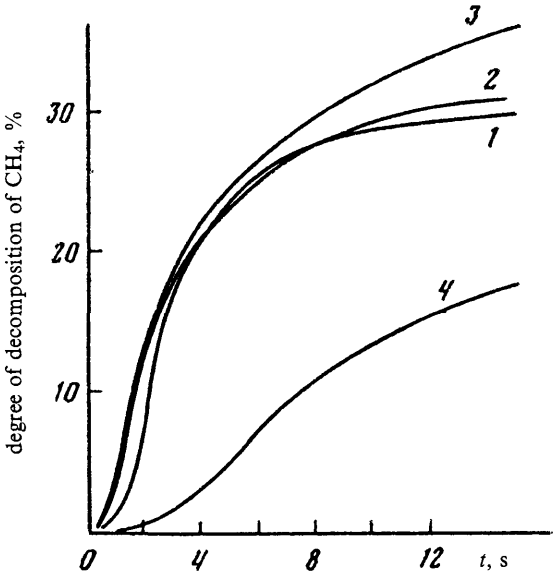


Figure 10. Kinetics of the decomposition of methane on dilution of the mixture with N_2 and H_2 (T = 1273 K, P = 1 atm):[26] *1*, 100% CH_4; *2*, CH_4/N_2 = 50/50; *3*, CH_4/N_2 = 33/66; *4*, CH_4/H_2 = 50/50.

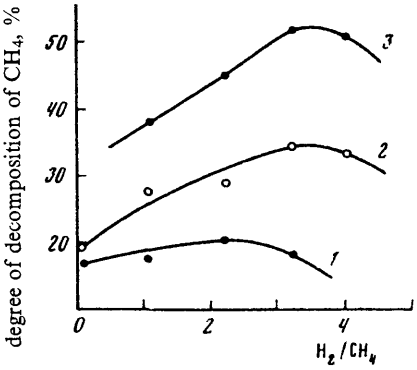


Figure 11. Dependence of the degree of conversion of methane into C_2H_6 on the H_2/CH_4 ratio at different temperatures (T, K):[30] *1*, 1473; *2*, 1573; *3*, 1673.

VII. Composition of the methane pyrolysis products

Thermodynamic calculations of the equilibrium composition of the gaseous pyrolysis products (of the gaseous C/H system), taking into account the existence of more than 70 seperate components, have been carried out[56] for C/H ratios from 1/10 to 3, at temperatures of 500–5000 K, and at pressures of 0.1, 1.0, and 10 atm. Calculations taking into account the formation of solid carbon were performed separately. In all cases the main gaseous product in the relevant temperature range is H_2 (up to 70%) (Fig. 13). In this temperature range the stable hydrocarbons with a small number of atoms reached their maximum concentrations, after which their concentrations decreased monotonically with increase in temperature. At T > 1400 K the dominant hydrocarbon is acetylene (Fig. 13), whose concentration reaches 25% of the total volume of the gas phase. The concentrations of the remaining stable hydrocarbons are appreciably lower and even for ethylene the maximum concentration does not reach 1%. In this temperature range, there is an appreciable amount of methane at thermodynamic equilibrium in the gas phase. The equilibrium concentrations of atoms and radicals are extremely low at such temperatures. When the ratios C/H and the pressure do not vary appreciably in this system, the situation does not change significantly.

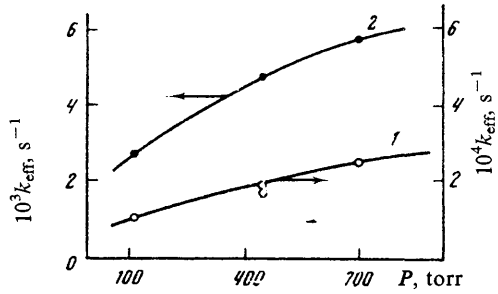


Figure 12. Dependence of the effective unimolecular rate constant k_{eff} for the decomposition of methane on pressure at different temperatures (T, K): *1*, 1100; *2*, 1200.[39]

The picture changes sharply when account is taken of the formation of the solid carbon phase. In this case, in the temperature range from 1000 to 3000 K the gas phase consists almost exclusively of hydrogen (~100%). The equilibrium concentration of methane falls sharply (<1% at T > 1200 K) and the concentrations of all the remaining hydrocarbons decrease. Since it is difficult to claim that the solid phase was taken adequately into account in the above calculations (one of two ratios, C/H = 10^3/1 or 10/1, was adopted for the composition of the solid phase), the practical value of the results of these calculations is primarily an indication of the qualitative trends associated with the presence of the solid phase. However, the real formation of the solid phase precludes a direct comparison with experiment of the results of thermodynamic calculations on a single-phase system, although it may be that such single-phase description reflects to some extent the ratio of the gaseous products of the initial stage of pyrolysis. Thus the uncertainty of the results of the thermodynamic calculations, associated with the inadequate allowance for the formation of the solid phase during pyrolysis, necessitates the analysis of the available experimental yields of the final methane pyrolysis products.

The kinetics of the formation and the final composition of the gaseous methane pyrolysis products in the range of moderate temperatures have been investigated in many studies. Germain and

Vaniscotte[25] studied the formation of C_2 hydrocarbons at 1273 K at atmospheric pressure in quartz reactors with S/V ranging from 2.8 to 25.3. Under these conditions, the concentration of methane at the end of the experiment was about 50% of the volume of the gas phase, the concentration of ethylene was less than 1%, and the concentrations of ethane and acetylene were approximately an order of magnitude smaller (slow conversion of methane and of the remaining products continued also for the maximum observation time, which was 20 s in the given study). The concentrations of all the C_2 hydrocarbons passed through a maximum, the time of attainment of which diminished with increase in S/V, but neither the size of the maxima ($\sim$1.5% of the volume of the gas phase for ethylene) nor the degree of decomposition of methane depended significantly on this ratio. Similar results were obtained by Schneider[45] (temperature range 1323–1823 K). An increase in the maximum concentrations of ethylene and acetylene is observed with increase in temperature—$[C_2H_2]_{max}$ is approximately 10% at 1833 K and approximately 1% at 1323 K. Small amounts of added ethane (up to 4.5%) have a similar effect as an increase in S/V, diminishing the time of attainment of the maximum concentration of C_2 hydrocarbons but not affecting its value.[45]

The kinetics of the reaction of methane and the formation of the principal gaseous products in the temperature range 1100–1400 K in a static reactor at a pressure of 440 torr have been investigated.[39] The kinetic curves for T = 1200 K are presented in Fig. 14*a*. At this temperature the pyrolysis virtually terminates after 5 min and the final degree of conversion of methane is about 50%. Direct measurement of the final pressure and the decrease in the relative concentration of the nitrogen added to the mixture as a permanent reference standard ($\sim$10%) indicate a pressure rise by about 22% (Fig. 14*b*). Such a change in pressure combined with the insignificant content of C_2 hydrocarbons in the pyrolysis products lead to the formula CH for the solid product remaining on the walls of the reactor and partly deposited on the cold connecting tubes during its evacuation. The principal gaseous hydrocarbon pyrolysis product in this temperature range is ethylene, but, whereas at 1100 K its concentration exceeds by a factor of approximately 10 the concentrations of the hydrocarbons next in importance (acetylene and ethane), at 1300 K the concentrations of ethylene and acetylene are almost comparable. Nevertheless, even at 1300 K the maximum concentrations of these products remain at the level of 1% of the total volume of the mixture. Although the maximum concentration of ethane increases somewhat with increase in temperature to 1300 K compared with the value at T = 1100 K, it is still amost an order of magnitude lower than the maximum concentration of ethylene.

At 1300 K the maximum concentrations of ethylene and acetylene are attained almost simultaneously but later than the attainment of the maximum concentration of ethane, which is consistent with Gordon's data.[34] At 1200 K, the maximum concentrations of all three C_2 hydrocarbons are attained almost simultaneously (Fig. 14*a*). Apparently the dehydrogenation scheme involving the successive transformation of methane during pyrolysis,[14] which describes satisfactorily the kinetics in the region of low temperatures (T < 1000 K), [2] becomes less suitable with increase in tempereature. An increase in temperature entails a sharp shortening of the time of attainment of the maximum concentrations of ethylene and acetylene—from 60 s at 1200 K to 5 s at 1300 K. At 1100 K the ethane and ethylene concentration profiles have very broad maxima, which are virtually converted into quasi-stationary concentrations, attained after 7–15 min and maintained for periods exceeding 30 min. Only the concentration of acetylene passes through a maximum at t = min and then falls sharply, so that at t > 15 min acetylene cannot be detected at all.[39] The time of attainment of the maximum in the ethane concentration coincides with the time of attainment of the maximum rate of decomposition of methane (induction period) (Fig. 14). This is clearly seen also on comparing the corresponding kinetic curves obtained under flow conditions at a higher temperature (1373 K).[35]

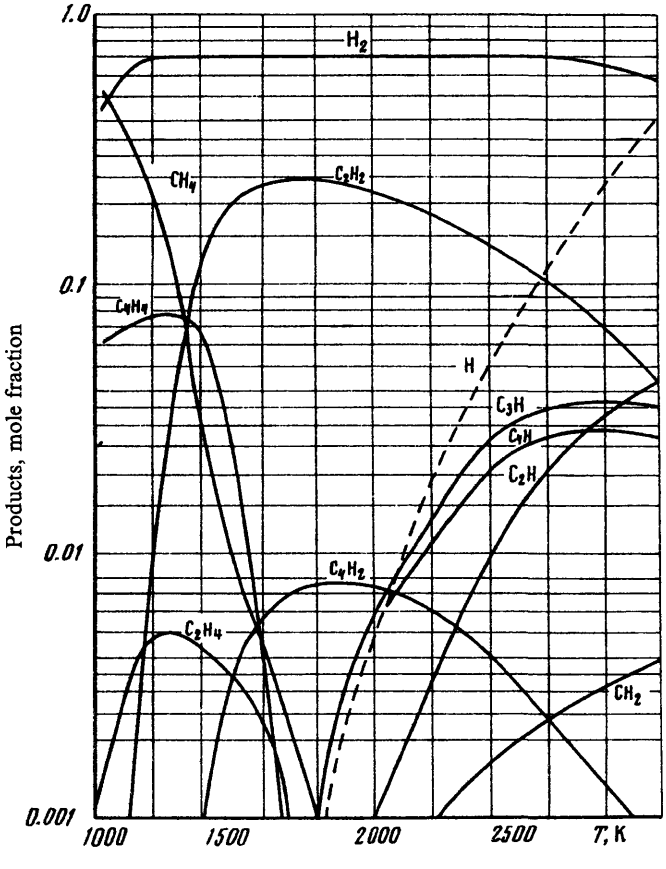


Figure 13. Results of the thermodynamic calculation for the C/H equilibrium system at temperatures in the range 1000–3000 K without taking into account the formation of a solid phase; P = 0.1 atm; C/H = 1/4 (methane).[33,56]

The temperature variation of the yield of the main final gaseous methane pyrolysis products is illustrated in Fig. 15. The results obtained can be compared with those of thermodynamic calculations[56] (Fig. 13) although the system is apparently still fairly far from thermodynamic equilibrium. Whereas the final concentrations of methane and hydrogen are virtually identical with the values calculated without taking into account the solid phase, the final amounts of C_2 hydrocarbons are several times lower than the calculated values. The results of the calculations of the equilibrium composition taking into account the solid phase[56] show that, in the experimental temperature range used by Arutyunov et al.[39]

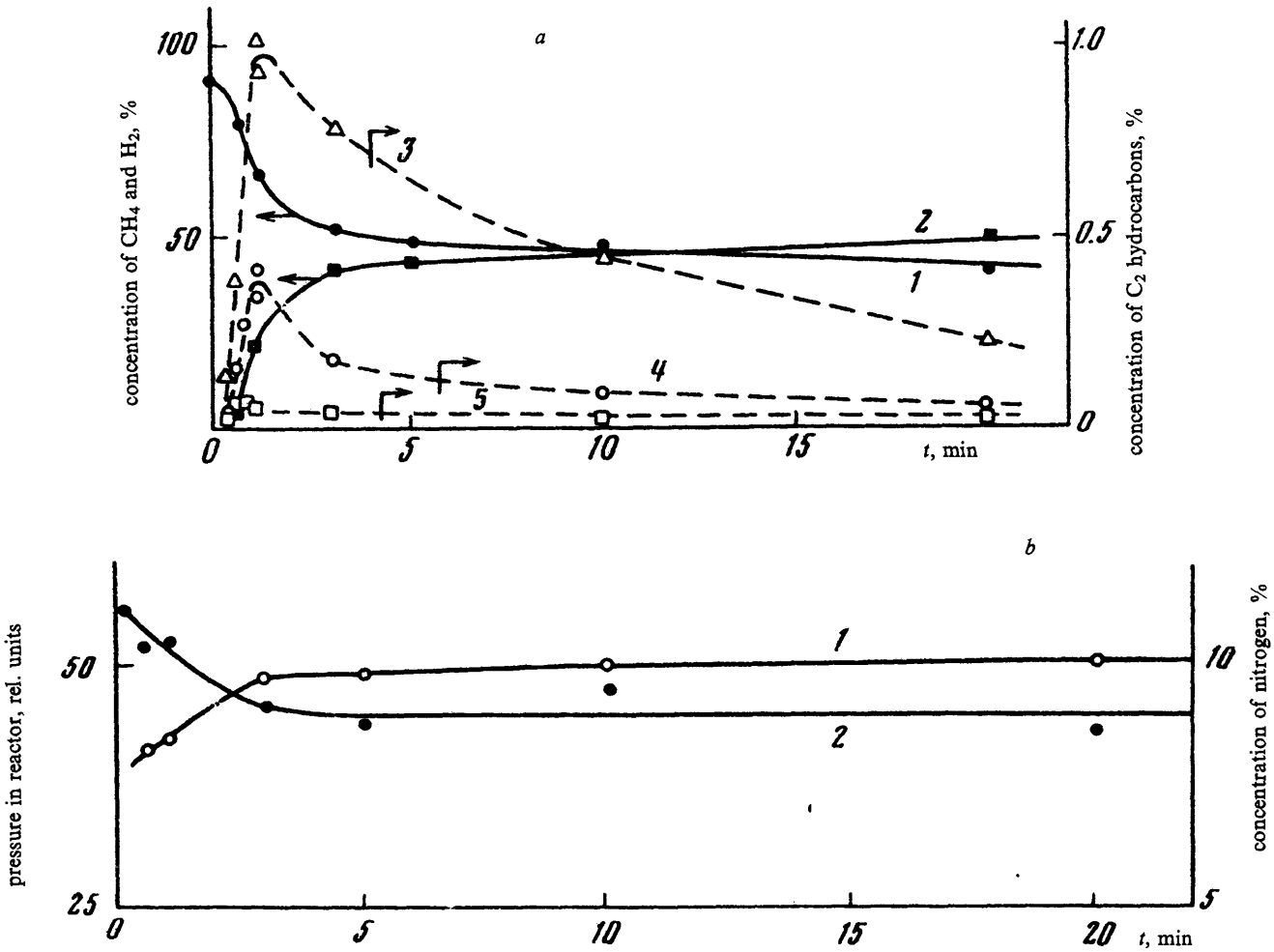


Figure 14. Kinetics of the variation of the concentrations of the principal gaseous products (*a*) and variation of the pressure and concentration of nitrogen in the pyrolysis of methane (*b*); initial mixture: CH_4 (90%) + N_2 (10%); T = 1200 K, P = 438 torr;[39] *a*: *1*, CH_4; *2*, H_2; *3*, C_2H_4; *4*, C_2H_2; *5*, C_2H_6; *b*: *1*, variation of pressure; *2*, variation of N_2 concentration.

(1100–1400 K), almost the only gaseous product should be hydrogen, since even the calculated residual concentration of methane is less than 1%, and those of the remaining hydrocarbons are lower by several orders of magnitude. The cause of such appreciable discrepancy may be either inadequate allowance for the composition of the solid phase in the calculation or appreciably longer times of attainment of equilibrium in the heterophase system.

The temperature variation of the yields of methane, ethylene, and acetylene obtained in a flow reactor at a pressure of 5–10 atm and over a very wide temperature range (1573–2473 K) has been published.[42] The detection of small amounts of C_3–C_4 products (propene, allene, methylacetylene, buta-1,4-diene, and vinylacetylene) is indicated in the above communication. These substances are the products of the thermal transformation of ethylene and acetylene at high temperatures. At lower temperatures, a wide range of high-molecular-weight products can also be detected.

Chen and Back[46] followed the kinetics of the formation of pyrolysis products ranging from ethylene to fluoranthene at 1118 K and 307 torr. The maximum concentration of fluoranthene reached $\sim 1.5 \times 10^{-6}$ M, which is only an order of magnitude lower than the maximum concentration of actylene under these conditions. The formation of the solid product followed directly the formation of the most complex of the aromatic compounds detected—fluoranthene. Since in the overall amount of aromatic compounds formed on pyrolysis of methane on silica gel those with an even number of carbon atoms constitute 97%,[57] it was concluded that they are formed from C_2 hdyrocarbons. Apparently the mechanism of the formation of polyatomic hydrocarbons involves both radical and molecular processes, their relative roles in the formation of any product depending on the process temperature and pressure. Products with a low molecular weight are formed mainly in radical reactions. The rate of formation of large polyatomic molecules can be determined by addition reactions of the Diels–Alder type.[2] We shall not dwell on a detailed consideration of the mechanisms and

kinetics of the formation of macromolecular pyrolysis products and solid carbon, because these questions are outside the scope of the present review.

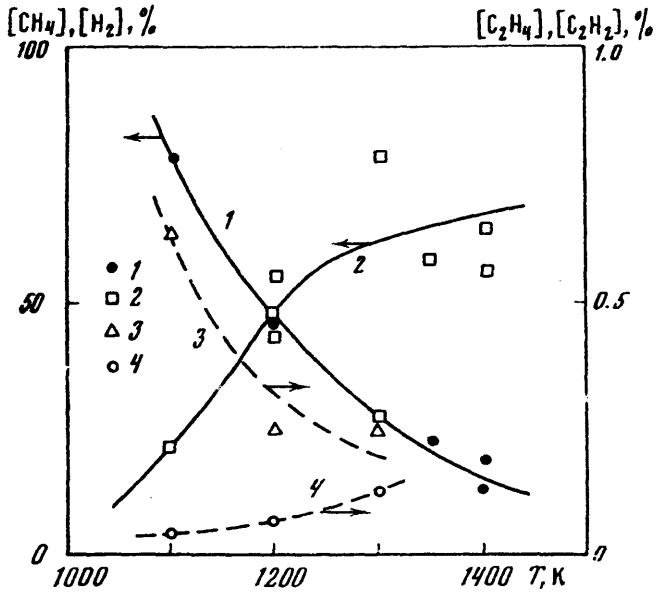


Figure 15. Temperature variation of the yields of the principal gaseous methane pyrolysis products:[39] *1*, CH_4; *2*, H_2; *3*, C_2H_4; *4*, C_2H_2.

Since the concentrations of C_2 hydrocarbons pass through a maximum in the course of the pyrolysis of methane (Fig. 14*a*), there is in principle a possibility of obtaining them in amounts greatly exceeding the values corresponding to thermodynamic equilibrium. Fig. 16 presents the maximum degrees of conversion of methane into ethylene and acetylene $C_{max}/\Delta[CH_4]_{t_{max}}$ obtained by Arutyunov et al.[39] The results of experiments at higher temperatures are also presented.[30] At 2100 K the maximum concentrations of ethylene and acetylene reach respectively ~35 and ~65%,[58] i.e. in the region of 2000 K the maximum concentrations C_{max} reach their highest values.

VIII. Temperature dependence of the pyrolysis of methane

The temperature dependence of the effective unimolecular rate constant for the pyrolysis of methane has been determined in numerous studies, the activation energies obtained varying from 63 to 104 kcal mol^{-1}. Many studies undertaken to determine the rate constants and activation energies for the initial stage of the pyrolysis [reaction (6)] in the range of temperatures from 1700 to almost 3000 K were carried out by the shock wave method.[59] The rate constant for reaction (6) was determined by Chen et al.[38] for the region of 1000 K. All these results refer to a transitional range of pressures, which makes it possible to determine also the pressure dependence of the rate constant for reaction (6). The recommended values of this constant for the temperature range from 300 to 2500 K have been published,[59] the recommended activation energy amounting to 104.4 kcal mol^{-1}. In the region of moderate temperatures 1100–1700 K, the experimental activation energies for the pyrolysis of methane differ from the activation energy for reaction (6) and are close to 80–85 kcal mol^{-1}. Certain activation energies obtained for this process in the range of moderate temperatures are given blow (in kcal mol^{-1}): 79.4,[14] 85,[53] 87,[26] 87.3 [45] and 83.2.[42] Fig. 17 illustrates the temperature variation of the effective unimolecular rate constant for the decomposition of methane obtained by Arutyunov et al.[39] Evidently, although the rate of pyrolysis depends on the pressure, the activation energy remains constant at 82 ± 3 kcal mol^{-1}. The expression obtained[39] for the effective unimolecular rate constant for the pyrolysis of methane, i.e.

$$k_{eff} = (3.0 \pm 1.0) \cdot 10^{12} \exp[-(82\,000 \pm 3000)/RT],\ s^{-1}$$

described satisfactorily the majority of the experimental results for the temprature range 1100–1700 K.

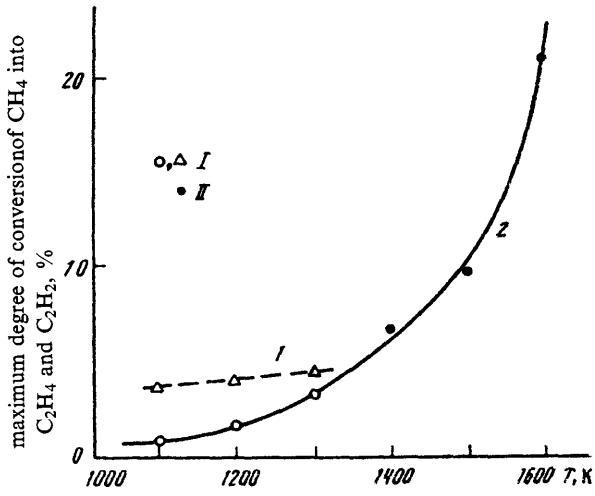


Figure 16. Maximum degrees of conversion of methane $C_{max}/\Delta[CH_4]_{t_{max}}$ into C_2H_4 (curve *1*) and C_2H_2 (curve *2*) at P = 440 torr: *I*, according to the data of Arutyunov et al;[39] *II*, according to the data of Kunugi et al.[30]

Fig. 18 presents the literature data for the rate of pyrolysis of methane under various conditions in the temperature range 1100 to 1700 K. Mathematical treatment of these results by the method of least squares yields a pyrolysis activation energy of 82 kcal mol^{-1}, which agrees with the value obtained by Arutyunov et al.[39] It is readily seen that, with the exception of several clearly deviating results, the entire set of experimental data is described satisfactorily by the expression quoted above, which may be recommended for these conditions.

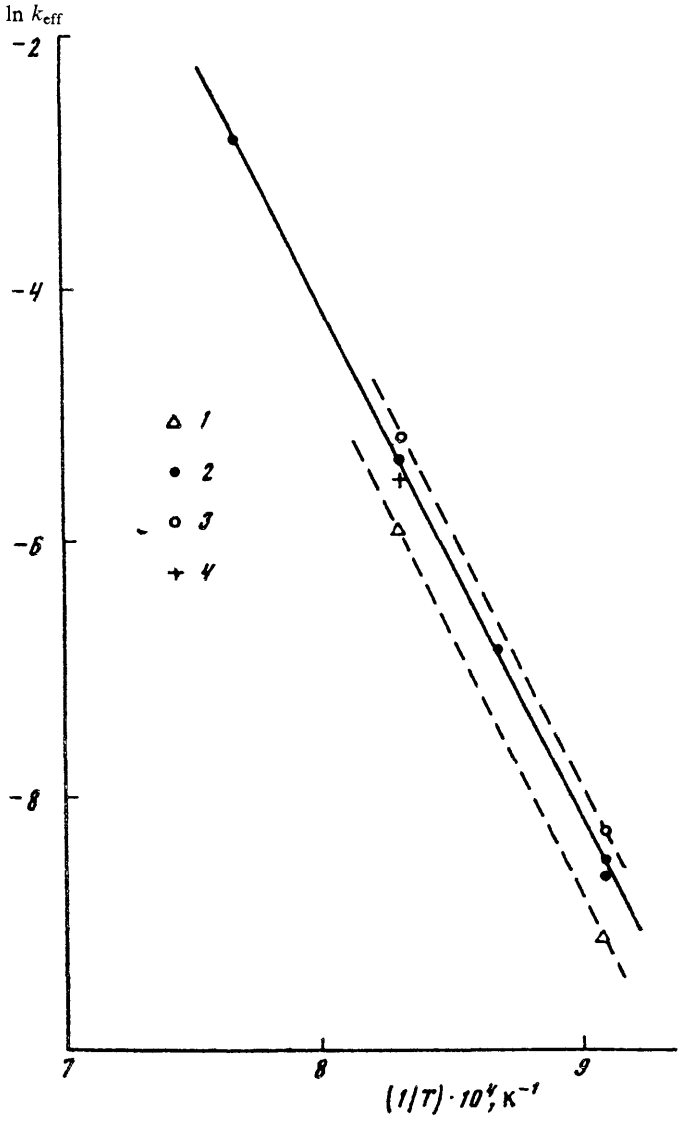


Figure 17. Temperature variation of the effective unimolecular rate constant for the decomposition of methane in reactors 46 mm (*1*–*3*) and 21 mm (*4*) in diameter at different pressures (*P*, torr):[39] *1*, 115; *2*, 440; *3*, 700; *4*, 435.

IX. The mechanism of the pyrolysis of methane

There is at present no generally accepted mechanism of the pyrolysis of methane up to the carbon formation stage. The problem of devising such a mechanism is extremely complex, since it is necessary to take into account a large number of parallel processes occurring simultaneously in this complex system, their relative roles varying markedly as the external conditions are altered. At moderate temperatures, the initial stages of the pyrolysis of methane are apparently fairly well described by a simple scheme taking into account the parallel occurrence of chain dehydrogenation and methylation reactions, which explains and describes the formation of both simple hydrocarbons (C_2) and the highest unsaturated hydrocarbons with increasing molecular weight and descreasing hydrogen content up to the formation of carbon.[2] The key hypotheses on which the above scheme is based are (1) the dominant role of methyl radicals, chain reactions with the latter constituting the main pathway leading to the removal of all the hydrocarbon products, (2) the insignificant role of the thermal dissociation of secondary hydrocarbon products and the mainly thermal decomposition of higher hydrocarbon radicals, and (3) the involvement in the reaction with methane molecules of almost all the hydrogen atoms formed. These hypotheses are entirely realistic for temperatures in the region of 1000 K and a little above.

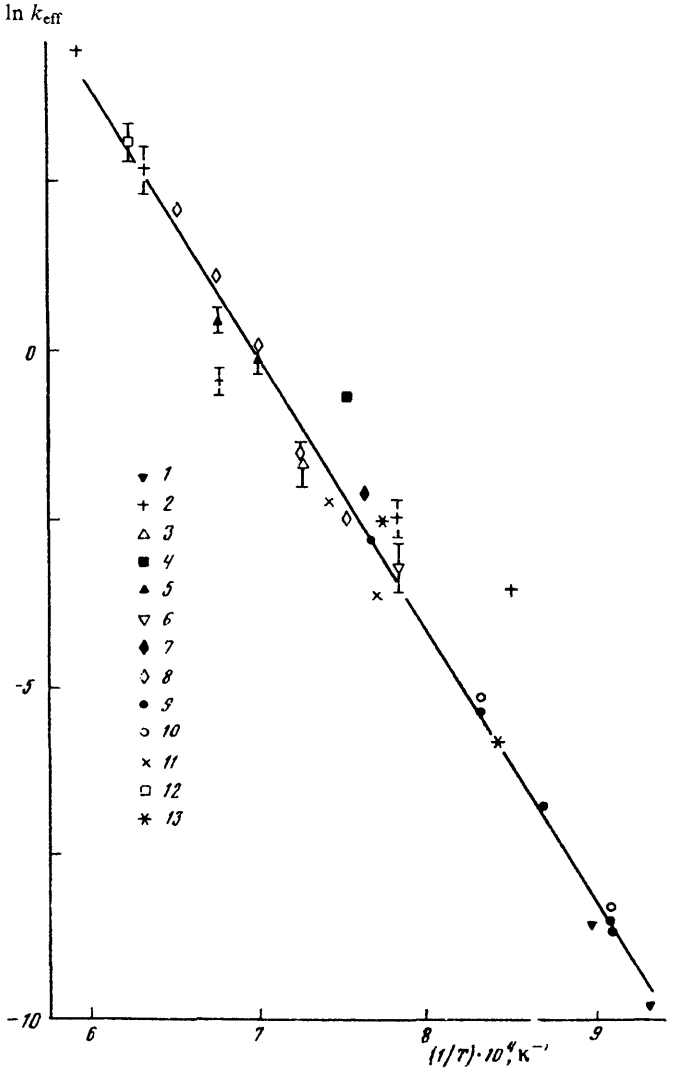


Figure 18. Temperature variation of the effective unimolecular rate constant for the decomposition of methane in the temperature range 1100–1700 K plotted on the basis of the set of literature data: *1*, Ref. 14; *2*, Ref.16; *3*, Ref. 19; *4*, Ref. 20; *5*, Ref. 21; *6*, Ref.25; *7*, Ref.34; *8*, Ref. 35; *9*, Ref. 39 (P = 440 torr); *10*, Ref. 39 (P = 700 torr); *11*, Ref. 43; *12*, Ref. 60; *13*, Ref. 61.

The mathematical modelling of the pyrolytic process carried out[47] on the basis of this scheme for $T = 1038$ K and $P = 433$ torr made it possible to explain the phenomenon of autocatalysis in the formation of ethane, which was observed experimentally by Chen et al.[38] Calculations confirmed the hypothesis[2] that the most important causes of autocatalysis are secondary initiation and subsequent methylation propagated by the addition of methyl radicals to olefins. The same model makes it possible to describe satisfactorily the experimental profiles for the formation of ethane, ethylene, acetylene, and propene in the pressure range $5 < P < 50$ atm and the temperature range $1073 < T < 1148$ K in the initial stage of the reaction (up to the onset of autocatalysis).[55] According to the results of Barnes and Pratt,[55] the main cause of autocatalysis under the given conditions is secondary initiation, mainly via the reaction

$$C_3H_6 \rightarrow C_2H_3 + CH_3.$$

However, the model proposed[47] has been criticised[48] because of the lack of consistency in many instances between the constants adopted for the forward and reverse reactions. After the adjustment for such consistency in the case of reverse reactions, the results changed significantly and the phenomenon of autocatalysis vanished from the model. A new mechanism has been proposed[48] for the pyrolysis, according to which the acceleration of the reaction is achieved as a result of the dissociation of cyclopentadiene formed in large amounts even for the very lowest degrees of conversion of methane (~0.1%). However, even if this mechanism is the real cause of the autocatalysis at 1000 K, it is difficult to say to what extent it is valid at higher temperatures, especially those exceeding 1500 K.

There exist several models† for the description of the high-temperature pyrolysis under shock wave conditions. However, the question of the modelling of the pyrolysis in the range of moderate temperatures remains essentially open.

* * *

The data considered in the present review refer to the study of the pyrolysis of methane in the range of moderate temperatures which is of greatest practical importance. Attention was concentrated on the process kinetics, the composition of the products, their influence on the course of the process, and the role of external factors (pressure and temperature) on the reactor surface. The limited size of this review precluded the consideration of many aspects of the pyrolysis of methane which are of practical importance, in particular, the questions of promotion, for example, by halogen compounds. All the technological aspects of the process remain outside the scope of the review. Apparently it would be desirable to devote a separate review to these questions. As regards further investigations, in our view attention should be concentrated on the construction of a quantitative kinetic model of the pyrolysis of methane in the region of moderate temperatures taking into account all the reliably established facts, including the occurrence of autocatalysis, the acceleration by hydrocarbon additives, and the influence of hydrogen on the yield of hydrocarbons, the rate of the process, and the composition of at least the principal pyrolysis products. The existence of such a model would make it possible to predict reliably the course of high-temperature processes involving methane, which is extremely important bearing in mind the rapid expansion of the range and scale of the industrial applications of natural gas.

† See, for example, one of the latest studies.[3]

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Translated from *Uspekhi Khimii* **60** 2685–2717 (1991) U.D.C. 547.313.2-31

Inorganic anion exchangers

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ABSTRACT. Data on inorganic substances showing basic and anion-exchange properties have been reviewed. The structural dependence of the number and strength of the basic centres has been discussed.

The bibliography contains 162 references.

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I. Introduction

Ion exchange materials are widely used in the most varied spheres of human activity. Ion exchange processes are acquiring particular importance in attempts to create waste-free technologies and closed technological schemes.

The need to prepare and purify water, to purifiy effluents and air from harmful impurities, and to obtain pure substances has for the last 50 years stimulated the development of research in the field of ion exchange and the production of new ion exchangers. The development of the industrial production of various ion exchangers has been no less intensive. There has been an extremely rapid increase in the number of publications on the synthesis and production of ion exchangers and the theory and practice of ion exchange, and a number of reviews have appeared.[1–3]

A basis for this rapid development has been provided by progress in the field of macromolecular compounds. The great majority of ion exchangers that have been studied, to say nothing of those used in industry, have been based on organic polymers.

It is appropriate to remember that the ion exchange process was first detected and studied in inorganic compounds—soils, earth, clays, and zeolites. A new stimulus to the development of ion exchange in inorganic materials was provided by progress in nuclear energy and radiochemistry. It became necessary to produce ion exchange materials with high stability to heat and radiation. It also became clear that the development of polymeric materials containing functional groups with a higher stability to heat and radiation is not promising,[4] since the stability of an ion exchanger is determined by the stability of the polymer matrix.[5]

Data on the properties of compounds such as aluminosilicates, oxides, hydroxides, sulphides, phosphates, salts of heteropolyacids, ferrocyanides, graphite oxides, and complex hydrated oxides have now been accumulated and systematised.[6,7] Zeolite aluminosilicate ion exchangers have been particularly well studied.[8,9]

Zeolites and the other compounds listed above, however, are almost all acidic substances, that is they are cation exchangers. Inorganic anion exchangers are much less familiar, and there are no published data on their use in industry.

The aim of the present review was to systematise published data on inorganic anion exchangers.

II. Terminology

Traditionally,[10–12] an "anion exchanger" is an ion exchanger containing fixed ions (or ionogenic groups) and exchanging anions. An ion exchanger is a two-phase heterogenous system, capable of dissociation and containing fixed ions, etc.

This definition is not comprehensive, however. In general, all anion exchangers are solid bases (ion exchangers in the salt form can be regarded as potential solid bases). The term solid base can be applied to a substance which is a proton acceptor or an electron donor.[13]

We shall use the term anion exchanger to describe a solid insoluble substance which contains Brönsted or Lewis basic centres and which shows basic properties over a wide pH range. It is assumed that the basic form of an anion exchanger can be obtained from the salt form by ion exchange.

The complete characterisation of an anion exchanger should include the following parameters:

1, the total concentration (mmol g^{-1}) of basic centres relative to the highest theoretically possible value;

2, the concentration of basic centres on the surface of the anion exchanger and in its bulk;

3, the strength distribution of the basic centres;

4, the physicochemical properties (specific surface, pore volume and radius, chemical, thermal, and radiation stability, accessibility of the centres in relation to steric factors);

5, the ion exchange properties (the form of the isotherms, and selectivity coefficients and series).

III. Determination of the basic properties of anion exchangers

To obtain a picture of the basic properties of solids, it is necessary to know the total quantity, nature, and strength distribution of the basic centres.

A solid base can convert an adsorbed acidic molecule into the conjugate base form. The basic centre may be a proton acceptor, taking them from the adsorbed molecule (Brönsted basic centre) or an electron donor, transferring them to the adsorbed molecule (Lewis basic centre).

The most complete information on the state of a surface is given by the indicator method. When an electrically neutral acidic indicator in a non-polar solvent is adsorbed on a solid base, the colour of the indicator changes to that characteristic of the conjugate base form. This indicates the presence of centres whose basic strength is sufficient to transfer electrons to the acid molecule.

By successively adsorbing indicators with different pK_a values on fresh specimens it is possible to obtain a qualitative picture of the basic strength distribution.

The concentration of basic centres (usually expressed in millimoles per unit weight or unit surface area) is determined quantitatively by titrating a suspension of the powdered solid base in a non-polar solvent with an acid solution. The quantity of acid required to convert the indicator into the acidic form corresponds to the number of basic centres whose basic strength is lower than pK_a for the indicator used in the titration. By using a range of indicators it is possible to obtain the distribution of the number of centres with respect to basic strength (Table 1).

Table 1. Indicators used to obtain information on the basic properties of solids.[7]

Indicator	Colour		pK_a
	acidic form	basic form	
Bromothymol Blue	yellow	green	7.2
2,4,6-Trinitroaniline	"	orange	12.2
2,4-Dinitroaniline	"	violet	15.0
4-Chloro-2-nitroaniline	"	orange	17.2
4-Nitroaniline	"	"	18.4
4-Chloroaniline	colourless	pink	26.5

The main disadvantage of the indicator method is that the basic strength is measured in a given specific medium, and with change in the conditions, both the concentration and the distribution of the basic centres may be quite different. Moreover, the large indicator molecules cannot penetrate to the centres inside fine pores.[9] This last restriction does not appear to be significant, however, since it is more important that the basic centres be accessible to the acid titrant, and to observe the indicator change the quantity adsorbed on the outer surface is sufficient. Thus the results obtained by titrating mercarbides with benzoic acid in the presence of Bromothymol Blue are close to those obtained by other methods, although this indicator cannot penetrate into the mercarbide pores.

A more significant limitation of the indicator method is that it cannot be used to determine the basic properties of solid anion exchangers in forms other than the hydroxide form. If the Brönsted centres are in the hydroxide form, the indicator method gives the total Brönsted and Lewis basic strength; otherwise, it gives only the Lewis basic strength.

Titration using aqueous solutions of acids makes it possible to determine the total quantity of basic centres, and Brönsted centres present in salt forms can also be titrated. Here it is necessary to be sure that the affinity of the titrant acid for the anion is appreciably greater than its affinity for the counter-ion, otherwise an equilibrium is established, and the number of centres found in this way is too low. In this case, naturally, the concentration of anions in the solution, and not the change in the pH of the medium, is followed.

In the titration with acid it is necessary to be certain that the solid framework does not break down.

The concentration of Brönsted basic centres on the surface of a solid can be estimated from data on exchange between the hydroxide groups of the surface and the anions from salt solutions.

If the number of centres is being determined for a new substance, it is necessary to carry out at least several measurements with different solutions containing different ions, since the selectivity of anion exchangers may be different.

This method can sometimes be used to determine the number of centres in a solid in different anion forms; here, the limitations are the same as those for aqueous titration with acids.

Calorimetric titration can be used to determine the basic strength by observing the increase in temperature due to the liberation of heat in the reaction of the anion exchanger with an acid in the liquid phase.

When gravimetric methods are used, gaseous acidic compounds such as phenol and carbon dioxide are used as adsorbates. After adsorption at a given pressure and temperature, the acid is desorbed from the anion exchanger, and the quantity of desorbed acid determined by DTA [12] or chromatography.[11]

Calorimetric and gravimetric methods can be used to find the quantity of Lewis basic centres and Brönsted centres in the OH form. Gravimetric methods also give a qualitative picture of the strength distribution of the centres, which can be made the basis of quantitative calculations.[11,12]

Important information on the basic strength of anion exchangers could be obtained by spectral methods. The spectra (infrared, ultrviolet, EPR) of acidic substances adsorbed on anion exchangers can be used to determine the nature of their interaction with the basic centres. The reactions of adsorbed molecules with Lewis basic centres and with hydroxide groups should give different spectra. There are no published data, however, on the spectroscopic study of the basic properties of solids.

Thus there is at present no general method for determining the nature, strength, and number of basic centres in all cases. The situation is particularly complicated if the anion exchanger is in the salt form. For a complete estimation of the basic strength of anion exchangers it is necessary to use several methods in succession. The study of the basic properties of solids should include the following stages:

1, conversion of the anion exchanger to the OH form (the degree of conversion can be followed, for example, by elemental analysis);

2, determination of the total basic strength by one of the methods;

3, determination of the Brönsted basic strength by one of the methods;

4, determination of the strength distribution of the basic centres by the indicator method;

5, conversion of the Brönsted centres to the salt form (with determination of the degree of conversion);

6, determination of the distribution of Lewis basic centres by the indicator method;

7, determination of the strength distribution of the Brönsted basic centres from the data balance.

The number of basic centres is expressed in mol g^{-1} or equiv g^{-1}; we shall use the dimensions given in the original works.

The great majority of inorganic anion exchangers are products of isomorphous replacement in the crystal lattice. The replacement of one element by another in a higher oxidation state leads to the production of an excess positive charge, whose compensation requires an anion. This structure is shown by many compounds which at present are assigned to different classes: mixed hydroxides, cyanides, insoluble salts, and inverse zeolites. We shall retain the traditional classification, although the above compounds have many similar properties; in particular, they show similar structure–property relationships.

IV. Double hydroxides

Double hydroxides form the most widespread class of inorganic anion exchangers. A very large number of representatives of this class are known, and they have been studied in considerable detail and are beginning to be used in industry. Related to the hydroxides is the class of mixed oxides, since most double oxides are obtained from double hydroxides and, most importantly, the oxides formed by heating double hydroxides with basic properties may also have a considerable number of basic centres. Moreover, it is impossible to draw a distinct boundary between oxides and hydroxides, or for that matter between mixed oxides and salts.

The discovery that preciptitating metal hydroxides form a mixture of solutions of the salts gives a new double hydroxide phase with anion exchange properties[13,14] was followed by further studies in this direction.[15–19]

For convenience, double hydroxides can be divided into three groups:

1, hydroxides formed by metal ions whose oxidation states differ by 1, for example $Ca_2Al(OH)_7$;

2, hydroxides in which the oxidation states of the metals differ by more than 1, for example $LiAl_2(OH)_7$;

3, hydroxides in which the metals have the same oxidation state, for example $MgNi(OH)_4$.

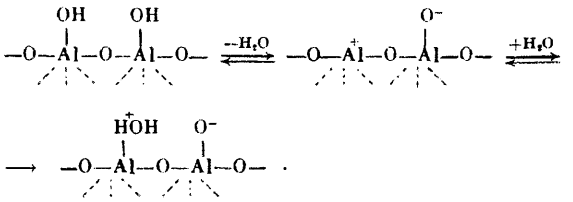
There also exist more complex hydroxides containing three or more metal cations with different oxidation states,[20] but these can be regarded as combinations of the above double hydroxides.

The structure and basic properties of complex hydroxides are best studied by regarding them as synthetic analogues of anionic clays. All clays are layer compounds made up of metal oxides. For example, clays of the simples type (kaolins) contain two layers: a tetrahedral silicate layer and an octahedral aluminate layer. At the edges and corners of each layer there are hydroxide groups, which on immersion in a salt solution can exchange with anions, but exchange between protons and various cations is also possible. Since cation exchange and anion exchange take place on the same groups, the exchange capacity of kaolins is approximately the same for cations and anions.[6]

Since clay minerals and double and other hydroxides have terminal hydroxide groups, they all are both cation exchangers and anion exchangers, and their ion exchange properties are determined primarily by the pH of the medium:

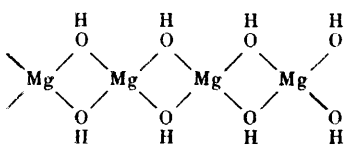
$$\underset{\text{pH}<7}{M^+ + OH^-} \rightleftharpoons \underset{\text{pH}>7}{MOH \rightleftharpoons MO^- + H^+}$$

The exchange capacity of ion exchangers in which exchange takes place on terminal groups is extremely low, and proportional to the surface area. The basic strength of these neutral hydroxides can be increased by covering the acidic centres, for example with water:[7]

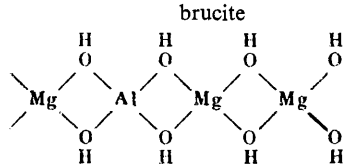


The ion exchange capacity of hydroxides increases considerably on isomorphous replacement of the metal cations. For example, the cation exchange capacity of layers of the type present in kaolins can be increased considerably by replacing Al^{3+} cations in the octahedral layer by Mg^{2+} or Fe^{2+}, and by replacing the Si^{4+} cations in the tetrahedral layer by Al^{3+}. The layers acquire a negative charge, which is compensated by alkali and alkaline earth metal cations situated between the layers, and also by solvating water molecules. These cations can be replaced by others, and this is responsible for the cation exchange properties of clay minerals. The ion exchange capacity depends on the extent of the isomorphous replacement, and in most cases it is much greater than that due only to exchange at edges and corners. Anionic clay minerals are mostly synthetic, but they are also found in nature.

Hydroxides with anion exchange properties can also be obtained by the isomorphous replacement of the cations of the basic layers. Naturally, in this case the oxidation state of the replacing cations must be greater than that of the replaced cations. For example, hydrotalcite can be obtained by the isomorphous replacement of Mg^{2+} ions by Al^{3+} ions in brucite.[15]



brucite



hydrotalcite

From the same elements it is possible to obtain both a cation exchanger and an anion exchanger. The isomorphous replacement of Mg ions by Al ions produces an excess positive charge, and therefore gives a substance anion exchange properties, and the replacement of Al ions in $Al(OH)_3$ by Mg gives cation exchangers. Thus it is always possible to calculate the degree of replacement of ions giving the greatest anion exchange capacity. This degree of replacement usually also corresponds to the most stable structure $M^I_xM^{II}_y(OH)_x$. The weakest basic centres are those in complex hydroxides containing metals with the same oxidation state. Their strength is determined only by the weak inductive influence due to the displacement of the electron density.

Mixed hydroxides can be prepared by different methods. The most frequently employed and well developed method is by precipitating the hydroxides from salt solutions.[21–31] Liquid-phase methods for synthesising anionic hydroxides have been reviewed.[15] From the advantages and disadvantages examined,[15] the following method, close to the optimal, was proposed for synthesising anionic hydroxides. A solution of the metal salts with concentrations of about 100 g litre^{-1}, taken in stoichiometric proportions, is added with stirring to a solution containing an approximately two-fold excess of alkali and carbonates (final pH 8–10). The precipitate is crystallised with heating for not less than 18 h. The higher the temperature and the longer the crystallisation time, the higher the quality of the product. At low temperatures, undesirable secondary phases may be formed.[32]

The properties of the hydroxides obtained, in particular their ion exchange properties, may be influenced by the nature of the precipitant and solution, the rate of precipitation, the nature of the salts used, the intensity of stirring, and various other factors. By varying these parameters it is possible to increase the yield of the desired product, to improve its properties, and, which is most important, to avoid the formation of secondary phases. Solutions of KOH, NaOH, Na_2CO_3, or ammonia are used as precipitants. Their selection requires justification. For example, the presence of super-stoichiometric quantities of sodium hydroxide increases considerably the range of crystallisation of double calcium aluminium hydroxide sulphate as a result of a decrease in the range of crystallisation of aluminium hydroxide.[33] Further increase in the concentrations of lithium, sodium, or potassium, however, may lead to breakdown of the compound obtained and conversion of the components into different phases.[34]

Not all double hydroxides can be obtained using strongly basic precipitants. Double copper aluminium hydroxides are formed only in hydroxide carbonate solutions, since at high pH values copper is precipitated as hydroxide carbonates.[35] Precipitation by ammonia is of limited application, because of possible complex formation.

The pH of the solution has a marked influence on the precipitation of hydroxides; the rate of precipitation and the stability of the compounds formed generally increase with increase in pH,[36] but on the other hand the selectivity of the process decreases. The formation of double hydroxides and their salts may take place over a period of several months or even years.[37] The highest selectivity is achieved by precipitating with dilute solutions of alkali or ammonia, taken in stoichiometic quantities.[38]

The formation of double hydroxides by precipitating with ammonia shows interesting features.[39] In the preparation of double hydroxides of zinc and chromium it was found that increase in temperature from 20 °C to 60 °C leads to the appearance of various secondary phases, both as a result of their parallel formation and as a result of decomposition of the principal phase. The ratio of the reagents being precipitated has less influence on precipitate formation than the basic strength of the solution; at different pH values, precipitates with different atomic ratios Zn : Cr are obtained from solutions with the same composition. The ratio also depends on the rate of the process. In general, increase in temperature and decrease in the rate of the process lead to the formation of secondary phases as a result of more extensive hydrolysis.

Danilov and co-workers[39] observed an extremely interesting fact, namely that the selectivity of formation of double zinc chromium hydroxide nitrate increases sharply when a very small quantity of acetic acid is added to the reaction mixture. The authors cited give no explanation for this phenomenon; it is quite possible that acetate ions (or acetic acid itself) are applicator anions. This is also indicated by the fact that the precipitate does not contain amorphous zinc- and chromium-containing hydroxide phases.

Decrease in the concentrations of the salts being precipitated and of the precipitant is accompanied by an increase in the degree of solvation of the hydroxides obtained,[2] and this also influences their properties, including the ion exchange properties. If however the precipitate is subsequently subjected to ageing[40] or thermal treatment, then this factor has no significant influence.

The nature of the metal being precipitated determines the conditions for its precipitation. Thus under the same conditions, selective precipitation of double magnesium aluminium hydroxides takes place but the formation of mixed nickel and cobalt hydroxides is accompanied by the formation of $Ni(OH)_2$ and $Co(OH)_2$.[15]

It is considered that the ability of zinc to form double hydroxides is weak.[13] Nevertheless, mixed hydroxides based on zinc have been studied in detail.[41–46] Only synthetic hydrotalcite $[Mg_xAl_y(OH)_x].X_n$ has been more intensively studied than anionic hydroxides based on zinc. The great majority of double hydroxides that have been synthesised, studied, and described are compounds based on divalent and trivalent metals. Double hydroxides containing alkali metals (except lithium) have not been studied in such detail.

Table 2 lists double hydroxides containing M^I and M^{II} whose properties were studied in the works cited.

Table 2. Literature sources containing information on the methods and characteristics of the preparation of synthetic anionic double hydroxides.

M^{II}	M^I							
	Al	Cr	Fe	Sc	Zr	Zn	Co	In
Mg	+	[15]	[47]	[15]				[48]
Zn	[49]	+	[50]					[48]
Li	[51]							
Fe	[15]		[27]		[52]			
Co	[15]		[53]	[54]				
Ni	[55]	[15]	[56]				[56]	
Cu	[15]	[57]	[50]	[57]		[58]		
Mn	[54]							
Ca	[59]	[48]						
Cd	[22]							
Sn	[60]	[60]						

Note. The symbol "+" indicates that the information can be found in many sources.

The double hydroxides listed in Table 2 show anion exchange properties only at certain M^I/M^{II} ratios and with the condition that certain requirements are met in their synthesis. When these requirements are not met and at other ratios, the products may show not anion exchange but cation exchange properties, or may not be formed at all.

Table 3 lists double hydroxides with anion exchange properties, but these data were taken from the patent literature, and should be approached with care.

Double hyroxides with anion exchange properties are not formed for all M^I-M^{II} combinations. In particular, they are not formed if one of the ions M^{n+} oxidises the other M^{m+} (for example Fe^{3+}/Mn^{2+}). Moreover, although transition metals (Cr, Co, Ni, etc.) form double hydroxides, this is accompanied by the secondary formation of the oxides, hydroxides, and carbonates of the metals, and their mixtures. Solutions containing ions which can be readily oxidised in air must be treated in an inert atmosphere.

Table 3. Literature sources containing information on synthetic double hydroxides having anion exchange properties.

M^{II}	M^I								
	Al	Fe	Cr	Sc	Y	Ti	In	B	Bi
Mg	+	[47]	[61]	[61]	[61]	[61]	[62]	[62]	
Ni	[63]	[64]	[63]						
Zn	[63]	[64]	+			[62]	[62]	[62]	
Ca	[67]	[64]	[64]						
Ba	[68]	[64]	[64]						
Cu	[64]	[65]	[64]						
Co	[66]	[66]	[64]			[69]			
Fe	[64]	[64]	[64]						
Mn	[70]								
Al						[71]			
Cd	[62]	[62]	[62]				[62]	[62]	[62]

Note. The symbol "+" indicates that the information can be found in many sources.

The starting materials for preparing double hydroxides may be not only the salts but also the alkoxides of the corresponding metals, and the precipitation can be carried out by alkaline hydrolysis.[72] All the regularities described above should be observed in this case also, but by using the alkoxides of the appropriate alcohols an attempt can be made to produce the required structure in the process of synthesis.[73]

The mechanochemical method for obtaining double hydroxides appears more promising. Thus hydroxides based on zinc and chromium are obtained[42,46] either by grinding for 24 h at pH 4 a paste of zinc oxide and chromium salt (with an excess of the chromium salt) or by mechanically mixing dry zinc oxide and chromium(VI) oxide.[42] In the last case the mixture was moistened slowly with grinding, after which an equivalent quantity of water (16% of the total mass of the oxides) was added. The double hydroxides obtained by these methods had different properties; in particular, the specific surfaces of different specimens prepared by the "dry" method were 5, 13, and 22 $m^2 g^{-1}$, whereas those of specimens obtained by precipitating were 77 $m^2 g^{-1}$ and 99 $m^2 g^{-1}$. Coprecipitated hydroxides synthesised at different temperatures also have different specific surfaces (for hydrotalcite, 120 $m^2 g^{-1}$ at 65 °C and 12 $m^2 g^{-1}$ at 200 °C[35]).

The most promising method for obtaining complex hydroxides is by the sol–gel method, used to obtain hydrated salts.[28] Electrolytes are removed by decomposing the acid formed by passing an electric current. The decomposition gives sols of the corresponding hydrated oxides.

The most suitable initial salts are of course the chlorides, iodides, etc. The redox potentials of the metals may also influence the selectivity of the process, but by using different membranes—semi-permeable ion exchange membranes and porous crystalline membranes—it is possible to obtain various metal hydroxides. The sol–gel method has been used to obtain various sorbents based on metal hydroxides,[74–76] but there are no published data on the synthesis of complex basic hydroxides.

The alkali metals, except lithium form hydroxometallates or double basic salts with corresponding trivalent metals. Lithium also forms compounds with basic and anion exchange properties, but with a different structure. The lithium aluminium compound $[LiAl_2(OH)_6]OH$ has been studied in most detail.[24,30] Most workers tend to regard it not as product of the isomorphous replacement of some cations by others but as a product of the intercalation of lithium ions into the aluminium hydroxide lattice.[51] Lithium aluminium hydroxide can be obtained both by the traditional method of precipitation[77] and by solid-phase synthesis from crystalline $Al(OH)_3$ and lithium hydroxide[51] or the corresponding salts.[78] The yield is quantitative only when $Al(OH)_3$ particles are impregnated with LiOH. The optimum ratio of the liquid and solid phases is 5 : 1.[79] $Li_2Al_2(OH)_8$,[80] which also shows anion exchange properties, is less stable.

Theoretically, the exchange capacity of double hydroxides can reach high values—up to 5 mequiv g^{-1} for the hydroxides of light metals. A value of the anion exchange capacity of 3 mequiv g^{-1} (Mg, Al) has been given.[81] The real values differ considerably from the theoretical, however.

The factors responsible for the anion exchange or cation exchange properties of double hydroxides can be considered.

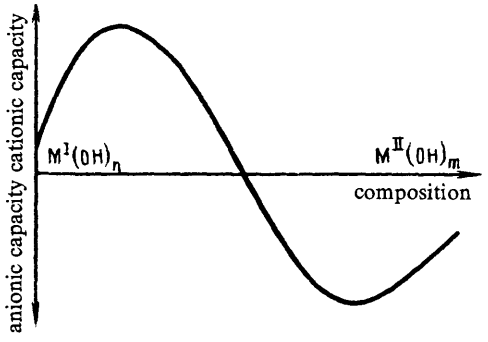


Figure 1. Composition dependence of the ion exchange capacity of a complex hydroxide.

If metal cations with charges lower than that on the original cations are introduced by isomorphous replacement into a polymeric hydroxide layer [for example if some Al^{3+} in $Al(OH)_3$ are replaced by Mg^{2+}], then the layer acquires an overall negative charge and begins to show cation exchange properties. If on the other hand cations with higher charges are introduced into the hydroxide layer [for example if some Mg^{2+} in $Mg(OH)_2$ are replaced by Al^{3+}], then the positively charged layer acquires anion exchange properties.

The ion exchange capacity should obviously depend on the degree of isomorphous replacement; a double hydroxide of metals in different oxidation states can be both a cation exchanger and an anion exchanger. The presence of ion exchange centres is determined by the displacement of electron density and the redistribution of charges.[82] There exists an optimum degree of isomorphous replacement, at which the maximum ion exchange capacity is reached.

Although lithium aluminium hydroxide is formed not by isomorphous replacement but by the introduction of Li^+ ions oetween two $Al(OH)_3$ layers, leading to the production of a positive charge,[77] all that has been said about the relationship between the isomorphous statistical replacement and the strength and number of basic and acidic centres remains applicable in this case also. The other alkali metal hydroxides show genuine isomorphous replacement.[83–86]

The approximate form of the composition dependence of the acid–base properties of a double hydroxide is shown in Fig. 1. The overall or observed exchange capacity is characterised, for example, by the pH of a salt solution when the ion exchanger is immersed in it; this pH is determined by the cation exchange and anion exchange reactions.

The dependence of the number of basic centres E on the surface of MgAl hydroxide in the carbonate form on the degree of replacement[87] is given as an example in Fig. 2.

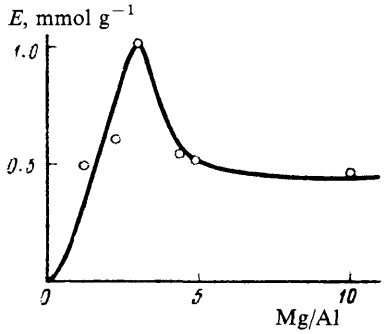
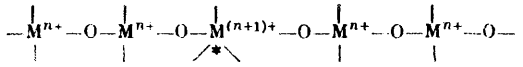


Figure 2. Composition dependence of the capacity of magnesium aluminium hydroxide.[87]

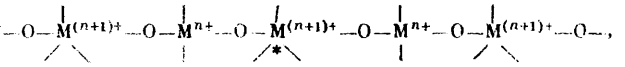
Similar observations were reported in another paper.[88] The curve shown in Fig. 1 was not obtained completely in any case, although the extremal character of the composition dependence of the capacity is mentioned in many papers. This curve naturally cannot be continuous, since the double hydroxide phases do not exist at all M^I/M^{II} ratios.[39] A study[29] of the formation of $Fe^{II}-Fe^{III}$ hydroxides gave the following results (the plus sign indicates that a double hydroxide is formed, the minus sign indicates that it is not formed, and i indicates impurity)

Fe^{II}/Fe^{III}	5.1	4.1	3.2	2.9	3.1	6.9	3.0	6.6	4.7	7.6
Hydroxide	+	+	+, i	–	+	+, i	+, i	–	–	–

The chief factors determining the number of basic centres (the exchange capacity) and their strength are the number of isomorphous replacements and their frequency. A centre of the type indicated by the asterisk



should obviously have a much higher basic strength than a centre of the type



because of the greater displacement of electron density. Account must of course be taken of the fact that the inductive influence decreases rapidly with increase in the distance, and becomes practically insignificant after two chain units.

What has been said about the relationship between the degree of isomorphous replacement and the strength and number of basic centres remains applicable when the oxidation states of the metals are equal, as for example in $Mg_xNi_{1-x}(OH)_2$.[89] In the examination of these systems it is necessary to compare the effective charges on the atoms; strictly speaking, this should also be done in all other cases.

The strength of the basic centres and the exchange capacity are inversely proportional to one another. The greatest strength should be shown by the basic centre in a specimen in which isomorphous replacement of one single atom has taken place; this specimen will have the lowest capacity. Correspondingly, the strength of the basic centres will be lowest in the specimen with the highest capacity.

The strength distribution of the basic centres can be predicted qualitatively by examining the structure of the specimen. Restricting the treatment to an idealised one-dimensional model, the following cases can be distinguished:

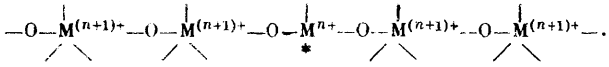
1) –A–A–A–A–B–A–A–A–A–
2) –A–A–A–B–A–A–B–A–A–B–A–A–A–
3) –A–A–A–B–A–B–A–B–A–A–A– .

Combinations of these are also possible. The inductive influence extending over more than three atoms can be neglected. The spectrum of the basic strength of real octahedral and tetrahedral systems in layer hydroxides is more complex, but the general approach remains the same.

For any ratio M^I/M^{II}, the real structure of layer hydroxides is far from ideal, that is from a regular alternation of isomorphous replacement centres ...AABAABAAB...

When the structures of double hydroxides is discussed, we refer to the isomorphous replacement of some cations by others. This treatment is extremely convenient, but it does not necessarily take place in practice. It is most likely, at any rate in hydrothermal synthesis, that the process taking place is not replacement but growth of the oxide chain, the sequence in which the cations are arranged in this chain being determined statistically, with allowance for their reactivity. Since the statistical factors are decisive, in real

complex hydroxides at all stoichiometric ratios, acidic centres of the following type exist



The number and strength of acidic centres undoubtedly also depend on the degree of isomorphous replacement.[90,91] A study[90] of the dependence of the number of basic and acidic centres on the degree of isomorphous replacement, that is on the ratio M^{I}/M^{II}, gave the following results:

Molar ratio MgO/Al_2O_3	2.49	3.8	5.23	9.33	17.6
Acidity, mmol g^{-1}	0.41	0.32	0.21	0.06	0
Basic strength, mmol g^{-1}	0.63	0.54	0.73	0.85	0.94 .

The basic centres were determined by titrating with a 0.1 M solution of benzoic acid in benzene in the presence of 2,4-dinitroaniline.

The strength of the basic centres lies mainly in the range $18.0 > H_0 > 17.2$. Thus the curve given in Fig. 1 is in fact the result of the summation of two curves giving the change in the number of basic and acidic centres (Fig. 3).

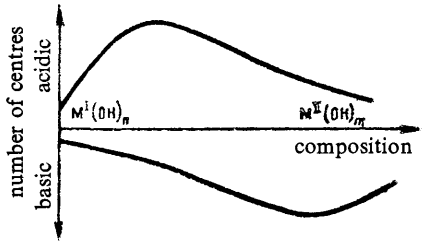


Figure 3. Dependence of the number of basic and acidic centres on the composition of double hydroxides.

Table 4. Observed and calculated exchange capacities of double magnesium aluminium hydroxide.

Capacity, mmol g^{-1}		Anion	References
theoretical	observed		
1.7	0.1	SO_4	[18]
1.6	1.0	SO_4	[74]
4.5	1.5	CO_3	[36]

The actual magnitude of the exchange capacity of double hydroxides differs considerably from the theoretical value calculated from elemental analysis data. There are two main reasons for this—inaccessibility of the centres and the presence of structural defects. The term structural defects is applied to the above-mentioned isomorphous replacements and breakdown of the sequence in the arrangement of the cations in the three-dimensional structures, shown in Fig. 4.

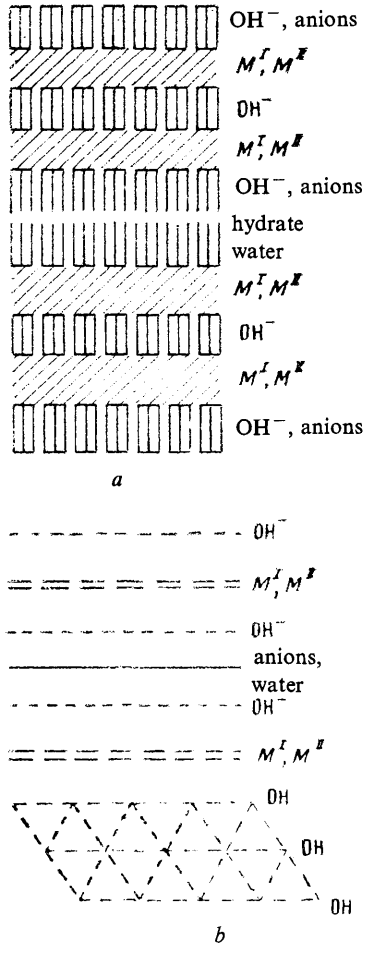


Figure 4. Diagram of the structure of a double hydroxide (*a*)[16] and the structure of hydrotalcite (*b*).[56]

The exchange capacity of a complex hydroxide cannot be regarded as the sum of the capacities of the individual hydroxides, as has been done.[52]

The exchange capacities of hydroxides of the $M^{I}_{x}M^{II}_{y}$ type also are not additive quantities, as indicated by the composition dependence of the anion exchange capacity of the double nickel magnesium hydroxide (Fig. 5).[92]

The observed exchange capacities are practically never equal to the theoretical values (Table 4).

Although the observed exchange capacity is much lower than the value calculated from the elemental analysis data, there is no reason to suppose that exchange involves only those centres on the outer

surface. This can be illustrated by the following example. Theoretically, the exchange capacity of ZnCr hydroxide in the carbonate form is about 1.6 mmol g^{-1}, but in practice the value is about 1.0 mmol g^{-1}; on the other hand, the specific surface of the specimen is about 150 $m^2 g^{-1}$, and the outer surface is about 3 $m^2 g^{-1}$.[45] If only the centres on the outer surface functioned, then the exchange capacity values should also differ by a factor of 50.

The internal centres in double hydroxides are accessible even to extremely complex organic molecules. The view is held that ion exchange taking place does not prove that the centres are accessible, and that the actual exchange may take place on the external surface after migration of ions from the internal space.[45] These suggestions, however, are not consistent with a large amount of data on the relationship between the size of the internal cavities and the size of the exchanging anions. The interplanar spacings in various double hydroxides are given in Table 5.

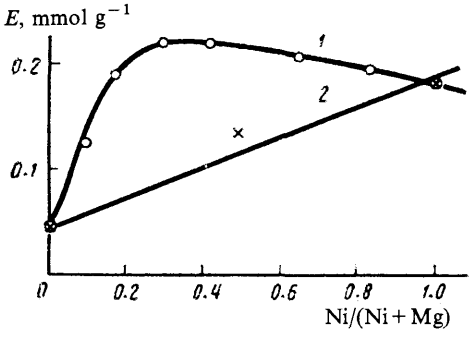


Figure 5. Dependence of the capacity of a hydroxide on its degree of isomorphous replacement:[92] *1*, complex NiMg hydroxide; *2*, mechanical mixture of Ni and Mg hydroxides.

The interplanar spacing is determined not only by the type of anion.[101] On ion exchange in which anions of one type are replaced by anions of another type, the change in the distance between the layers takes place abruptly,[44,56] and the appearance of phases with mixed anions in the space between the layers is unlikely, since this is energetically unfavourable because of the high activation energy of anion transfer. If nevertheless the hydroxide contains either alternating layers or separate regions with different anions within a given inter-layer space, which leads to deformation of the layers, then the determination of the interplanar spacings is complicated by the marked broadening of the X-ray diffraction lines.

The interplanar spacings also depend on the crystal structure of the complex hydroxide. This dependence is not so great, however; for example, the difference between the interplanar spacings for the hexagonal and trigonal forms of pyroaurite is 0.16 Å.[102]

The interplanar spacing is influenced much more strongly by the type of solvent in which anion exchange takes place and which acts as solvating agent. If water is used as solvent, there are usually 1–3 molecules of solvating water for every basic centre.

Table 5. Dependence of the interplanar spacings in double hydroxides on the nature of the anion.

Anion *	Interplanar spacing	References	Anion *	Interplanar spacing	References
Magnesium–aluminium			**Zinc–chromium**		
OH^-	7.55	[81]	C_2	4.6	[22]
F^-	7.66	[81]	C_3	5.0	[22]
Cl^-	7.87	[81]	C_4	6.0	[22]
Br^-	7.95	[81]	C_6	7.4	[22]
NO_3^-	8.79	[81]	C_{10}	8.4	[22]
I^-	8.16	[81]	Cl^-	7.7	[44]
CO_3^{2-}	7.65	[81]	I^-	8.3	[44]
NY	13.0	[81]	NO_3^-	9.1	[44]
SO_4^{2-}	8.58	[81]	ClO_4^-	11.9	[44]
$SiV_3W_9O_{40}^{7-}$	14.5	[93]	CH_3COO^-	12.9	[44]
$H_2W_{12}O_{40}^{6-}$	14.5	[93]	MoO_4^{2-}	10.45	[45]
$SiW_{11}O_{39}^{8-}$	14.5	[93]	F^-	7.51	[46]
$PW_9O_{34}^{9-}$	14.5	[93]	Cl^-	7.73	[46]
$Ru(DPS)_4^{4-}$	22.0	[94]	Br^-	7.85	[46]
$ReO_2(CN)_4^{3-}$	22.0	[95, 96]	I^-	8.4	[46]
Cl_4^-	22.0	[97]	N_3^-	7.62	[46]
CrO_4^{2-}	8.94	[23]	NO_3^-	8.88	[46]
$Fe(CN)_6^{3-}$	11.18	[98]	ClO_4^-	11.8	[46]
ClO_4^-	9.15	[98]	$^1/_2SO_4^{2-}$	11.8	[46]
CO_3^{2-}	7.7	[99]	$^1/_2HPO_4^{2-}$	10.9	[46]
Cl^-	7.7	[99]	AC_8	21.1	[46]
$HGaO_3^{2-}$	7.96	[99]	AC_{10}	23.7	[46]
MoO_4^{2-}	7.8	[99]	AC_{12}	26.1	[46]
SO_4^{2-}	8.6	[99]	AC_{14}	28.0	[46]
HPO_4^{2-}	8.29	[99]	AC_{16}	28.6	[46]
CrO_4^{2-}	8.73	[99]	AC_{18}	32.6	[46]
SiO_3^{2-}	8.74	[99]	**Nickel–iron**		
HVO_4^{2-}	9.33	[99]	CO_3^{2-}	7.97	[56]
Nickel–cobalt			Cl^-	7.86	[56]
CO_3^{2-}	7.66	[56]	NO_3^-	8.28	[56]
Cl^-	7.78	[56]	SO_4^{2-}	10.6	[56]
NO_3^-	8.53	[56]	ClO_4^-	11.94	[56]
SO_4^{2-}	11.19	[56]	CH_3COO^-	12.02	[56]
ClO_4^-	11.76	[56]	**Lithium–aluminium**		
CH_3COO^-	12.55	[56]	OH^-	7.5	[100]
			Cl^-	7.75	[100]
			HCO_3^-	7.6	[100]
			NO_3^-	8.8	[100]
			CH_3COO^-	13.0	[100]
			$^1/_2SO_4^{2-}$	8.7	[100]
			CO_3^{2-}	7.67	[100]

*Notation used: NY = Naphthol Yellow; anions of dicarboxylic acids: C_2 = oxalic, C_3 = malonic, C_4 = succinic, C_6 = adipic, C_{10} = sebacic; normal alkyl sulphates: AC_8 = octyl sulphate, AC_{10} = decyl sulphate, AC_{12} = dodecyl sulphate, AC_{14} = tetradecyl sulphate, AC_{16} = hexadecyl sulphate, AC_{18} = octadecyl sulphate; DPS = 4,7-diphenyl-1,10-phenanthroline disulphate.

Change in the degree of solvation leads to a change in the interplanar spacings,[103,104] and this may take place gradually or abruptly. Miyata and Okada[23] obtained two values for the interplanar spacing, depending on the moisture content of the specimen; no intermediate values were observed. Replacing water by another solvent with bulkier molecules leads to an increase in the interplanar spacing.

Table 6 shows the change in the interplanar spacings when a double zinc chromium hydroxide in the alkyl sulphate form is kept in different alcohols.

Table 6. Change in the interplanar spacing when a layer double hydroxide of zinc and chromium is kept in various normal alcohols.[46]

Alcohol	d, Å	Alcohol	d, Å
C_3H_7OH	28.3	$C_{10}H_{21}OH$	38.2
C_4H_9OH	29.2	$C_{12}H_{25}OH$	41.1
$C_6H_{13}OH$	30.8	$C_{14}H_{29}OH$	42.4
$C_8H_{17}OH$	33.7	$C_{16}H_{33}OH$	44.9

The influence of both the length of the hydrocarbon group in the anion and the length of the group in the solvent molecule on the interplanar spacing is given by the equation

$$d=a+bn,$$

where a and b are the contributions to the increase in the interplanar spacing made by the terminal (methyl and functional) groups and the CH_2 group respectively.[29] This relationship is possible for mutually perpendicular or almost mutually perpendicular arrangements of the hydrocarbon groups in the basal plane. In fact, it is known that the ions of dibasic acids can bind neighbouring hydroxide layers.[98,105] It is also known that after the ion-exchange replacement of the NO_3^- ion in zinc chromium hydroxide by alkyl sulphate anions and the alkylglycol sulphate anion $C_{12}H_{25}(OCH_2CH_2)SO_4^-$, the chains of the surface-active substances are arranged in a monomolecular layer strictly perpendicular to the layers of the hydroxide, and after drying the angle of slope is only 56°.[106] After drying, these heterolayer compounds retain the solvate molecules of the C_6-C_{18} alcohol solvents. A double layer consisting of alcohol molecules and the ions of the surface-active substance is formed.

Some workers assume that the interplanar spacing is determined not so much by the size of the counter-ions as by the structure and size of the anions present during the synthesis in the liquid phase. Thus when bulky alkyl sulphate anions are used in the synthesis, the interplanar spacing is increased by 2–3 Å, but when anion exchange involves lauryl sulfate, toluenesulphonate, dihydroxybenzene-sulphonate, terephthalate, or $Mo_7O_{24}^{6-}$, $W_7O_{24}^{6-}$, and $V_{10}O_{28}^{6-}$ anions, the interplanar spacing remains unchanged.[107]

The change in the interplanar spacing and exchange capacity of MgAl hydroxide during the sorption of various C_1-C_{20} primary and secondary alcohols has been studied.[108] A correlation was observed between the length of the group of the alkyl alcohol and the exchange capacity of the anion exchanger, and it was shown that the active centres are blocked by the hydrocarbon groups. At the same time, the absence of any significant change in the interplanar spacing indicated parallel arrangement of the planes.

The interplanar spacing depends significantly on the degree of isomorphous replacement. This can be seen for the double hydroxide of magnesium and aluminium:[24]

Mole fraction Mg	0.09	0.69	0.71	0.73	0.95
d, Å	7.55	7.60	7.64	7.7	7.8

Thus the interplanar spacing is influenced by different factors. In certain cases, one or two of these factors are decisive (for example, the interplanar spacings in various double hydroxides of the types Zn_2Al, Zn_2Cr, and Ni_3Al containing the $V_{10}O_{28}^{6-}$ ion have the same value, 11.9 Å [109]), and in other cases the different factors have comparable effects.

Thermal treatment of the hydroxides leads to appreciable changes in their structure and composition and hence in their physico-chemical properties. These changes are naturally greatest when the thermal treatment is carried out in air or in another gaseous medium. In the liquid phase the changes are slight. Thus MgAl and ZnCr hydroxides undergo no changes when heated to 150–170 °C in an aqueous or alcohol medium.[143]

In the thermal treatment of hydroxides in a gaseous medium, two main processes take place—the loss of solvating water and dehydration with breakdown of the brucite-like layer. Typical thermal analysis curves are shown in Fig. 6. The first endothermic effect, corresponding to the loss of the solvating water and breakdown of the carbonium ion [sic. carbonate ion? Ed. of Translation)], is observed in the range 200–250 °C, and the second, corresponding to dehydration is observed at 400–450 °C. The position of the peaks depends on the molar ratio of the cations and on the nature of the anion.

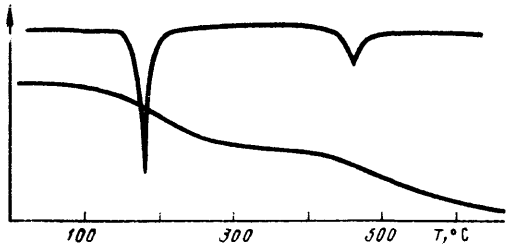


Figure 6. Typical thermal analysis curves for a double hydroxide.[55]

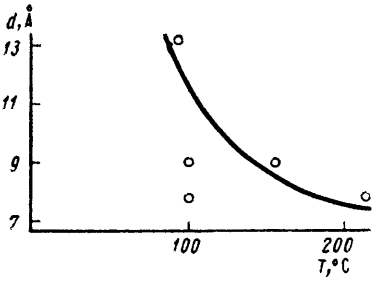


Figure 7. Dependence of the interplanar spacing in lithium aluminium hydroxide on the temperature at which dehydration starts.[100]

The temperature at which the first endothermic effect appears for lithium aluminium hydroxide (°C) has the following values for different anions:[110] CO_3^{2-} 120, SO_4^{2-} 130, OH^- 139, NO_3^- 201, Cl^- 250.

At the same time, the dependence of the interplanar spacing in this hydroxide on the temperature at which dehydration starts has the form shown in Fig. 7.

For the thermal treatment of MgAl hydroxide,[111] completely different values were obtained for the temperature at which dehydration starts, °C: OH^- 165, CO_3^{2-} 200, SO_4^{2-} 200, Cl^- 240, NO_3^- 140.

The strength of the retention of water in the space between the layers is most probably determiend by the strength of the hydrogen bond, with allowance for the mutual repulsion of the anions.

In general, the greater the bond strength, the higher the temperature at which water is removed. The first endothermic process involving the loss of water of crystallisation is completely reversible; when the product obtained by heating is placed in water, all its physicochemical properties are restored. Breakdown of the brucite-like layer on dehydration leads to the production of spinel-like structures. Contrary views that this process is completely irreversible[90] and that it is completely reversible[99] have been expressed.

A study of the behaviour of MgAl hydroxide when treated with water after heating at 600 °C showed[108] that the original hydroxide, with the same anion exchange properties is restored.

The structure and properties of MgAl oxide obtained by heating the corresponding hydroxide have been studied.[99] Specimens heated at 900 °C sorbed water from the gas phase, with complete restoration of the original hydroxide structure. An interesting feature is that the properties and structure of the restored hydroxide depended on the type of anion in the solution, although its concentration did not exceed 0.05%.

The reversibility of the processes taking place on thermal treatment is confirmed indirectly by the fact that the double hydroxides can be obtained by hydrolysing the corresponding oxides.[112]

Thermal treatment generally decreases the interplanar spacings, as a result of a rearrangement and a decrease in the width of the internal layers.

The temperature dependence of the interplanar spacing in Mg-Al hydroxide is shown below.[98]

T, °C	20	100	150	200	250
d, Å	11.18	10.91	10.39	10.80	8.04

In the gas phase the distance between the layers is determined not only by the type of anion but also by the degree of hydration, which in turn depends on the partial pressure of water vapour.[59,100]

The thermal treatment of double hydroxides influences their sieve properties, and also the number and strength of the basic centres. The dependence of the number of basic centres on the treatment temperature is generally extremal in character.

The highest number of basic centres is produced in MgAl oxide obtained by heating the hydroxide at 450 °C; the basic strength of specimens heated below 400 °C is too low.[113]

The indicator method has been used to determine separately the change in the numbers of Brönsted and Lewis basic centres when ZnCr hydroxide is heated in air (Fig. 8).[108]

There are insufficient published data on the change in the strength of the basic centres on thermal treatment, and the solution of this problem lies in the future. Published data[87] show that the dependence of the strength of the basic centres on the treatment temperature is complex. At higher temperatures, thermal treatment of double hydroxides gives spinel structures,[43] and the temperatures of their formation are lower than those when a mixture of the hydroxides is heated.[114]

Thermal treatment at high temperatures leads to the appearance of acidic centres. The formation of acidic centres when Zn-Cr hydroxide was heated was observed only above 500 °C (the number of centres was less tha 0.1 mmol g^{-1-1}).[108] The change in the number of acidic centres when double Mg-Al hydroxide is heated is shown in Fig. 9.

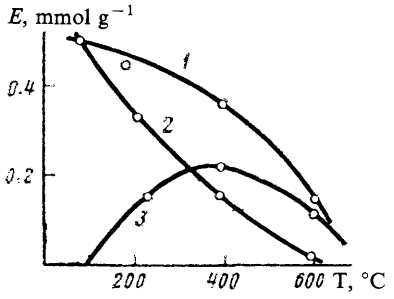


Figure 8. Change in the number of basic centres when zinc chromium hydroxide is heated in air:[108] *1*, total; *2*, Brönsted; *3*, Lewis.

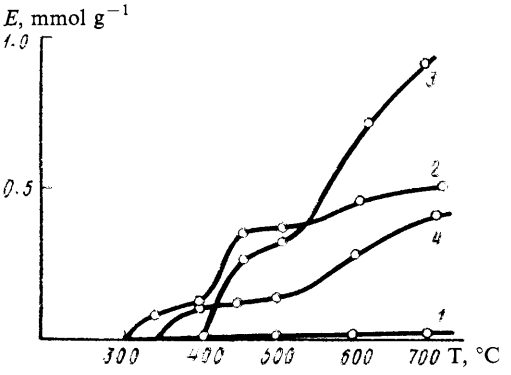


Figure 9. Change in the number of acidic centres when double magnesium aluminium hydroxide is heated in air; Mg/Al molar ratio: *1*, 0.05; *2*, 4; *3*, 6; *4*, 10.[87]

The specific surface of complex hydroxides can vary over a wide range, but there are no definite data on which parameters determine this quantity. The dependence of the internal surface of the pores on the average pore radius has been given.[115] The specific surface is influenced by the crystallisation temperature (in the hydrothermal synthesis[35]). Thus crystallisation at 65 °C for 18 h gives platelets with dimensions of 0.5 μm and a surface are of 120 $m^2 g^{-1}$, whereas crystallisation at 200 °C for 18 h gives crystals with dimensions of 1–2 μm and a surface area of about 12 $m^2 g^{-1}$.

The external specific surface of double hydroxides obtained under industrial conditions has been measured by the diffraction of laser beams in suspensions of the hydroxide in water and in glycol solution. All the hydroxides were obtained by precipitating from concentrated solutions at low temperatures. Different double hydroxides had the following surface areas, $cm^2 g^{-1}$: Mg-Al 674, Zn-Cr 298. When Zn-Cr hydroxide was kept for a long time in aqueous methanol, its specific surface increased to 592 $cm^2 g^{-1}$.[116] This is of course much smaller than hundreds of square metres per gram,[15,35] so that when the specific surface is mentioned, it must always be made clear whether the total surface or only the external surface is meant.

The surface area of hydroxides changes on thermal treatment, the changes being very different for different compounds, and also for the same compound obtained in different ways.[34,42] In most cases, thermal treatment leads to an increase in the specific surface. This is most probably due to the formation of a large number of fine pores (there is a two-fold increase in the surface area and the volume),[115] possibly as a result of the conversion of an appreciable proportion of the specimen from the octahedral to the tetrahedral state. Contrary data indicating a marked decrease in the specific surface on thermal treatment have also been published.[117]

In the liquid phase, double hydroxides have an extremely high thermal stability. They are very stable in basic media, but even in neutral media their stability is extremely high.[118] All double hydroxides undergo changes, however, in acidic solutions. The reaction with acids, as far as complete solution of the mineral framework, limits the possible applications of double hydroxides in acidic media.

Table 7. Anion exchange properties of various double hydroxides.

Anion exhanger	Selectivity series	References
Mg-Al	$I^- < Br^- < Cl^- < F^- < SO_4^{2-} \leqslant OH^- < CO_3^{2-}$	[81]
Li-Al	$AcO^- < CO_3^{2-} \approx NO_3^- < Cl^- < SO_4^{2-}$	[75]
Ca-Al	$AcO^- < NO_3^- < Cl^- < CO_3^{2-} \approx SO_4^{2-}$	[59]
Fe-Zr	$I^- < Br^- < Cl^- < MoO_4^{2-} \approx PO_4^{3-} < SO_4^{2-}$	[52]
Ni-Fe Ni-Co	$AcO^- < NO_3^- < ClO_4^- < Cl^- < SO_4^{2-} \ll CO_3^{2-}$	[56]
Zn-Cr	$AcO^- < ClO_4^- < MnO_4^- < NO_3^- < Cl^- < CO_3^{2-}$	[44]

The stability of hydroxides in basic and neutral media depends on many factors, however.[119] In solution, for example, calcium aluminium hydroxide sulphate reacts with carbon dioxide in the pH range 9–12 and is converted completely into the corresponding carbonates and hydrogen carbonates.[114] The same reaction takes place between CO_2 and the dry hydroxide sulphate, Zinc chromium basic nitrate is also fairly unstable in neutral solutions; it is hydrolysed to give the individual basic salts, or zinc oxide if the process is prolonged sufficiently.[24] This question was examined in more detail in a study[40] of double hydroxides of chromium and nickel to determine how and why their sorptive capacity changed. No definite correlation was found between the concentration of hydroxide groups and the exchange capacity (the capacity gradually decreases, and the concentration of hydroxide groups and structural water increases slightly).

Published data[39] would seem to indicate that the structure of double chromium zinc hydroxide is completely unstable. For example, at 20–60 °C and pH 6.5–7.0 the hydroxide is hydrolysed rapidly to zinc oxide and the basic nitrate. In fact, however, double zinc chromium hydroxide can exist for an extremely long time, and the exchange capacity of the corresponding nickel chromium hydroxide decreases by only about 15% after 6 months.[40] Double hydroxides can be kept for an unlimited time at high pH values.[33,120]

The effective exchange capacity also depends on the pH of the solution, the effect being greatest for amorphous compounds.[121] The stronger the basic properties of a compound, the weaker the influence of the pH of the medium on the exchange capacity.

Ion exchange in double hydroxides has been studied in considerable detail. The selectivity series for ion exchange by various hydroxides are given in Table 7.

The selectivity series given in various other sources are less complete than those in Table 7. Deviations from these sequences are observed.

The selectivity series given correspond almost completely to the magnitude of the interplanar spacings (see Table 5) and hence to the sizes of the ions, although in general the selectivity of inorganic anion exchangers depends on the characteristics of the synthesis.[122,123] The interplanar spacings in double hydroxides, unlike those in ion exchange resins, correlate with the sizes of the non-hydrated ions. The CO_3^{2-} ion shows the highest stability to exchange, probably because of the planar arrangement of the oxygen atoms and the high effective ionic charge.

Since practically all double hydroxides show a high selectivity with respect to carbonate ions, the preparation of double hydroxides as the pure sulphates, chlorides, etc. by ordinary ion exchange is not always possible, although theoretically there are no problems.[81] A much more effective method has been proposed.[124] MgAl and NiAl hydroxides in dilute acid solutions lose carbon dioxide rapidly and completely as a result of the exchange

$$DH.CO_3 + 2HCl \rightarrow DH.Cl_2 + CO_2 + H_2O.$$

This reaction can take place with any acid stronger than carbonic acid.[125]

Anion exchange in double hydroxides takes place not only with ordinary inorganic anions but also with the anions of dicarboxylic acids,[22] anionic complexes,[21,52,99] complex alkyl sulphates and alkanesulphonates,[46,126] optically active compounds,[127] alkyl halides,[45,128] and hydroxyalkylated alcohols.[162]

Double hydroxides are anion exchangers not only in liquid media but also in gaseous media.[45]

The rate of ion exchange in a liquid phase depends markedly on the pH of the medium. Anion exchange by NiFe hydroxide at pH 0–3 takes not more than a few minutes, whereas at pH > 6 no exchange has taken place after several hours. The $Cl^- \rightleftharpoons OH^-$ exchange rate constants in NiAl hydroxide in neutral and basic media are 1.4×10^3 s^{-1} and 9×10^3 s^{-1} respectively.[129] The types of cation present in the solution have a marked influence on the rate of exchange.[21]

V. Natural double hydroxides

Inorganic anion exchangers belonging to the class of complex hydroxides can be synthesised, and also occur naturally as various minerals. Almost all these minerals belong to the pyroaurite–sjögrenite group, since their elementary structure corresponds fairly closely to the general formula of pyroaurite (trigonal form) or sjögrenite (hexagonal form).

Table 8 lists minerals of this group and corresponding minerals having anion exchange properties. This Table can be reduced considerably if account is taken of the fact that all the minerals listed in it are capable of ion exchange. The name can be based on the hydroxide form of the mineral, correpsonding to the traditional nomenclature of ion exchange resins: "meixnerite carbonate" or "meixnerite in the carbonate form" instead of "hydrotalcite". Alternative names can be formed in accordance with accepted mineralogical nomenclature, taking as a basis the most stable natural form, that is the carbonate form. It is then necessary to use the name "hydroxohydrotalcite" instead of "meixnerite", and "sulphotakovite" instead of "carrboydite".

Table 8. Natural anion exchange minerals.

Name	Formula	Symmetry	Impurities	References
Hydrotalcite (Faulknerite)	$Mg_6Al_2(OH)_{16}CO_3\cdot 4H_2O$	trigonal	Ni, Cl	[102, 130]
Manasseite	$Mg_6Al_2(OH)_{16}CO_3\cdot 4H_2O$	hexagonal		[102]
Stichtite	$Mg_6Cr_2(OH)_{16}CO_3\cdot 4H_2O$	trigonal	Fe	[102, 130]
Barbertonite	$Mg_6Cr_2(OH)_{16}CO_3\cdot 4H_2O$	hexagonal		[102]
Pyroaurite (Igel'stremit)*	$Mg_6Fe_2(OH)_{16}CO_3\cdot 4H_2O$	trigonal	Fe, Al, Ni	[102]
Sjögrenite	$Mg_6Fe_2(OH)_{16}CO_3\cdot 4H_2O$	hexagonal		[102]
Brugnatellite	$Mg_6Fe(OH)_{13}CO_3\cdot 4H_2O$	trigonal		[102, 130]
Kolingit*	$Mg_{10}Fe_2(OH)_{24}CO_3\cdot 2H_2O$	hexagonal		[102, 130]
Cyanotrichite	$Cu_4Al_2(OH)_{12}SO_4\cdot 2H_2O$	–		[130]
Woodwardite	$Cu_4Al_2(OH)_{12}SO_4\cdot(2\div 4)H_2O$			[124, 130]
Meixnerite	$Mg_3Al(OH)_9\cdot 2H_2O$	trigonal		[131]
Motukoreaite	$Mg_{10}Al_6(OH)_{28}(CO_3)_3\cdot(SO_4)_2\cdot 14H_2O$	hexagonal		[130]
Takovite	$Ni_6Al_2(OH)_{16}CO_3\cdot 4H_2O$	trigonal		[124, 132]
Reevesite	$Ni_6Fe_2(OH)_{16}CO_3\cdot 4H_2O$	"		[133]
Carrboydite	$Ni_3Al_2(OH)_{10}SO_4\cdot H_2O$	hexagonal		[134, 135]
Aiovatit*	$Mg_4Fe(OH)_{16}Cl\cdot H_2O$	"		[124]
Hydrocalumite	$CaAl_2(OH)_6OH\cdot 6H_2O$	–	$\frac{1}{2}SO_4$	[124]
Khonessit*	$Ni_6Fe_2(OH)_{16}SO_4\cdot 4H_2O$	–		[124]
Comblainite	$Ni_6Co_3(OH)_{18}(CO_2)_2\cdot 9H_2O$	orthorhombic		[136]
Erdlegit*	$Zn_6Al_2(OH)_{16}CO_3\cdot 4H_2O$	–		[137]
Ettringite	$Co_6Al_2(OH)_{16}(SO_4)_3\cdot 26H_2O$	–		[33]
Aurichalcite	$Cu_2Zn_3(OH)_6(CO_3)_2$	–		[138]

[*Transliterations. Equivalents in Western nomenclature are not clear. (Ed. of Translation)].

It would be quite incorrect to use names such as, for example, "chromobrugnatellite"[102] instead of "stichtite", since when M^I or M^{II} is replaced the structure and properties of the mineral may be changed considerably.

Of the minerals having anion exchange properties, only hydrotalcite is widely encountered, and all the others are relatively rare or very rare minerals.

Like the other minerals, the compounds showing anion exchange properties have been studied mainly from the mineralogical viewpoint, that is most attention has been paid to their structure and chemical composition.

For an understanding of the characteristics of ion exchange and an evaluation of the minerals as possible anion exchangers, most information is given by the following mineralogical data: chemical composition, interplanar spacing, stability in aqueous solutions, thermal analysis data, and data on the isomorphous replacement of cations and anions.

The chemical compositions of the minerals have been determined fairly accurately, and the data obtained by different authors show no discrepancies. Sometimes, minerals with complex compositions are encountered, for example $Mg_3Zn_3Al_2(OH)_{16}CO_3$, or isomorphously substituted minerals in a background of the basic mineral, for example ferristichtite in mixtures or intergrowths with stichtite.[130] The isomorphism is often determined by the rock in which the given mineral occurs.

The interplanar spacings depend mainly on the anion. Replacement of the anion has a much greater effect on the interplanar spacing than the isomorphous replacement of a cation. The interplanar spacing changes little in the series hydrotalcite (Mg, Al)–stichtite (Mg, Cr)–pyroaurite (Mg, Fe), the values being 7.83, 7.8, and 7.6 Å respectively.[102,130] Anion exchange leads to a greater change in the interplanar spacing: 7.64 Å for meixnerite (Mg, Al, OH), 7.83 Å for hydrotalcite (Mg,Al,CO_3), and 11.32 Å for motukoreaite (Mg,Al,SO_4).[102,130]

The polymorphic form has comparatively little influence on the interplanar spacing. The interplanar spacings for different minerals are (Å): pyroaurite (trigonal form) 7.6, sjögrenite (hexagonal) 7.78; and hydrotalcite (trigonal) 7.83, manasseite (hexagonal) 7.67.[130]

The interplanar spacings in minerals are influenced not only by the nature of the anion but also by the solvated state of the ion being exchanged. Anionic minerals can sorb both solvated and non-solvated anions. The transfer of solvating water from the solid to the gas phase and back takes place readily even at room temperature, the direction of the process depending on the humidity of the surrounding medium. For example, carrboydite loses water reversibly, as a result of which the interplanar spacing decreases from 10.5 Å to 8.6 Å.[134] When the humidity of the medium changes from 0 to 100%, only two values of the interplanar spacing are observed in takovite — 10.8 Å at a high humidity and 8.9 Å at a low humidity.[124] The same phenomenon is observed for motukoreaite (11.1 Å at a high humidity and 8.7 Å at a low humidity).[132]

If however the solvating agent is not water, the increase in the interplanar spacing may be even greater. Thus after hydrotalcite is treated with ethylene glycol,[124] the interplanar spacing is at first 12.9 Å, after which it gradually changes to 10.0 Å; when water is removed by drying, the spacing decreases to 7.87 Å. An additional ethylene glycol layer is apparently first produced in hydrotalcite, after which ethylene glycol solvates the exchange centres with the anions present there together with hydrate water, and finally ethylene glycol remains only as the solvating agent.

Diagnostic tests on minerals invariably include the action of various acids. In the study of practically all the minerals, breakdown of their structure and complete solution under the influence of strong mineral acids was observed; solution is generally accompanied by slight "effervescence".[98] Published data on the effect of aqueous solutions of mineral and organic acids are somewhat contradictory. Thus it has been reported[98] that brugnatellite dissolves readily in dilute acid solutions in the cold, and also[132,139] that treating pyroaurite minerals with dilute solutions of various acids does not lead to breakdown of the basic structure. The action of 0.1 M solutions of nitric, sulphuric, and hydrochloric acids on takovite and hydrotalcite has been studied.[124] X-Ray diffraction and infrared spectroscopy established that specimens treated with HCl and HNO_3 are identical to the untreated materials, except that they are in a different salt form. The diffraction patterns of the sulphate materials differ from those of the starting materials; the interplanar spacings increase as a result of the geometric differences between the leaving carbonate ion and the sulphate ion.

The stability of the anionic minerals in solutions of salts and bases has not been reported, but if the minerals are analogous to the synthetic layer double hydroxides, they should be extremely stable in these solutions.[33]

Thermal studies have been carried out only for the anionic minerals containing the carbonate ion.[130] Practically all of them give differential thermal analysis curves of identical form. Two endothermic effects are observed, the first in the temperature range 180–250 °C (300 °C for manasseite) due to the liberation of water of crystallisation, and the second in the range 420–500 °C (320 °C for kolingit) due to the loss of hydroxide water and carbon dioxide. Spinel formation takes place at higher temperatures.

The first process is completely reversible; keeping the heated specimen in a moist atmosphere restores the original structure. The second process, however, involving the loss of water and carbon dioxide, is irreversible, although restoration of the structure in a solution saturated with CO_2 has been reported.[131]

The non-carbonate forms of the anionic minerals have not been studied by thermal analysis, but the form of the DTA curves should be the same in this case also, apart from the appearance of additional peaks corresponding to the decomposition and removal of the anions.

Of much greater interest is the fact that although different anions are encountered in the minerals being considered, the structure of a mineral, usually determined by X-ray diffraction, remains unchanged. This indicates again the possibility of replacing the anions in the minerals, that is their anion exchange properties.

The anion exchange properties of the layer minerals have been studied only for takovite and hydrotalcites.[124] Their selectivity with respect to anions changes in the same order:

$$CO_3^{2-} > NO_3^- > OH^- > Cl^- > SO_4^{2-}.$$

The position of the sulphate ion in this series is unexpected. The existence of such minerals as cyanotrichite, woodwardite, and others encountered in nature in the sulphate form indicates stability of the sulphate forms. Carrboydite is found in weathered rocks, and if its selectivity with respect to the carbonate ion were a maximum, it should have been converted completely into takovite after a geologically momentary time interval. The work cited[124] in fact points out that the carbonate groups of the original mineral are readily exchanged for sulphate ions at room temperature. For the synthetic analogues, the following order of selectivity has been given:[81]

$$CO_3^{2-} > SO_4^{2-} > OH^- > F^- > Cl^- > Br^- > NO_3^- > I^-.$$

VI. Inverse zeolites

The most promising anion exchangers are undoubtedly the inverse zeolites, which represent a completely new class of solids having basic properties; they were first described in 1987.[140]

Inverse zeolites, like other inorganic anion exchangers, are products of isomorphous replacement. In contrast to mixed hydroxides, salts, etc., however, in inverse zeolites it is not the metal ions that are replaced, but silicon ions, which are replaced by phosphorus ions. The introduction of an ion with a higher oxidation state produces an excess of positive charge, whose compensation requires anions.

The replacement of silicon by phosphorus in zeolites presents no problems. Inverse zeolites of the types NaX, NaA, KY, and 4A have been prepared and studied. Inverse zeoliites can apparently be obtained from zeolites of any type, and in general from any aluminosilicates. An important feature is that inverse zeolites retain practically completely the structure of the cavities of the original materials, although they do not contain the same quantity of water.

Inverse zeolites, like other anion exchangers obtained by isomorphous replacement, show the dependence of the strength and number of the basic centres on the degree of isomorphous replacement described above.

The exchange capacity of various inverse zeolites that have been studied[140] is 2–3 mequiv g^{-1}. Unfortunately, the composition dependence of the exchange capacity was not examined; it was merely reported that in the range of molar ratios P/Si from 0.002 to 0.05 there is no correlation between the exchange capacity and the phosphorus concentration. This result is somewhat unexpected, since if static isomorphous replacement is assumed, the number of centres should be practically linearly dependent on the concentration of the element introduced.

The concentration of phosphorus in inverse zeolites based on NaA,for treatment times of 17, 22, and 23 h, had the values 2, 4, and 50 mg g^{-1} respectively.[140] In a study by the present author, the anion exchange capacity of the same zeolite for treatment times of 9, 15, and 21 h had the values 0.56, 0.8, and 0.52 mequiv g^{-1} respectively; the concentration of acidic centres remained at practically the same level. The number of Brönsted basic centres was greater than the number of Brönsted acidic centres (more accurately, not the number but the sum of the products of the number of centres and their dissociation constant, $\Sigma k_i C_i$). The rate of ion exchange was not very high, since the contact time for its study was not less than one week. The selectivity of inverse zeolites with respect to the anions F^-, Cl^-, and NO_3^- is different; the isotherms of the $F-NO_3$ and $Cl-NO_3$ exchange processes have a sigmoid form. The selectivity of inverse zeolites with respect to carbonate ions is particularly high.

The thermal stability of inverse zeolites is determined practically by the properties of the starting material, so that they have a high thermal stability. The temperature at which the main dehydration begins for all the compounds studied is not lower than 400 °C. Their chemical stability is also similar to that of the original zeolites.

VII. Mercarbide

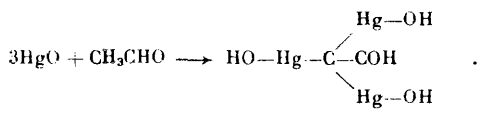
Salts of mercarbide, or simply mercarbides, are unique basic compounds. They have a high concentration of basic centres, a unique stability, and a well developed three-dimensional structure.

Salts of mercarbide are readily obtained by heating the yellow form of mercuric oxide for a long time in a highly concentrated solution of alkali in alcohol.[142] Red mercuric oxide can also be used, but the reaction rate is then lower. The rate is even lower if potassium or sodium alkoxides are used instead of the corresponding hydroxides.

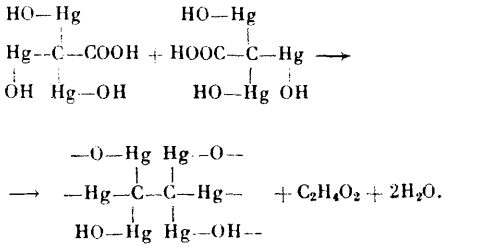
The initial stage of the process is possibly the oxidation of ethanol to acetaldehyde:

$$HgO+C_2H_5OH\rightarrow CH_3CHO+Hg+H_2O.$$

This is confirmed by the fact that an appreciable quantity of the original mercuric oxide is reduced to metallic mercury; the reaction is much more difficult in the absence of alcohol. The acetaldehyde formed is mercurated by three molecules of the oxide:



This compound is then oxidised by another molecule of mercuric oxide to give the sodium salt of the corresponding acid. Up to 40% of the original oxide is reduced to metallic mercury. Intermolecular removal of water gives mercarbide (water is also removed from the hydroxide groups of mercury):



In addition to ethanol as starting material it is possible to use saturated alcohols, aldehydes, cellulose, starch, and acids. Ethanehexamercarbide (the correctness of this name will be discussed below) can be obtained from ethanol and primary and secondary propanol. If the starting materials used are compounds which are not alcohols, or are alcohols whose molecular weight differs greatly from that of ethanol, the properties of the mercarbides obtained are quite different. Neither methanol nor formaldehyde give mercarbides or analogous products.

From the formula $C_2Hg_6O_2X_2$, where X is the exchangeable anion,

$$C_2Hg_6O_2X_2+2Y^-\rightleftharpoons C_2Hg_6O_2Y_2+2X^-,$$

the theoretical exchange capacity is about 1.5 mequiv g^{-1}. The actual values of the exchange capacity are extremely close to the theoretical value: 1.4 for the bromide ion, 1.5 for the hydroxide ion, and 1.5 for the chloride ion;[6] or 1.34 for the iodide ion, 1.37 for the ethoxide ion, and 0.052 for the chloride ion[143] (values in mequiv g^{-1}). The low value of the exchange capacity with respect to chloride ion in the last case is evidently due to the higher strength of the bond formed with the hydroxide ion compared with that with the chloride ion. Since the theoretical and actual values of the exchange capacity of mercarbides are approximately equal, the centres on the mercarbide surface and the centre in its bulk are evidently both accessible.

In some cases the exchange capacity of mercarbide can be increased considerably by carrying out the reaction

$$[C_2Hg_6O_2](OH)_2 \xrightarrow{HCl} [C_2Hg_6O_2]Cl_2 \xrightarrow{HCl} C_2Hg_6Cl_6.$$

This reaction is reversible, and treating the chloride with sodium hydroxide gives the original mercarbide. In this case, however, the structure undergoes significant changes.

The structure of ethanehexamercarbide, also called Hofmann's base in honour of the man who first studied it, indicates that it has active centres of only one type, namely Brönsted centres. The exchange capacity of mercarbide, established in a study of the basic centres by the indicator method in the presence of 2,4-dinitroaniline with $pK_a = 15.0$, was 1.5 mmol g^{-1}.[144] The same value was obtained when the exchange capacity was determined in KI and HI solutions. In the presence of 4-chloroaniline, however, the concentration of basic centres was 0.8 mmol g^{-1}. This may indicate that the mercarbide molecule contains centres of two types.

There is lack of agreement on whether mercarbides are derivatives of ethane[144,145] or methane.[146–149] The detection of centres of two types with different strengths in approximately equal quantities apparently indicates that the name "ethanehexamercarbide" is correct.[144] Further evidence that this compound is a derivative of ethane is provided by the fact that an exchange capacity higher than 1.5 mmol g^{-1}, that is higher than the theoretical value for ethanehexamercarbide, has never been observed, whereas the theoretical exchange capacity of methanetetramercarbide is 2.3 mmol g^{-1}.

A striking feature is that in all cases the elemental analysis data confirm the structure proposed by the authors concerned, although the same method was used to obtain the mercarbide.

Mercarbides have a rigid structure, and contain fairly large cavities, accessible to ions such as Br^-, I^-, SCN^-, ClO_4^-, SO_4^{2-}, and CrO_4^{2-}. C_7-C_{10} normal alcohols and benzoic acid can penetrate into the pores of mercarbide.[143]

The unique chemical stabilty of mercarbides is due to the strength of the C—Hg bond. The stability of mercarbide in acid solutions is particularly striking. Hydroxomercarbide reacts with acids to give the corresponding salts, which are stable in concentrated mineral acids, even aqua regia. It is also stable to oxidising agents such as potassium permanganate, chromic acid, hypochlorites, and hypobromites, but reacts slowly with reducing agents when heated (when heated with hydrazine hydrate it gives a mixture of gases, one of which is ethane[142]).

Treating mercarbide with acids gives salts of two types—the product of the replacement of two hydroxide groups and the product of the replacement of all the oxygen groups. There arises the question of how to characterise this property of mercarbides in terms of the basic properties and the ion exchange properties. On the one hand, the solid may sorb anions from the liquid (and gas) phase by a reversible process, that is apparently ion exchange. On the other hand, this basic or exchange centre cannot be determined *a priori*, either by the indicator method or by anion exchange. Hexaequivalent exchange can be detected only by titrating with highly

concentrated mineral acid, which leads to an unacceptable change in the structure.

The thermal stability of mercarbide is not as high as its chemical stability. When heated in air, hydroxomercarbide explodes with the effect of a high explosive; the published temperatures of the explosion vary from 120 °C [145] to 250 °C.[142] Our DTA studies showed that in air, mercarbide explodes at 140 °C, but in a liquid phase it is stable for an indefinite period at 200 °C.[143]

The order of selectivity of mercarbide with respect to various anions is as follows:[6]

$$NO_3^- < Cl^- < Br^- < OH^- \leqslant CN^- < I^-.$$

VIII. Heteropolar salts

Insoluble salts can often act as ion exchangers.[75] Their properties have been studied in detail.[6] All the compounds that have been described, however, are either cation exchangers or amphoteric substances. Only a few compounds based on salts and showing clearly defined basic properties over a wide range are known. One group of compounds of this kind is formed by transition metal tellurides.[150,151]

As noted above, it is difficult to draw a boundary between hydroxides and complex oxides obtained by heating hydroxides. A criterion is apparently provided by the conversion of the oxides into the hydroxides in an aqueous phase, observed, for example, for spinels obtained from mixed hydroxides, but not for the above-mentioned tellurides.

The tellurides of zirconium[150] and tin,[151] and also various molybdates,[152] are good anion exchangers with an extremely small number of acidic centres. The tellurides are obtained by hydrothermal synthesis in a strongly acidic medium. The precipitate is usually aged for a long time at increased temperature.

The anion exchange capacity of tellurides has been determined with respect to chloride ions, but it was subsequently established that these compounds show a low selectivity with respect to these anions. Tin telluride has a capacity of 1.12 mequiv g^{-1}, and zirconium telluride a capacity of 0.98 mequiv g^{-1}.[150,151]

The ideas about the statistical formation of exchange centres are also applicable to complex oxides and salts, but the deviations from the ideal distribution are much smaller in this case.

Tellurides are true ion exchangers, and anion exchange in these materials is completely reversible. For zirconium telluride, the selectivity decreases in the following anion order:[150]

$$CrO_4^{2-} \gg MoO_4^{2-} > SO_4^{2-} > PO_4^{3-} > AsO_4^{3-} > Fe(CN)_6^{4-} > Br^- > Cl^-.$$

For tin telluride the order is:[151]

$$SO_4^{2-} > PO_4^{3-} > Fe(CN)_6^{4-} > MoO_4^{2-} > CrO_4^{2-} > AsO_4^{3-} > SCN^- > NO_3^- > Cl^- > Br^-.$$

The tellurides are white solid amorphous substances, and their structure should be fairly rigid. They have a high chemical stability, and are stable for an indefinite period in acid (1–5 M), alkali (1–2 M), and salt (5 M) solutions.

The maximum replacement of anions in tellurides requires 36 h at a concentration of 0.8–0.9 M.[150,151]

IX. Carbon anion-exchange materials

Activated carbons show both cation exchange and anion exchange properties. Carbon obtained by heating saccharose acquires its maximum basic strength after heating to 400 °C.[7] The values of the capacity obtained by titrating with benzoic, acetic, and hydrochloric acids are 48.2, 26.5, and 0.43 mmol g^{-1} respectively.

To increase the basic strength of carbons, various methods of activating their surface have been studied. A remarkable feature is that the greatest number of basic centres was observed for specimens heated at 800 °C.[7]

Both the acidic and the basic properties of activated carbons are determined by the presence of oxygen groups on their surface. In a study of the acid–base properties of carbons obtained by oxidising swollen graphite in a liquid phase with hydrogen peroxide, a correlation was observed between the composition of the liquid phase and the ratio of the acidic and basic centres. This ratio can vary over a wide range; the anion exchange capacity for the lowest concentration of acidic centres is ~2 mequiv g^{-1}. Significant suppression of the acidic groups could not be achieved.

The number and ratio of the acidic and basic centres may change by a factor of several tens with change in the oxidising agent.[153]

With increase in the oxidation time, the concentration of both basic and acidic groups on the surface of carbon oxidised by nitric acid or potassium dichromate increased; the number of basic groups on unit surface area remained approximately unchanged[154] (Table 9).

Table 9. Dependence of the concentration of basic centres on the surface of oxidised carbon, heated at 800 °C, on the oxidation time.[154]

Concentration of basic centres	Oxidation time, h					
	0	0.5	1	2	4	6
Quantity, mmol g^{-1}	94	149	164	173	208	210
Surface concentration, centre nm^{-2}	0.54	0.58	0.53	0.54	0.58	0.45

The basic groups on the surface are carboxyl, lactone, phenol, carbonyl, and pyrone groups. On thermal treatment the carboxyl, carbonyl, and phenol groups decompose readily, whereas the number of lactone groups changes to a much smaller extent. The number of basic groups increases approximately ten-fold on heating, but increase in the treatment temperature above 800 °C leads to a decrease in their number.

X. Other anion exchangers

There are a number of compounds which do not belong to the above groups or which are amphoteric but show clearly defined basic character, at least under certain conditions.

Thus a new anion exchanger which shows its properties in neutral and in basic media and which is formed by the reaction of aluminium ions with 2,2′,2″-nitrilotri(ethanol) has been described.[155]

In it, two molecules of 2,2′,2″-nitrilotri(ethanol) are combined with one aluminium atom, but the molar ratio nitrogen : aluminium is always equal to 3. The formula and structure of the substance have not been established. Strictly speaking, this compound cannot be described as "inorganic". Anion exchange properties are also shown, however, by the substances obtained by heating it at temperatures up to 300 °C. This anion exchanger has an exchange capacity of about 1 mequiv g^{-1}, which correlates with the concentration of $-\overset{|}{\underset{|}{N^+}}-$ groups. It is stable in neutral and alkaline (2 M) solutions, but decomposes readily in acidic solutions. The anion exchanger has a particular affinity for the hydroxide ion. Other anions can be arranged in the following order:

$$CrO_4^{2-} > PO_4^{3-} > SO_4^{2-} \gg Cr_2O_7^{2-} > S_2O_3^{2-} > S_2O_8^{2-} > IO_3^- > MoO_4^{2-} \approx Fe(CN)_6^{3-} \approx SO_3^{2-} \geqslant HSO_4^- > AsO_2^- > Cl^- > BrO_3^- > Fe(CN)_6^{4-} > AsO_3^{3-} \approx SCN > Br^- > I^-.$$

The selectivity can be altered slightly by changing the pH and composition of the liquid phase. Equilibration is fairly rapid, and takes several minutes.

The following compounds with anion exchange properties have been used: polyantimonic acid, hydrated tin oxide, and hydrated titanium oxide.[156] These compouunds are produced industrially as anion exchangers. Their capacity is fairly low, 0.2–0.5 mequiv g^{-1}. None of the ion exchange processes studied is truly reversible, and in some cases, in particular in the case of iodide ions, the process is most probably not exchange but simply addition. The selectivity series for the compounds studied are approximately the same:

$$SO_4^{2-} \gg Cl^- > I^- > Br^- > NO_3^-.$$

These compounds are stable both in basic and in acidic (0.1 M) media, but they are dehydrated at about 130 °C when heated in air. All the substances studied have a large number of cation exchange centres.

The exchange capacity of hydrated cerium oxide[137] decreases with increase in the temperature of drying, possibly due to a decrease in the specific surface. The following selectivity series has been obtained for this compound:

$$ClO_4^- < Br^- < BF_4^- < NO_3^- < Cl^- < F^-.$$

Anion exchange on the hydrated oxides studied by different authors[122,123] was carried out in neutral and weakly acidic media, since hydrated oxides are mainly amophoteric, and are generally unstable in acidic media. The properties of hydrated oxides depend markedly on the method of synthesis.

Hydrated tin oxide[157] is stable to nitric and sulphuric acid solutions. Its anion exchange capacity reaches 2 mg-equiv g^{-1} (cation exchange capacity 1.5 mg-equiv g^{-1}), and the selectivity series is

$$I^- < Br^- < MoO_4^- < Cl^- < Fe(CN)_6^{3-} < Fe(CN)_6^{4-} < Cr_2O_7^{2-} < SO_4^{2-} < CrO_4^{2-} < PO_4^{3-}.$$

The use of amophoteric ion exchangers for absorbing and separating anions does not require their additional treatment. In some cases, however, the presence of acidic centres is quite inadmissible. It is then necessary, before using the anion exchanger, to "poison" the acidic centres using a strong base, for example KOH solution. This process, however, like any ion exchange process, is reversible, and when an ion exchanger of this kind is used it is necessary to control the reverse transfer of base to the liquid phase.

Transition metal phosphates, in particular zirconium phosphates, are widely known as cation exchange materials.[6] The properties of zirconium phosphate as an anion exchanger have been much less extensively studied.[158] Anion exchange properties are also shown by salts of antimonic acid, arsenic acid, and heteropolyacids.[159]

The ion exchange properties of ferrocyanides and cyanides in general are fairly widely known.[2,6] Mainly their cation exchange properties have been studied, however, although there are reports that certain cyanides act only as anion exchangers.[6]

It has been suggested that basic properties should be shown by cyanides containing metal cations in different oxidation states.[160] Methods for obtaining the anion exchangers $[Zn_2Co(CN)_6]OH$ and $[Zn_2Fe(CN)_6]OH$ have been described in detail,[161] and some of their properties studied. The structure of these compounds is very similar to that of double hydroxides. Cyanides, however, have a rigid hexgonal structure, so that they are excellent molecular sieves, capable of separating various organic molecules. The anion exchange capacity of $[Zn_2Co(CN)_6]OH$ is 2.5–2.7 mmol g^{-1}, and the number of acidic centres is low. These anion exchangers are extremely promising, but they have not yet been studied in detail.

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